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Project Title:	**Developing and Testing a Multi-Level Package of Interventions for an Integrated Care Delivery Model of HIV Prevention and Treatment Targeting Adolescent Girls in Zambia**
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Principal Investigator's Name — **Date**

***Sections updated July 2025 to clarify intervention components**

Running title: HIV Prevention & Treatment: Adolescent Girls in Zambia

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List of Acronyms

AGEP	Adolescent Girl Empowerment Program
AGYW	Adolescent girls and young women
ART	Antiretroviral therapy
CAB	Community advisory board
CFIR	Consolidated Framework for Implementation Research
CFR	Code of Federal Regulations
cRCT	Cluster randomized controlled trial
DCE	Discrete choice experiment
DREAMS	Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe women
DSMB	Data Safety Monitoring Board
FGD	Focus group discussion
FTP	File transfer protocol
GCP	Good Clinical Practice
GEE	Generalized estimating equation
GRZ	The Government of the Republic of Zambia
HCT	HIV counselling and testing
HIPAA	Health Insurance Portability and Accountability Act
HPV	Human papillomavirus
ICH	International Council on Harmonization
IDE	Investigational Device Exemption
IDI	In-depth interview
IND	Investigational New Drug Application
IRB	Institutional Review Board
IWC	Integrated wellness care
MOH	Ministry of Health
NAC	National HIV/AIDS/STI/TB Council
NIH	National Institutes of Health
PATC3H	Prevention and Treatment through a Comprehensive Care Continuum for HIV-affected Adolescents in Resource Constrained Settings
PI	Principal Investigator
PN	Peer navigator
PopART	Population Effects of Antiretroviral Therapy to Reduce HIV Transmission
PrEP	Pre-Exposure Prophylaxis
PTID	Unique study identification number
SDG	Sustainable Development Goal
SHIELD	Support for HIV Integrated Education, Linkages to care, and Destigmatization
SOP	Standard Operating Procedure
SRH	Sexual and reproductive health
UNC	University of North Carolina
YAB	Youth advisory board

Summary of Proposed Research

Zambia is among countries in sub-Saharan Africa experiencing one of the highest incidences of HIV, and adolescent girls and young women (AGYW)are particularly affected. This has placed priority on innovations that are likely to make a positive impact and catalytic in national efforts to curb new infections and attain the global 95-95-95 targets. Prior studies and initiatives to provide youth-friendly services through adolescent antiretroviral therapy (ART) clinics that offer a range of services, but these clinics have faced challenges because of the loss of privacy and the stigma associated with HIV. To address this gap**,** the Zambian Ministry of Health, RTI International, the Population Council, and the University of North Carolina are collaborating to develop and test an integrated wellness care (IWC) delivery model that targets all HIV-affected AGYW, both those that are HIV negative or do not know their status (HIV-/u) and those that are HIV positive (HIV+).

The proposed study will test a multilevel package of interventions to connect AGYW with a source of regular care to provide a sustainable platform for successful implementation of regular HIV testing and support for linkage to care and adherence to antiviral treatment. Prior tools will be adapted to create the SHIELD intervention (Support for HIV Integrated Education, Linkages to care, and Destigmatization) to educate and empower AGYW and their families, and to create community-based youth clubs to foster peer support.

1. Background and Introduction

1.1 Background, Rationale and Significance

Zambia is experiencing one of the highest incidences of HIV in the world, and adolescent girls and young women (AGYW) are a particularly affected group because of their social and economic vulnerability.[1,2] Approximately 5% of girls aged 15 to 19 years and 11% of young women aged 20 to 24 are HIV positive in Zambia, with about 14,000 new infections among AGYW annually.[1,3,4] As part of the DREAMS initiative, the Zambian government recognized the importance of addressing the unique needs of AGYW and their vulnerability during transition from childhood to adulthood.[5,6] Zambia adopted the "test and start" approach, which is based on recent evidence on prioritizing treatment to enhance prevention.[7] Successful implementation requires high levels of adherence along the HIV care continuum, including repeated HIV testing and compliance with treatment regimens, which are particularly problematic for AGYW. They face multiple barriers, including lack of youth-friendly services, HIV stigma, low levels of self-efficacy, and generally weak peer and family support.[1] GRZ's response effort requires complementary research-driven innovations that identify and harness opportunities for enhancing prevention and care coverage of AGYW.

Prior studies and initiatives have attempted to provide youth-friendly services through adolescent antiretroviral therapy (ART) clinics that offer a range of services, but these clinics have faced challenges because of the stigma associated with HIV and loss of privacy.[8-10] To address this gap**,** the Zambian Ministry of Health (MOH), RTI International, the Population Council (PC), and the University of North Carolina (UNC) are collaborating to test an integrated wellness care (IWC) delivery model that targets all HIV-affected AGYW, both those HIV negative or status unknown (HIV-/u) and those HIV positive (HIV+). The study will adapt the successful Zambian cervical cancer screening program, which provides a range of services to older women who are HIV- and HIV+, to offer tailored services to AGYW.[11,12] The availability of the human papillomavirus (HPV) vaccine, which is targeted at AGYW (ages 10 to 24 years included in this study) and well-accepted in Zambia,[13,14] provides an ideal opportunity to address the dual burden of HIV and cervical

cancer. The IWC clinic will provide services related to HIV testing, HIV treatment (in coordination with HIV clinic and dispensary in the same facility), HPV vaccination, and other sexual and reproductive health (SRH) care needs.

The study team will also include a community-based behavioral intervention for AGYW and their families that is specifically tailored to the development stage of the AGYW. The overall goal is to test a multilevel package of interventions to connect AGYW with a source of regular care to provide a sustainable platform for successful implementation of regular HIV testing and support for linkage to care and adherence to antiviral treatment. This approach will avoid siloes and provide a comprehensive HIV care continuum with a holistic and integrated health care delivery approach that is recommended by the Zambian HIV guidelines.[7]

1.2 Study Goal and Objectives

Our overall goal of the study is to test a multilevel package of interventions to connect AGYW with a source of regular care to provide a sustainable platform for successful implementation of regular HIV testing and support for linkage to care and adherence to antiviral treatment.

The objectives of the study are to:

1. Objective 1: Assess efficacy at 6, and 12 months of a multilevel integration intervention on HIV testing and viral load suppression.
2. Objective 2: Obtain feedback on the integrated care delivery model to assess sustainability, document best practices, and update SOPs to support scaling up of integrated services for AGYW.
3. Objective 3: Perform cost-effectiveness and budget analysis to evaluate and describe impact along the HIV care continuum and disseminate findings to national partners and the international community.

1.3 Ethical Issues

Ethical approval to conduct this study will be sought from ERES Converge IRB, Population Council IRB and University of North Carolina at Chapel Hill (UNC) IRB. The final approval will be sought from the Ministry of Health, through the National Health Research Authority. All participants will be required to provide written informed consent or assent. Before implementation, all informed consent and assent forms will be reviewed by the Youth Advisory Board, approved by the study institutional review boards, and field-tested to ensure comprehension and completeness.

In Zambia, the legal age for consent for health research is 18 years. For minors under age 18 who are interested in participating in the study, PN will obtain written consent for participation from a parent or legal guardian (referred to as “parent” hereafter). After parental permission is obtained, the minor will be asked to provide assent for study participation (referred to as “child aged 10–17 years”). Parental consent forms will specify that parents may not have access to their children’s study data.

