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HRP-503B – BIOMEDICAL RESEARCH PROTOCOL
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Protocol Title: Engaging providers, community members, and young women to adapt and pilot a youth-friendly sexual and reproductive health package in low-income communities in India

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(*If applicable*) **Clinicaltrials.gov Registration #:** NCT04307849

INSTRUCTIONS
This template is intended to help investigators prepare a protocol that includes all of the necessary information needed by the IRB to determine whether a study meets approval criteria. **Read the following instructions before proceeding:** 1. Use this protocol template for a PI initiated study that includes direct interactions with research subjects. Additional templates for other types of research protocols are available in the system Library. 2. If a section or question does not apply to your research study, type "Not Applicable" underneath. 3. Once completed, upload your protocol in the "Basic Information" screen in IRES IRB system.

UTHealth Houston
IRB NUMBER: HSC-SPH-21-0834
IRB APPROVAL DATE: 12/06/2022

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SECTION I: RESEARCH PLAN

1. **Statement of Purpose:** State the scientific aim(s) of the study, or the hypotheses to be tested.

   This study will systematically adapt, pilot test, and evaluate an integrated community/facility intervention to improve the uptake of adolescent-friendly services for married and unmarried adolescent girls and young women (AGYW; ages 15-25) in a low-income area with a population of approximately 700,000 in Mumbai, India. The specific aims and hypotheses to be tested are as follows:

Aim 1: Adapt the health club curriculum and provider/staff sensitization training using ADAPT-ITT.

I will collect formative mixed methods data from stakeholders to assess the landscape of adolescent-friendly care and gaps to adapt the intervention. Intervention sessions will be presented to groups of stakeholders to elicit feedback on adaptations.

Hypothesis Aim 1: Community engagement and mixed methods data will yield insights into current treatment seeking patterns and needs for AGYW and effective adaptation strategies to improve the proposed intervention.

Aim 2: Implement a pilot of the intervention and assess implementation outcomes.

The provider and staff component will consist of two groups to facilitate participation and accommodate provider/staff schedules. Four separate groups of AGYW will participate in the adolescent health club component, using a wait-list control group design. Separate groups are needed due to the group nature of the intervention activities which limits the number of people who can participate at one time. Intervention participants will be surveyed pre- and post-intervention to examine acceptability, feasibility, and uptake. Qualitative process data will also be collected and analyzed.

Hypothesis Aim 2: AGYW's satisfaction with services will improve 20% post-intervention compared to pre-intervention.

Aim 3: Assess a pilot set of health outcomes for future research.

Quantitative pre- and post-tests will also assess pilot effectiveness health and behavioral outcomes.

Hypothesis Aim 3: Sexual and reproductive health (SRH) knowledge will show statistically significant improvement post-intervention. Behavioral elements of SRH will show positive trends, but will not be statistically significant.

2. **Probable Duration of Project:** State the expected duration of the project, including all follow-up and data analysis activities.

   5-6 years

3. **Background:** Describe the background information that led to the plan for this project. Provide references to support the expectation of obtaining useful scientific data.

A.1. Status of adolescent sexual and reproductive health (SRH) and adolescent-friendly health services

Most of the over one billion people between the ages of 15-25 in the world live in low- and middle-income countries (LMICs). Among youth living in LMICs, 70% are in Asia.[1] Among health, education, and employment challenges facing young people, SRH need specific action.[2-7] Adolescent girls and young women (AGYW) are particularly vulnerable with adolescent pregnancy, maternal morbidity and mortality, STIs/HIV, gender-based violence, and psychological trauma stemming from these issues given their precarious status in patriarchal cultures.[8-11] While striving to achieve the Millennium Development Goals, the global health agenda largely

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focused on maternal and child health and infectious disease, which has contributed to gains in child health, but made little progress addressing the needs of the growing AGYW population.[12] **LMICs seeking to improve AGYW's health and make progress on the Sustainable Development Goals must promote gender equity and integrated SRHR services.**[13-16]