Separate sets of consent forms will be used for each research activity and each participant population, where a “set” of forms includes adult information sheets, informed consent forms plus parental consent and child assent forms for AGYW populations. For additional recruitment of any AGYW living with HIV, a pre-consent form will be administered by the health facility staff or staff from organizations that provide treatment support and care to seek for permission from the parent/guardian/caregiver of adolescent girls

aged 16–17 years or young women aged 18–24 years for Population Council research staff to contact them.

2.0 Literature Review

The proposed study is designed against the following background contexts:

- **AGYW are less likely to be tested for HIV and less adherent to antiretroviral therapy (ART).** HIV counseling and testing (HCT) is the key entry point for many HIV prevention interventions and is essential for early linkages to HIV treatment.[2] With optimal use of ART, early diagnosis can reduce transmission to others and improve health outcomes.[15-17] Latest estimates indicate that only 42% of youth aged 15 to 24 years know their HIV status, 78% of those diagnosed with HIV are in treatment, and 71% of those in treatment have achieved viral suppression, resulting in a community viral load suppression (at the population level) of less than one-third.[18] Evidence indicates that girls have less-comprehensive HIV knowledge than boys, face male gender norms that increase their susceptibility, and lack access to sexual and reproductive health (SRH) services to support their reproductive rights.[19,20] Therefore, to decrease the disparities faced by this vulnerable group, the study team will focus on interventions to improve HIV testing and treatment adherence among AGYW and on linkages to services to reduce HIV risk behaviors (two priority areas addressing the key population of AGYW). The planned interventions will be embedded within the broader framework of ongoing studies in Zambia, addressing HIV risk and treatment among other populations, including boys and adults.

- **The Zambian government prioritizes HIV services for adolescents and encourages evaluation of new models of care delivery to support "test and start" guidelines.** Zambia has introduced comprehensive sexuality education, which is fully integrated in school curriculums, and is in the early stages of initiating facility-based ART adherence clubs. To spearhead further progress, the government is interested in evaluating new models of HIV testing and treatment. Under the new "test and treat" guidelines,[7] linkage to HIV care is crucial to the success of ART treatment. Community-based testing approaches, such as the Population Effects of Antiretroviral Therapy to Reduce HIV Transmission (PopART) trial in Zambia,[21] do face some barriers, including challenges around parents and AGYW not being present at home and the high level of resources required in terms of labor hours and travel costs. A recent systematic review, investigating acceptability of HCT in children and youth aged 5 to 19 years in sub-Saharan Africa, reported that provider-initiated testing and counselling achieved the highest acceptability (86%), followed by home-based HCT (84.9%) and school-linked HCT (60.4%).[22] There is also some evidence that locating testing and care services within the same facility can improve care linkage and ART initiation.[23-25] Additional evidence is required on whether provider-initiated HCT in an adolescent-friendly, clinic-based setting that is co-located with HIV services can increase HIV testing and improve linkages to HIV treatment among AGYW.

- **Create a Comprehensive Continuum of Care for HIV-affected AGYW by adapting the successful Zambian Cervical Cancer Screening Program.** The government of Zambia runs a successful cervical cancer screening program[26] integrated with HIV care that targets women aged 25 to 49 years and was selected as a top-10 sustainable solution by *Sustainia Award* (http://www.sustainia.me/sustainia-action-forum). Full countrywide scale-up of the program is in progress. The program began in the Lusaka area to address the dual burden of HIV and cervical cancer, as HIV-positive women have up to a six-fold higher risk of developing cervical cancer. Women who attend the clinics can request on-site

HIV testing from the program nurses; the nurses are trained to provide holistic care, which include comprehensive SRH services. RTI International's evaluation of the program (1R01CA200845-01A1) indicates that because of the stigma associated with HIV, women often prefer to receive testing in the privacy of cervical cancer clinics rather than HIV clinics. Program staff also support HIV+ women by collecting their ART medication from the HIV dispensary, which protects their privacy, while they receive care in the cervical cancer screening clinic.

The successful cervical cancer screening program model will be adapted and create IWC clinics. The IWC clinics will offer integrated SRH services along with HPV vaccination. Vaccine implementation guidelines support a two-dose schedule for girls before becoming sexually active (generally 9 to 14 years of age) and a three-dose schedule for the older AGYW cohort (15 to 24 years of age). HPV vaccination is well-accepted in Zambia,[13,14] and vaccination could serve as one key entry point to provide HIV testing in the privacy of the IWC clinics.

- **Individual and interpersonal factors, such as self-efficacy and social support, are key facilitators of HIV testing and ART adherence among AGYW.** The transitions from being a child, to a teenager, to a young adult are crucial developmental phases that require age-appropriate interventions.[27] Training tools such as the Stepping Stones program and those developed by the study team for the Adolescent Girl Empowerment Program (AGEP) are proven to improve self-efficacy and increase HIV knowledge.[28-31] Additionally, during adolescence, both family support and peer influence are important.[32,33] Youth clubs are an important venue to help young people establish friendships and social bonds to support optimal HIV prevention and treatment behaviors.[34] Prior tools will be adapted to create the SHIELD intervention (Support for HIV Integrated Education, Linkages to care, and Destigmatization) to educate and empower AGYW and their families, and to create community-based youth clubs to foster peer support.

3.0 Methodology

3.1 Overview of the Intervention Trial

We conducted a cluster randomized trial to assess the efficacy of the multi-level interventions, through the measurement of both the primary and secondary endpoints of the intervention. We also conducted a post-intervention follow at about 12 months after the end of the intervention.

3.2 Overview of the interventions

SHIELD intervention. The SHIELD intervention is based on social cognitive theory, which posits that positive behavior change requires knowledge and skills to increase behavioral capability, development of self-efficacy to increase the belief that one can achieve the desired outcomes, and social support to provide positive reinforcement and develop positive outcomes expectations.[46] We developed a modular program for AGYW that increases knowledge, skills, and self-efficacy to engage along the HIV prevention and care continuum, and a program for family members (up to four participants in addition to the AGYW; 10 years and older) to increase social support. To reflect AGYW's evolving cognitive and decisional capacity, judgement, emotional development, risk, and health-seeking behaviors, intervention content for both AGYW and families were tailored for five distinct groups to reflect development stage and

AGYW's HIV status. Content areas were adapted from existing evidence-based interventions, such as Stepping Stones[30,31] and Families Matter![47,48] based on CAB and YAB input and formative research with AGYW, caregivers, and community leaders. Modules address HIV prevention and treatment, general wellness and SRH, approaches to combat stigma and discrimination, and skills for better communication, and include new content on health service availability and access to increase self-efficacy in seeking health care services. SHIELD educational materials were pre-tested. The SHIELD sessions will be offered to AGYW and their families in the 4 communities randomly assigned to intervention arms. The AGYW in the usual care arm will receive one education session focused on stigma and HIV care. SHIELD education session content is presented in **Exhibit 1** for the AGYW sessions and **Exhibit 2** for the family sessions. We have noted content that will be included in core sessions along with content that will be included in the basic education provided to the control group participants. The core sessions will be provided to all participants in the intervention communities while all other sessions will be optional content for future meetings within the intervention communities.

Exhibit 1. SHIELD Content Areas for Adolescent Girls and Young Women Program

	Stigma and discrimination around SRH and HIV care and treatment	HIV knowledge, prevention, and treatment	Health service availability and access	Combatting stigma, building self-esteem
HIV+ 16+	1. How we are the same, how we are different (all ages/groups) 2. Naming stigma through pictures (13-24)*^ 3. Coping with stigma*	1. Taking care of your health when living with HIV*^ 2. Adherence case studies* 3. Healthy sexuality* 4. Pregnancy prevention 5. STIs	1. Where to access services* 2. Barriers and challenges to accessing health services* 3. Claiming rights to quality care through assertive communication*	1. The voice in your head (all)* 2. Loving me, loving you (all)* 3. Introduction to human rights (all)* 4. Assertiveness – Be the change (13+)*
HIV- 10-12	1. How we are the same, how we are different (all ages/groups) 2. Naming stigma through pictures (10-12)*^ 3. Supporting your friends who are living with HIV (10-12)*	1. HIV transmission and prevention*^ 2. Living with HIV* 3. Good hygiene and managing menstruation 4. Pregnancy and menstruation 5. Puberty 6. STIs	1. Where to access services* 2. Barriers and challenges to accessing health services* 3. Asking adults for information through assertive communication*	1. The voice in your head (all)* 2. Loving me, loving you (all)* 3. Introduction to human rights (all)* 4. Assertiveness – Be the change (10-12)*
HIV- 13-20	1. How we are the same, how we are different (all ages/groups) 2. Naming stigma through pictures (13-24)*^ 3. Supporting your friends who are living with HIV (13-20)*	1. HIV transmission and prevention*^ 2. HIV testing* 3. Living with HIV* 5. Pregnancy and menstruation 6. Pregnancy prevention 7. STIs	1. Where to access services* 2. Barriers and challenges to accessing health services* 3. Claiming rights to quality care through assertive communication*	1. The voice in your head (all)* 2. Loving me, loving you (all)* 3. Introduction to human rights (all)* 4. Assertiveness – Be the change (13+)*

** Indicates core topic area*

^ Indicates inclusion in basic education for control group

Exhibit 2. SHIELD Content Areas for AGYW and Family Program

	Information on AGYW SRH and HIV	Stigma and Social Support
AGYW and Families	1. What you see in me (All) 2. Making puberty easier (parents of AGYW ages 10-12) 3. HIV, AIDS and STIs- Myth or Fact (All)* 4. Helping children express their feelings (ages 10-12) 5. Taking responsibility for pregnancy: Community responsibility (ages 13-24)*	1. Non-verbal communication (All) 2. Sharing information with family members: challenges and possibilities (HIV+ ages 16-24)* 3. Providing emotional support after a child learns that you or they are HIV positive (All) 4. Analyzing stigma against AGYW (All)*

** Indicates core topic area*

IWC Clinic

The Integrated Wellness Care (IWC) clinic for AGYW will be established in 2 randomly selected health centers participating in this study communities. The clinic will provide integrated HIV and sexual and reproductive health services to both participating HIV-/u and HIV+ AGYW facilitated by a trained nurse. Specifically, the IWC clinic will offer:

- HPV vaccination
- HIV testing & counselling
- ART adherence counselling (HIV+ AGYW)
- STI services information
- Family planning, including counselling, initiation of contraception, services related to current contraception, and pregnancy testing and counselling.
- Information on cervical cancer screening
- Referrals for services, such as mental health, gender-based violence, STI testing, cervical cancer screening, and other health services as needed

All services will be provided based on the standard of care guidelines and delivered by a trained nurse. IWC components and data collection was tested during the pilot-testing phase. In addition, selected staff at the health centers with the IWC clinic will receive stigma training to ensure team-based care is available for AGYW who are referred from the IWC clinic to received services in other departments at the health center. The training section includes four modules (2-hour session for each) that experienced trainers will deliver to give staff the skills to create a stigma-free health facility.[29,30]

Caregiver and provider support for AGYW. We will include caregivers who will participate with AGYW in the SHIELD family sessions. We will identify one caregiver for each participating AGYW in the 6

intervention communities (approximately 1,125 family members). The AGYW will select their caregiver upon enrollment into the intervention. We will also include approximately 60 clinic staff in health centers from the 6 communities included in the study. We plan to conduct interviews with these health center staff to seek general feedback on barriers and facilitators faced by youth receiving services at their health centers. We will include health center staff who have worked at the health center for at least 6 months, plan to stay in their current position during the 12-month study implementation period and have some interaction with girls and young women who visit the health center. The staff members at health centers hosting the IWC clinic will receive stigma training at baseline. The staff at each health center will be selected based on their likelihood to interact with AGYW seeking care at their facilities.

Peer navigators support for AGYW. We selected individuals 18 to 24 years to serve as peer navigators to support AGYW enrolled in the study intervention communities/clinics. These navigators were trained to deliver the SHIELD education sessions and they also supported the AGYW during IWC clinic visits.

3.3 Intervention – Cluster Randomized Trial Protocol

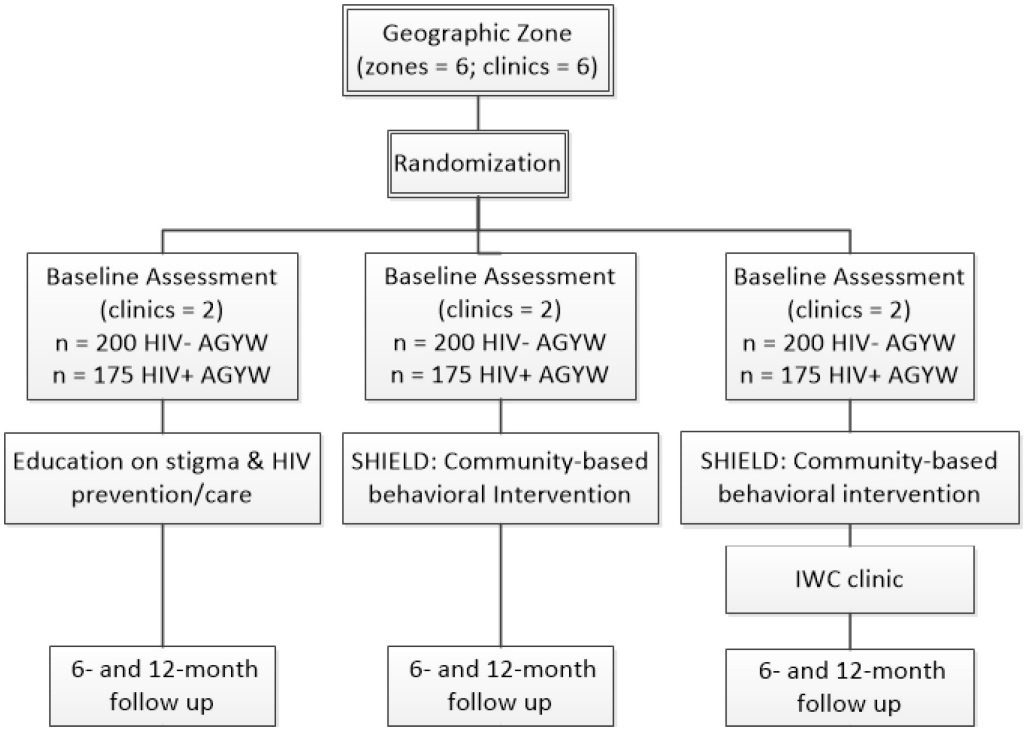
Recruitment of AGYW (core intervention recipient)