Since the International Conference on Population and Development (ICPD) in 1994 highlighted the unique and growing needs of the global adolescent and young adult population, countries, multi-lateral organizations, and practitioners have echoed the call for improved SRH.[12, 17-19] The WHO has developed guidelines around what constitutes adolescent-friendly healthcare, and worked with many LMICs to develop national strategies and programs to develop and improve their adolescent health services.[17, 20-22] Research and reviews have defined key elements of what "adolescent/youth-friendly" programs and healthcare consist of from the perspectives of adolescents and providers. The basic elements elaborated by these stakeholders are: youth accessibility and awareness of services, provider and staff attitudes (respect, friendliness and non-judgmental), patient/provider communication, clinical competency, guideline-driven and needs-based care, age-appropriate and appealing setting, confidentiality, community awareness and support of services, youth involvement in healthcare and health outcomes.[22-32] In addition to these indicators, some have noted that youth-friendly health care cannot exist unless nested within a context of supportive policy frameworks that advocate for youth SRHR and non-stigmatizing community norms.[26, 27, 33, 34]

A.2. Status of adolescent SRH and youth-friendly health services in India

India has generally been reflective of the global trends described above, with limited attention and resources provided for dedicated AGYW SRH services within public clinics and hospitals.[35-40] Challenges to the development and implementation of adolescent physical and mental health services in India include limited engagement of youth in the design of services, a lack of providers overall as well as a lack of providers who have limited time to spend per patient, poor health infrastructure that limit patient confidentiality and privacy, taboos concerning open discussion of sexuality and reproduction, and stigma surrounding mental and SRH treatment-seeking particularly for AGYW.[37, 41, 42] Further, adolescent-friendly services that have been attempted in India have suffered from inconsistent or poor quality evaluation data and limited sustainability.[43] Given these challenges, the Indian government recently sought to develop clearer guidelines and indicators for adolescent and youth health.

In 2006, the Government of India issued the Adolescent Reproductive and Sexual Health Strategy as a component of the Reproductive and Child Health Phase II Programme.[44] The strategy outlined ways in which adolescent-friendly services for married and unmarried women and men could be integrated into the existing public health infrastructure. However, researchers have noted that this strategy was not implemented in most of India, resulting in limited availability of services, limited knowledge of services and poor utilization by adolescents.[35, 37, 45] It was also noted that the 2006 strategy failed to incorporate mental health services and sufficient SRH education and counselling. In recognition of the limitations of the 2006 strategy, the Indian government launched the *Rashtriya Kishor Swasthya Karyakram* (RKSK; National Adolescent Health Program) framework for adolescent and young adult healthcare services.[35, 45, 46] RKSK suggests services that should be provided at each level of the public healthcare system, delivered by healthcare providers and staff after receiving training on adolescent healthcare. Basic elements of the framework are: 1) adolescent health clubs and adolescent health days, 2) adolescent friendly health clinics (AFHCs), 3) recruitment by community-based outreach workers, and 4) convergence of public and private sector organizations to support adolescents. RKSK is designed to address some of the gaps identified in the previous national strategy through incorporation of mental health services and health education. Researchers at the Population Council carried out an early evaluation of the implementation of RKSK from the perspective of providers[35] and from the perspective of adolescents and young adults.[45] This evaluation found that although some providers received sensitization training on appropriate, non-judgmental ways to educate and communicate with adolescents, this training was limited and practitioners often failed to implement best practices. In addition, providers continued to primarily

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focus on married and pregnant adolescents, rather than preventive care of unmarried female adolescent girls or boys. Providers identified problems with utilization of the services, including lack of knowledge that the services existed, limited mobility of adolescents and young adults, and reluctance of adolescents to access the services. Adolescents who accessed the services reported mixed experiences, especially with respect to privacy, adequacy of information provided, and providers' attitudes.

Despite the many policies, programs and movements towards the development of needed services, implementation at the local level has been a major impediment to impact. Most health and gender equity education is provided in schools, missing those adolescents who either never attended or have dropped out of school.[47-50] Thus, inadequate implementation of RKSK at the community/primary care levels has had the most negative effect on low-income girls and women in rural and urban slum communities who continue to be missed by these national changes. **As a result, many of the policies and programs described above have not yet achieved substantive, long-term impacts on the well-being of impoverished AGYW.**