. In each of the 6 clinic zones, the study team will use stratified random sampling, using age-group strata (based on age at cohort enrollment for each study community-clinic zones) drawn from the sampling frame recruited for formative research, to select AGYW for the HIV-/u and HIV+ study cohorts (IWC pilot study participants will be excluded and higher priority will be given to those who previously indicated that they were likely to reside over the long term in the study communities). Zones include the following communities and their clinic catchment areas: Chipata, Chawama, Kanyama, Kalingalinga, Mtendere, and George. The selection criteria will overall remain the same as the sampling frame recruitment with the following exclusions for the intervention: (1) girls and young women who are pregnant at enrollment (self-report); (2) young women who are older than 25 as our cohort would have aged; and (3) those not planning to live in the study communities or seek care at the study community clinics for at least 24 months so follow-up data collection can be completed. Those in the HIV- cohort who are diagnosed with HIV (self-reported) will be assigned to the HIV+ cohort if they meet the age criteria. The study team will oversample from the existing sampling frame cohort in each age subgroup to account for ineligibility. Additionally, to maintain balance in enrollment across age groups and communities, we may need to recruit few additional AGYW prior to implementing the intervention. As a consequence of the COVID-19 pandemic there may have been more dispersal among the already recruited AGYW cohort than anticipated. To add new AGYW (if required), we will follow the same procedures as previously approved to identify the cohort during formative research. The consent procedures for participation in the intervention will be the same for girls identified from the existing cohort or those newly recruited. Our overall goal is to select approximately 600 HIV-/u and 525 HIV+ AGYW to test the SHIELD and IWC interventions.

The sample size was calculated assuming conventional specifications (power = .80, alpha = .05, two-sided tests) and based on the primary endpoints. The sample sizes were determined to allow for the detection of a 15–percentage point improvement in the primary endpoints, our minimum threshold to consider the intervention to be successful. For the HIV-/u cohort, the current rate of HIV testing is estimated to be about 40%. With a sample size of 200 (each of the three cohorts), The study team will be able to detect a 13 to 14% difference, and even with a loss of 10% of the cohort during follow-up (the grant team achieved a 90% retention rate at 12 months in a recent study of AGYW),[28] the study team

will still have the statistical power for a minimum detectable difference in HIV testing of 15%. For the HIV+ cohort, viral load suppression is estimated to be 70 to 75% among AGYW. With a sample size of 175 per cohort, the study team will be able to detect a minimum difference of 15% even with a 10% loss to follow up. See **Exhibit 3** for details on sample size included in the cluster randomized trial.

Exhibit 3. Experimental design and sample sizes*



Post-intervention data collection: We will conduct one post-intervention survey with AGYW at about 24-months from study initiation (approximately 12 months after intervention completion).

Research Protocol

Assess efficacy of the multilevel interventions (hypothesis testing). Cluster randomization study design and interventions. We propose a cluster randomized study implemented in the six selected geographic zones in Lusaka, each served by a government-operated clinic providing HIV and cervical cancer screening services. Zones, with their respective clinics, will be randomized into three groups (zones with IWC clinics and SHIELD intervention, zones with only SHIELD intervention, and control zones with no IWC clinic or SHIELD interventions. AGYW in the control zones will be offered one education session on HIV prevention and treatment) to assess the impact of offering IWC clinics coupled with the SHIELD intervention compared to the standard of care (see Exhibit 1 above). The study team will also evaluate whether a similar impact can be achieved with control clinics when the SHIELD intervention is offered in the community. The SHIELD intervention, as described in Section 3.2, will begin with training sessions for AGYW and their families. This will be followed by PN-facilitated youth clubs that will meet about once a month during the 12-month study timeframe. Two-four PNs will be assigned to each clinic zone with the SHIELD intervention, and one-two PN each will be assigned to the two control clinic zones to assist with data collection and follow-up activities. The PNs in zones with the IWC clinics will also serve as community liaisons to support clinic-community linkages. The health centers in which the **primary endpoint for the HIV-/u** cohort is the proportion with any HIV testing at 12 months. **For the HIV+ cohort, we plan to assess the primary endpoint**: viral load suppression, measured as proportion with undetectable viral load at 12 months. The secondary endpoints are the proportion with decrease in HIV risk behavior, repeat HIV testing (each 6-month period), HIV infections diagnosed through voluntary HCT, linkages to HIV care, and adherence to ART. We will also conduct a targeted 6-month post-intervention data collection after the end of the 12-month intervention period. See **Exhibit 4** for endpoint definitions and biological, self-report, and clinic audit measures collected at 6- and 12-month follow up. To assess the impact of the SHIELD intervention on the medicating outcomes, the study team will collect data from AGYWs across all six clinic zones at baseline and at 6- and 12- month follow-up. The study team will also track health care service use by conducting clinic audits at all six clinic sites. We plan to retain the intervention cohort for a maximum of 24 months total to allow for initiation of the intervention and follow-up activities (12 months of intervention and follow-up after intervention completion).

Exhibit 4. Tables of measures at baseline, 6 months (6m), and 12 months (12m); few measures also collected at about 24 months (24m) during the post intervention period.

Constructs/Measures	Instrument and Specification	Source	Cohort
Primary and Secondary Endpoints—HIV Care Continuum and HIV Risk Behavior			
HIV testing; proportion tested for HIV in the past 6 and 12 months	Abstraction tool (serologic HCT); and self-report confirmed via clinic audit; repeat HCT at 6-month intervals will be assessed	Clinic audit Self-report	HIV-/u 6m,12m Self report only at 24m
HIV early detection; proportion with HIV identified through voluntary testing	All participants will be tested to determine HIV status (rapid finger prick and follow-up per Zambian guidelines)	Biological	HIV-/u 12m
Linkage to care: proportion enrolled at an HIV clinic in ≤ 30 days; *ART initiated* in ≤ *90 days*	Measured as days from testing HIV positive or from baseline when not on treatment (HIV+ but not on ART)	Clinic audit	HIV-/u HIV+ 6m & 12m

Adherence to ART; proportion filling prescriptions at least every 3 months	Zambian guidelines recommend dispensing 3-month supply of ART medications	Clinic audit Self-report	HIV+ 6m &12m Self-report only at 24m
Viral load suppression; proportion with undetectable viral load	HIV plasma viral load tests using the Roche platform	Biological	HIV+ 6m &12m
HIV risk behavior: proportion with delay in first intercourse, reduction in sexual partners; increases in condom use	Demographic and Health Survey and AGEP instrument (measures will be based on previous studies by grant team, including AGEP)	Self-report	HIV-/u Baseline, 6m, 12m & 24m
AGYW (Mediating outcomes, SHIELD intervention dose, and clinic-based services)			
Self-efficacy, social support, HIV stigma & gender roles	Tailored instrument based on supplemental survey completed at cohort recruitment	Self-report	HIV-/u & HIV+ Baseline, 6m, & 12m Self-report at 24m
Mental health and substance abuse	Brief assessment based on NICHD consortium common data elements	Self-report	
Unintended pregnancy	Tested at 12m	Urine test	
Education modules (AGYW & family)	Number of modules completed	Study database	
Youth club attendance	Number and proportion of meetings attended		
HPV vaccination	Proportion receiving 1, 2, or 3 doses (IWC clinic only)	Clinic audit & visit data collection	HIV-/u & HIV+; 6m & 12m
Number of clinic visits	Proportion with visits at 6m and 12m; total number of visits		
SRH services provided	Family planning, sexually transmitted diseases, and condoms		
Baseline Data for AGYW			
Demographics & socio-economic status	AGEP baseline instrument	Self-report	All AGYW 24m

Trained data abstractors will obtain the information from the clinical records at baseline and during the 6- and 12-month follow-up using prespecified abstraction forms. UNC's Zambia project manager will supervise the data collection at the IWC clinics that will manage the pre-screening processes, track visits, clinical services provided, and linkages for HIV care. Specially trained staff will perform biological data collection, which will include HIV testing at 12 months for the HIV-/u group, viral load testing at 12 months for the HIV+ group, and pregnancy testing for both groups at 12 months. All data collectors will be trained, data collection will undergo continual monitoring, and fidelity to protocol specifications will be confirmed by random in-person review of supervisors' data collection. IWC clinic staff will keep detailed records to track patient visits along with information on staff time spent across various clinic activities. Data will be stored locally at secure location at Population Council offices and reviewed for data completeness. Deidentified data then will be transferred securely to RTI and archived in secure,

password-protected servers. RTI staff will conduct further data quality review, produce reports, and develop analytic files.

SHIELD intervention exposure. Using attendance information entered in the study database, the study team will quantify the number of SHIELD education sessions AGYW and family members attend and the number of youth clubs AGYW attend. This will allow us to calculate the amount of exposure to the intervention (dose) for each participant. This dose estimate will be used as a covariate in sub analyses that examine the dose-response of the interventions on outcomes.

Hypotheses on intervention effect. The study team will test the following hypotheses: (1) HIV-/u AGYW from zones with IWC clinics and who receive SHIELD intervention will have higher HIV testing than AGYW in zones without the IWC clinics (including those receiving SHIELD intervention with usual care clinics); (2a) HIV+ AGYW from zones with IWC clinics and who receive SHIELD intervention will have higher viral load suppression (2b) than AGYW in zones without the IWC clinics (including those receiving SHIELD intervention with usual care clinics); (3) HIV+ AGYW from zones with IWC clinics will receive more-timely linkages to care than AGYW in zones without a IWC clinic; (4) AGYW from zones who receive SHIELD intervention will have improved self-efficacy (4a) and social support (4b), and reduced HIV risk behaviors (4c) compared to AGYW from zones not receiving the intervention.

Analysis of hypotheses. The **testing of the primary hypotheses** will be done by intent to treat, and the study team will examine the effects across the three randomization groups. Given the need to consider the influence of the cluster randomization by zone, The study team will use generalized estimating equation (GEE) models to estimate the effects of the randomization groups and will assess the need to apply small sample correction using approaches suggested by the NIH Health Care Systems Collaboratory Biostatistics and Design Core.[59] If the Hausman assumption of correlation between the random and fixed effects is violated, then The study team will include fixed effects representing cluster identification. The study team will adjust for baseline covariates, including sociodemographic factors and behavioral risks, should the initial descriptive analyses suggest differences in the distribution of these factors across study randomization groups. The study team will also explore the use of propensity scores to control for systematic differences between the groups. In further analyses, the study team will examine the potential mediating and moderating roles of key behavioral, social, and structural factors hypothesized to influence HIV testing and adherence along the HIV care continuum (e.g., social support; self-efficacy).. The study team will test the "dose" of the SHIELD training received as a covariate in these models. **Secondary analysis** will follow the same approach. As appropriate, the study team will perform analyses separately or pooled together for the HIV+ and HIV-/u cohorts. A key aspect of interest in this study is the developmental stage of the AGYW; using age as a proxy in our multivariate analysis, the study team will determine the differential effect of the IWC clinic and SHIELD intervention on outcomes reported by HIV status (see Exhibit 1 for groupings). In subsequent analyses, the study team will also consider both medium-term outcomes within the first 6 months after study enrollment and changes at any point during the 12-month follow-up period to assess longer-term outcomes. Additionally, for measures where we have baseline, 6-month and 12-month follow-up data (for example, self-efficacy, and other mediating outcomes for AGYW), the study team will perform difference-in-difference analysis, which will allow for comparisons between and across the study arms. The study team will also report all mediating factors, and 'IWC clinic utilization metrics stratified by age and HIV status to facilitate subgroup analysis. Importantly, the changes along the HIV care cascade, from HIV testing, linkage to care, ART adherence, and viral load suppression, will be documented to identify potential differential impacts of the interventions. This analysis is critical to assist in further tailoring the SHIELD training and IWC clinic services.

Obtain feedback on the integrated care delivery model and compare with current standard of care. Clinic staff and peer navigator data collection. Two complementary data collection approaches,

IDIs (qualitative) and survey (quantitative; **see Exhibit 2**), will be used to obtain data from about 10 health center staff (clinical and non-clinical) at each of the six health center sites to assess the impact of IWC on HIV care processes, AGYW health seeking behavior, and provider attitudes: The study team will develop an interview guide with key questions to explore staff experiences in providing care to AGYW and their perception about AGYW's satisfaction with the services provided. The study team will include a specific session for the IWC clinic health center staff on implementation procedures, clinic operations, and sustainability. This qualitative information will be supplemented by a survey that will be based on a validated instrument by Co-I Dr. Nyblade for measuring attitudes of providers towards those seeking HIV services (multiple statements that providers can agree or disagree with). This instrument will be adapted for this study and incorporate lessons from an ongoing RTI study in South Africa that is currently adapting the same instrument for vulnerable AGYW (1R01HD094629-01). Additionally, we will also collect details on the implementation climate using a short, tailored questionnaire. These data will be collected at baseline and at 6- and 12-month follow-up to provide a longitudinal assessment of potential changes in provider attitudes.

Furthermore, to assess the implementation of the interventions, we will conduct debrief activities to understand barriers and facilitators experienced by AGYW using surveys, interviews and group discussions with the study team members implementing the interventions. These activities will involve the PNs and the IWC clinic staff who will be working with the AGYW. Furthermore, to understand the level of effort required to implement the interventions and to estimate the cost, we will track time spent by the PNs, IWC clinic staff and others in implementing the SHIELD and IWC clinic interventions.

Data analysis and synthesis of findings. The study team will follow the same procedures outlined under our formative research to transcribe, code and analyze the qualitative data. The study team will identify themes that emerge around barriers to and facilitators of access to and use of HIV and SRH services. The study team will generate descriptive statistics based on the survey responses (percentage who agree or disagree with statements) and compare the proportions over time to identify patterns in health center staff attitude and PN feedback between those in IWC clinic zones and comparison zones offering standard-of-care health services. The qualitative analysis will provide contextual information to interpret the quantitative findings, and specific feedback provided on the integrated care delivery model will be evaluated to assess sustainability, document best practices, and update SOPs to support scaling up of integrated services for AGYW.

Cost-effectiveness, budget impact, and policy implications. The study team will use a previously validated instrument, The Cost Assessment Tool.[60] to create a tailored data collection approach to collect resource use information on the interventions. Our main goal is to estimate the implementation cost of the IWC and the SHIELD interventions from the program perspective (which will reflect MOH resources needed to sustain interventions), but the study team will also derive the start-up costs related to developing the interventions to inform future adaption of these interventions to other settings. The study team will estimate labor hours of IWC clinic staff, PN, and other staff by prospectively tracking time spent by each project staff member implementing the intervention on a pre-defined set of activities and use hourly wage to calculate cost. The study team will also document the expenditure on non-labor resources. Using standard economics methodology,[61,62] the study team will explore economies of scale that can be achieved during scale-up. The cost information, along with the effectiveness impact of the IWC and SHIELD interventions, will be used as inputs in previously validated models and approaches developed by RTI.[63] The study team will evaluate the tradeoff, or return on investment, between investing in HIV prevention and lowering HIV treatment cost over the long term. The usual care (base case) will be compared to the long-term effectiveness of including the IWC clinic-based intervention with and without the SHIELD community-based interventions to address barriers along the continuum of care. The study team will report the projected decrease in HIV incidence,

increase in community-level viral load suppression, and incremental cost per quality-adjusted life years. The study team will conduct policy simulations to assess the impact of scaling up the interventions to the population level; perform sensitivity analysis, varying the range of effectiveness and cost estimates; and generate potential best- and worst-case scenarios. The study team will create tornado and spider diagrams to display this uncertainty assessments graphically to policy makers. This cost-effectiveness analysis will be complemented by a budget analysis, which will identify the financial outlays that will be required annually to implement the intervention during the implementation trial in the scale-up process.

3.3.4 Limitations and approaches to minimize bias. First, although cluster randomization reduces contamination across study arms, it increases the risk that clinics and individuals in each arm may differ at baseline. The unique feature of this study is that the study team will create a sampling frame and therefore will be able to assess individual-level baseline differences before randomization. Additionally, through our planned situational analysis, the study team will explore clinic characteristics to select clinics that are similar. Second, data could be missing because of nonresponse as well as study attrition. All AGYW will be assigned to a PN who will ensure regular contact with the AGYW during the study period. The study team will also employ rigorous field data collection practices, including training data collectors, developing protocols, and monitoring fidelity on a continual basis. Using this approach, on the basis of a recent study among Zambian AGYW by the study team, we expect that retention will be 90% over the 12-month follow-up period.[28] Furthermore, the study team will address any missing data by including demographic covariates that will serve as proxies for dropout and conducting sensitivity analyses.

3.3.5 Dissemination, generalizability assessment, and policy forum. In addition to the PATC3H consortium meetings, regional conferences, and local YAB and CAB meetings, the study team will plan scientific, peer-reviewed journal articles and international conference presentations to disseminate formative research findings, interim results, and final results. The study team will involve all government partners in the communication plan and ongoing dissemination. The study team will use the PATC3H meetings to seek feedback on the extent to which the personal, interpersonal, and structural levels of the interventions included in our study are directly transferable to other settings. Key aspects of discussion will be differences in AGYW characteristics, community support, and health service delivery that may differ between Zambia and other Sub-Saharan African countries. The study team will also organize a policy forum in year 5 in Lusaka, Zambia, to present the outcomes to local health department and government officials and to share the findings from the modeling work and policy simulations. The study's formative research and hypothesis testing can inform the development of the Zambian government's policy on integrated service delivery and international guidelines regarding health service delivery for AGYW. The IWC model, if shown to be successful, will provide a comprehensive and sustainable approach to improving health outcomes of AGYW by using low-cost PNs and embedding integrated youth-friendly clinics within existing government facilities

Risks and Benefits

Although this study presents no greater than minimal risk to participating AGYW, and adequate provisions will be made for soliciting the assent of AGYW under age 18, there are some potential risks to participating in the proposed study:

Blood draws for HIV or viral load testing may lead to discomfort, feelings of dizziness or faintness, bruising, swelling, or infection.

Loss of confidentiality. There is a risk of loss of confidentiality for AGYW around study participation; HIV status; ART use; or data reported in project questionnaires. The intervention activities also carry a risk of participant disclosure of personal information during group activities such as the SHIELD intervention youth clubs, and during participant tracking for follow-up. It is also possible that other people may find out that participants have taken part in this research, and as a result, participants may be treated unfairly, discriminated against, or face problems being accepted by their families, communities, or both.

HPV vaccination. The World Health Organization recommends HPV vaccination. The Global Advisory Committee on Vaccine Safety has systematically investigated the HPV vaccine and found it to be safe. As with any vaccination, some people may have some side effects. These are usually mild and include a sore arm from the shot, fever, headache, or nausea. Brief fainting spells can happen immediately after any medical procedure, including vaccination.

Discomfort with learning HIV status or with interview topics and questionnaires. AGYW participants may experience psychological discomfort upon learning their HIV or pregnancy status. Sensitive interview topics related to HIV status, ART use, stigma, reproductive health, or sexual behavior may make some participants feel uncomfortable, worried, or embarrassed.

There is little to no risk for other participants, including clinic staff and stakeholders. All of the questions we will ask relate to their daily work as clinic staff or community leaders. Additionally, clinic staff and other government or private stakeholders who participate in IDIs will not be asked any sensitive questions. All responses will be de-identified and only reported in aggregate form. Clinic administrators will not have access to individual staff member responses.

COVID-19-associated risks

The COVID-19 pandemic may present health risks to both participants and the staff who engage with participants in the clinic and community setting. These health risks are significant but are not unique to our study. COVID-19 may pose a larger risk during group meetings, such as the SHIELD educational sessions, than for one-on-one contact. The project team is closely monitoring COVID trends in Zambia and has detailed our risk mitigation strategy in the below section.

Potential benefits

Participants may receive no direct benefit from participation in the study. Participants have the potential to contribute to and learn from research that will investigate how to improve uptake of HIV testing and adherence to ART among AGYW. If the proposed intervention is successful, the participants randomized to the interventions in Aim UH3-1 could benefit from improved linkages to services, including HPV vaccination and other sexual and reproductive health care. Although these services are already available in the public health facilities, proposed interventions may increase demand and accessibility. Intervention benefits could also include improved self-efficacy, improved social support, and a reduction in stigma.

Participants and others also may benefit in the future from information learned from these studies, if the intervention is scaled up to increase engagement in care in a larger population of AGYW. If

the intervention is not successful, the information will still be valuable to redirect future efforts toward other approaches.

Steps to Minimize Risks

Risks to participants will be minimized through the following procedures:

Risks associated with blood draws. The blood draw volume will be the same amount required for clinical care. Participants will be offered water, a snack, or both to minimize the risk of dizziness or faintness.

HPV vaccination. All those who receive the vaccination will be provided with information on how to notify the research team if they develop any symptoms, such as nausea, and need follow-up care (details on who to contact for care if they have symptoms will be provided). We will also ensure all AGYW sit or lie down for about 15 minutes after the vaccination to help prevent fainting and injuries caused by falls.

Data security to minimize loss of confidentiality. (described in detail in the below section for confidentiality)

Discomfort with interview topics and questionnaires. Procedures for minimizing risk and discomfort for participants during the qualitative and quantitative interviews will be monitored closely. Study staff interacting with participants will be female, and the interview team will be selected and trained with the goal of establishing rapport with the participants' age group. All study staff will be trained in ethical interviewing and discussion of sensitive topics, and staff training and debriefing will be conducted on an ongoing basis throughout the study, either weekly or as issues arise. Participants will be advised that they are not required to answer any questions, and reminded that they may withdraw from the study at any time without losing access to any clinical services. Referrals will be provided to participants who need or request clinical or psychosocial care at any point during study participation. In addition, participants will be encouraged to contact the peer navigators at any time during the study if they have questions or concerns.

COVID-19-associated risk mitigation

The study team has developed a detailed COVID-19 risk mitigation plan in conducting research and in the training of hired staff. The risk mitigation plan includes specific precautionary measures for all staff during trainings, when in contact with participants in the community and in the clinic setting, including wearing a mask, sanitizing, social distancing, avoiding crowds, and constant hand washing. Staff temperature will be checked prior to performing any fieldwork, and staff will wear a facemask and practice social distancing while performing any interviews or participant contacts. Researchers will also sanitize their hands prior to giving any materials or compensation to participants and will also ensure participants sanitize their hands after signing consent forms or receiving compensation. Research staff will also provide facemasks to guardians when obtaining parental permission, as well as for the respondents during consent and participation in the study. In addition, the IWC clinic staff will perform COVID-19 risk pre-screening by telephone to all participants prior to them coming to the clinic in-person. Staff will also perform an in-person COVID-19 screening questionnaire to participants.. Any participant experiencing flu-like symptoms will be advised to call the COVID helpline number and will not be interviewed or invited into the clinic. The IWC appointment will be scheduled for a later date following successful completion of pre-screening

requirements. For risk mitigation within the clinic, we are providing masks to participants, ensuring hand washing, providing hand sanitizer, cleaning the clinic space regularly, and keeping windows open to ensure air flow in the space. We are also limiting the number of participants per day to make sure that social distancing can take place.

Overall COVID trends in the Lusaka region will be closely monitored by the study team. The study team may decide to temporarily halt participant contact activities if the COVID risk level rises in the region or if advised by the Zambian Ministry of Health.

Overall risk mitigation

All reports of social harms, adverse events, and unanticipated problems will be reported to the Principal Investigator, site Lead Investigator, and Field Coordinator within 5 days, and will be reviewed by the Data Safety Monitoring Board, who may recommend additional action or modifications to the intervention or study protocol to ensure participant safety.

The knowledge gained in this study will address a critical gap in our understanding of effective public health interventions to improve engagement of AGYW along the HIV care continuum. It will test community- and clinic-based interventions to address key barriers to engagement in care at the individual, interpersonal, and clinic levels, including HIV knowledge, stigma, social support, and the need for youth-friendly services. If successful, the proposed interventions will improve HIV testing and treatment adherence among AGYW, and will contribute to meeting the 95-95-95 targets, reducing secondary transmission, and improving the quality of life of AGYW affected by HIV. If this multilevel intervention is successful in establishing a comprehensive care continuum for HIV-affected AGYWs, the Zambian Ministry of Health will advocate for expansion to additional settings to support national scale- up.

Risks to participants are low in this study, and we have designed careful safety reporting and monitoring mechanisms to ensure that the proposed intervention does not cause harm. Given the urgency of developing interventions that support engagement in care among AGYW, we feel the risks to participants are justified in relation to the potential benefits.

Confidentiality

The study team will bring its combined decades of experience working with young women in these settings to develop a detailed plan to protect participant confidentiality and minimize harms associated with loss of confidentiality. All staff will be trained to manage research with strict attention to appropriate counseling, disclosure, confidentiality, and secure storage of data in accordance with ICH-GCP, and these principles will be applied in the conduct of this study. Procedures will be documented in detailed standard operating procedures, which will be available at the study sites for reference. Staff will also receive instructions on how to report any violations of those policies and procedures.

All study interview and counseling sessions will take place in private rooms with closed doors. For the AGYW survey, participants will be offered the option to conduct the visit at a local community center if no private space is available at home. At enrollment, study staff will have a discussion with each participant about her home and partnership situation to assess the risks of participation. This will include

helping her make a plan for how she will respond to questions from family members or others about her attendance at the clinic or community sessions, to minimize the risk of stigma resulting from study participation.

All consent and data forms will be kept in locked files in the project office, with consent forms and locator forms stored separately from paper data collection forms. Data collection forms will be coded only with the unique study identification number (PTID) given to each participant. Computer records will be password-protected to prohibit illicit access. Audio recordings and interview transcripts from the qualitative activities will be labeled only with a PTID. All electronic data will be encrypted and stored on password-protected computers in locked rooms.

There is also risk of loss of confidentiality through participant follow-up procedures. We will minimize risk by using only methods of contact that are acceptable to participants, including using an alias or pseudonym of the participant's choosing to protect confidentiality.

The risk of loss of confidentiality and privacy during group activities such as SHIELD intervention sessions and FGDs will be minimized by ensuring that all participants are cognizant of the ground rules of participation in a group exercise. These ground rules include the fact that they do not have to reveal their full name and should not reveal personal information about others, but rather should talk in general terms. Ground rules will be introduced and participants will be asked to take a pledge that they will not disclose personal information about other group members to people outside the group. At the beginning and end of each session, participants will be reminded that it is essential to respect the confidentiality of other members of the group and not discuss other group members' personal information outside of the group meeting. However, participants will be told to keep in mind that the proceedings of the discussion may not be kept confidential, although all those present are encouraged to do so. Participants will also be reminded on a regular basis that participation in all study activities is voluntary and that withdrawal of consent will have no impact on their access to clinical services, including HIV testing and treatment.

Compensation

During the cluster randomized study, we will also offer a payment of 80 Kwacha to AGYW for transport reimbursement at baseline and at the 6-month, and 12-month. These reimbursement amounts are based on standard rates offered to participants in prior studies conducted by the research team.

Informed Consent Process

Study staff will be responsible for obtaining written informed consent or assent from all participants. Before implementation, all informed consent forms will be reviewed by the Youth Advisory Board, approved by the study institutional review boards, and field-tested to ensure comprehension and completeness.

In Zambia, the legal age for consent for health research is 18 years. For minors under age 18 who are interested in participating in the study, peer navigators will obtain written consent for

participation from a parent or legal guardian (referred to as "parent" hereafter). After parental permission is obtained, the minor will be asked to provide assent for study participation. Parental consent forms will specify that parents may not have access to their children's study data.

Separate sets of consent forms will be used for each research activity and each participant population, where a "set" of forms includes adult consent forms plus parental consent and child assent forms for AGYW populations.:

For the implementation trial, consent to participate in the cRCT will be obtained. According to national guidelines, those 18 years of age and older will be able to provide written consent for these services, and those under 18 years will require their parent's written consent.

The consent/assent process will address study procedures, confidentiality and limitations to confidentiality, time involved in study participation, risks and potential benefits of participation, the right to withdraw from participation, and the rights of research participants. For all activities, AGYW will be informed that their participation in the study is voluntary and that their decision will not affect their access to routine services at their schools, community agencies, or health clinics. Providers will be informed that their choice to participate is entirely voluntary and will not affect their employment status. All participants will be advised that they do not have to answer any questions that they do not want to and that they can withdraw from the study at any time. The names and telephone numbers of the site Field Coordinator and site Lead Investigator (Dr. Michael Mbizvo) will be given verbally to all participants and included in all consent or assent forms.

The staff will be extremely sensitive to issues of confidentiality and risk during all consent procedures. They will receive extensive training in ensuring participant confidentiality and comprehension of study procedures, and in confidentiality regarding the eligibility criteria when discussing the study with parents and other community members. All potential study participants will have the opportunity to talk with a member of the research team to clarify the study's purpose and procedures and to discuss the procedures to retain confidentiality during the interview. The informed assent and consent procedures will be conducted on a one-to-one basis in a private setting.

4.0 Data Management

Research materials obtained from individuals recruited into this study will include the following:

- Consent forms
- Contact information sheets ("locator forms" and eligibility assessments)
- Audio files and transcripts of interview and focus group sessions
- Completed surveys
- Clinic data (through clinic data abstractions)
- Intervention tracking details on education sessions and services provided

All participant data will be managed according to Zambian and U.S. regulations (45 CFR part 46) and ICH-GCP. Participants will receive a unique study identification number (PTID) that will be recorded on all study forms and interview transcripts. PTIDs will be maintained by the Population Council Field Coordinator, and a Screening and Enrollment Log will provide a link between participant name and PTID. The Screening and Enrollment Log will be stored in a secure, double-locked location in the Field Coordinator's office,

separate from participant data. Hard-copy (paper) consent forms and contact information sheets containing personally identifying information will likewise be stored in a secure, limited-access location separate from participant data. Personal identifying information will be accessible only to key study personnel and will not be transmitted to RTI.

All other data (transcripts) will be coded by PTID and will not contain any personal identifiers. The qualitative transcripts and audio files will be maintained as electronic records, which will be stored in encrypted, password-protected files, coded by PTID, and transmitted to RTI using a secure file transfer protocol (FTP) server. All electronic data and study databases will be stored on secure, password-protected computers in the project office computers, accessible by key study personnel only.

5.0 Training and Qualifications of Personnel

The team includes the Principal Investigator (PI) (Subramanian) who has led multiple studies related to integrated care delivery and on implementing best practices to scale up cervical cancer prevention for HIV- and HIV+ women. Dr. Sujha Subramanian has been working in close collaboration with the Zambian MOH to conduct a process evaluation of the Zambian Cervical Cancer Program. The Zambian Co-investigators (Co-Is) from the Population Council include Dr. Michael Mbizvo, Country Director, Dr Nkomba Kayeyi, an epidemiologist and demographer with extensive experience in managing large scale studies and field surveillance work in Zambia and Dr. Maurice Musheke, a social and behavioral scientist, who will continue to work on the study in an advisory role, while no longer full-time at the Council. Dr. Mbizvo, a professor who has trained public health and medical postgraduates, mentored and published in sexual and reproductive health and HIV prevention and care, is an expert in reproductive health, epidemiology and linkages between HIV and women's health services, and Dr. Musheke has extensive experience conducting research on HIV testing, ART adherence, key populations and adolescent's HIV care in Zambia. Ms Nachela Chelwa, a senior programme officer and public health specialist with expertise in qualitative and quantitative research methodologies and has conducted trainings and deployment of several field research assistants. Dr. Carla Chibwesha, Co-I from the University of North Carolina (UNC), is a clinician with extensive experience working in Zambia on the intersection of HIV and women's health. Technical Advisors from the Zambia MOH include Dr. Sharon Kapambwe, who was instrumental in developing the Zambian cervical cancer screening program, Dr. Tina Chisenga, the Associate Director for Infectious Diseases and Dr Matilda Simpungwe, Assistant Director for Adolescents Health. RTI Co-Is are Dr. Georgiy Bobashev, who has been a collaborator on modeling projects with the PI for more than 10 years and brings statistical and HIV modeling expertise; Dr. Sarah Roberts, who has expertise in implementing HIV research studies in Zambia; and Dr. Laura Nyblade, an expert in HIV stigma and discrimination among vulnerable groups, including AGYW. This team brings an extensive, intersecting, and multidisciplinary expertise to design and implement the proposed multilevel interventions to create a comprehensive HIV care continuum for AGYW. The team has well-established collaborations on the ground, including connections in the government health care sector, community organizations, and advocacy groups. To ensure the highest level of fidelity and adherence to the protocol, all data collectors will receive in-depth training and monitoring.

A study coordinator, from among the existing Population Council staff will be in charge of coordinating data collection. She will be responsible for the day-to-day supervision of PNs; planning and coordination of fieldwork activities.

Approximately 14 PNs will be recruited to the Population Council staff and will be responsible for leading youth club sessions and providing peer navigation across the participating communities. The PNs will have skills in conducting in-depth interviews and focus group discussions, and conversant in the two main local languages (Bemba and Nyanja) spoken in the study site. While many will have previous research

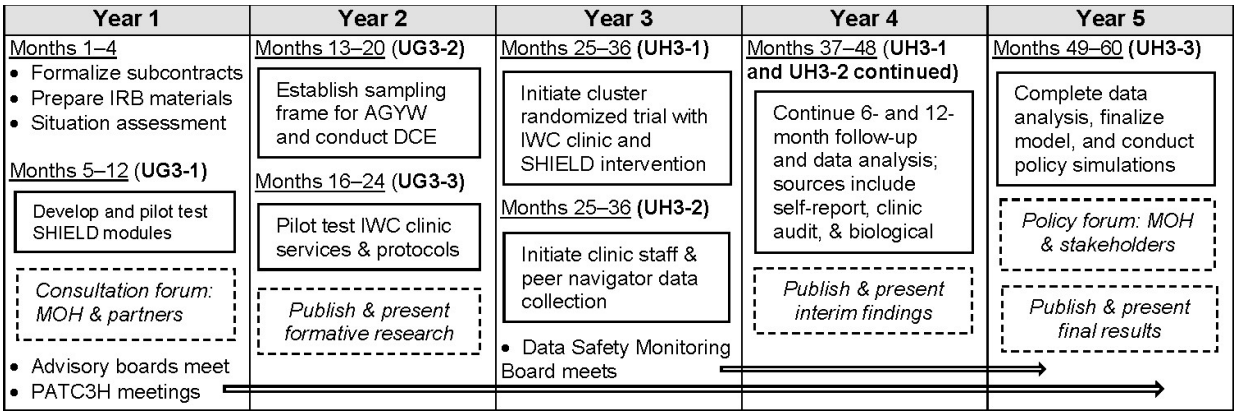
experience, they undergo a training program on conducting SHIELD sessions, stigma, clinic navigation, and research ethics, particularly on research with minors, prior to the start of data collection activities. PNs will also under training and receive certification for conducting mobile HIV counseling and testing (HCT) along with pregnancy testing. In addition to the PNs, 2 IWC clinic nurses will be hired to the UNC staff and will be responsible for facilitating the IWC clinic services, including HIV counseling and testing, HIV treatment and adherence counseling, contraception, pregnancy testing, HPV vaccination, along with making referrals for other services requested. The IWC clinic nurses will undergo training and will receive certification for HCT.

In addition to study staff, we have also established a data safety monitoring board (DSMB), which includes 5 Zambian experts or clinicians that work on adolescent health or HIV. The DSMB charter specifies the terms for project oversight, establishes regular DSMB meetings, and specifies the role of the DSMB in data monitoring.

6.0 Timeline

The study timeline is presented in **Exhibit 5.**

Exhibit 5. Project Timeline



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