A.3. The context of AGYW's SRH concerns in India

There is a well-established link between gender inequity, reduced opportunities for women, and heightened violence and poor health in LMICs.[38, 41, 51, 52, 61, 62] Gender inequity has long been considered a key barrier to empowerment of women and girls with consequent negative implications for sexual, reproductive, and mental health.[63] Globalization in India has exacerbated existing gender and economic inequities through continued exploitation of low-income women in low skilled jobs, disparities in pay and work conditions, and related negative health outcomes for AGYW.[48, 52, 54, 58, 64-72] Concurrently, gender norms are being reshaped by a rapidly globalizing society through expanded access to TV, internet, cell phones[73-79] and a growing emphasis on the potential for women to supplement household income with employment outside the household.[19, 20, 80] Over the past two decades, India has instituted policies and legislation to improve women's status through setting the legal age of marriage at 18, requiring universal education, outlawing dowry, and establishing tougher laws on gender-based violence. While these laws represent advances, enforcement has been inconsistent, and a patriarchal backlash has been observed.[81-90]

At the community level, many girls in India experience gender inequity early in life in the form of preferences for sons that produce a low female to male ratio[26, 91, 92] and poorer nutrition and less health care for girls than their male counterparts.[93-95] Gender discrimination that starts in infancy affects women's later development, status and empowerment as girls age.[96] The onset of menarche can result in restrictions that include withdrawal from school, reduced mobility and limitations on interactions with peers.[51-53] Gender-based violence and harassment, both within families, in communities, and in public spaces also disproportionately impact girls and women.[9, 54-59] In addition, the perception that communities are becoming more dangerous for young women has been used as a rationale to limit young women's mobility, access to education and a motivation for underage marriage.[27, 97-101] Underage marriage places young women at higher risk for maternal morbidity, mortality, and gender-based violence.[54, 60-63] Cultural taboos on discussing sexuality and reproduction continue to limit young women's knowledge of sexual and reproductive health, and ability to access services.[37, 42, 45, 47, 64] Unmet need remains high as contraceptive access continues to be restricted by both economic and cultural factors for young women in low-income communities.[65-68] Although STI/HIV risk remains low in the general population, young married women in the poorest sectors are vulnerable, as their husbands tend to work outside of the community, spending time in other parts of India or outside of India.[69, 70] Further, married AGYW remain at high risk for physical, sexual, and emotional abuse.[58, 71-75] **Thus, gender-sensitive community and facility-based approaches are required to improve AGYW's health.**

A.4. The interventions to be adapted and implemented

This study adapts two evidence-based curricula that have been tested in other LMICs, and addresses key elements in both supply and demand for adolescent-friendly care. EngenderHealth has developed and tested a

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sensitization program (the "Youth-Friendly Services Manual for Service Providers") for health providers and staff to reduce provider bias towards adolescents and arm providers with strategies for more effectively communicating with youth.[76] The adolescent sensitization training builds on EngenderHealth's COPE ("client-oriented, provider-efficient") process and package of tools. COPE establishes a process for health providers and staff to assess areas for improvement and develop solutions to promote sustained SRH healthcare improvement.[77] The Youth-Friendly Services curriculum is delivered as a four-day workshop, and provides both didactic and interactive portions, and also offers the opportunity for providers/staff to hear directly from adolescents about their needs. The EngenderHealth manual also provides sample evaluation instruments that can be adapted to low-income urban Indian communities. Originally developed and tested in Nepal, the curriculum employs client/patient-oriented approaches that have since been used in other LMICs.[76, 78, 79] The curriculum has typically been implemented as part of a package to increase access and use of youth-friendly services, and thus the impact of the provider curriculum alone has not been assessed. However, when used in conjunction with other approaches to improve uptake and use, evaluations found that it was associated with improved patient/client satisfaction.

The curriculum to be adapted for the adolescent health club component was developed by the International Sexuality and HIV Curriculum Working Group and published by Population Council.[80] The toolkit is called "*It's All One Curriculum: Guidelines and Activities for a Unified Approach to Sexuality, Gender, HIV, and Human Rights Education.*" *"It's All One"* employs a rights-based approach to provide SRH education and support youth empowerment, which is researchers believe is more effective and comprehensive than risk-based approaches.[81-83] The toolkit was developed and tested in both school and community-based settings in South Asia and Africa, and provides flexibility in terms of activities that address different types of learners and cultural contexts.[80] There are eight units providing information on sexual and reproductive health and rights, gender norms, empowerment, interpersonal relationships, and communication and decision-making. Qualitative case studies documenting implementation of the curriculum in a variety of contexts in LMICs found that the curriculum was associated with improved SRHR knowledge and attitudes, more equitable gender norms, and greater agency in negotiating sexual initiation and condom use.[84] A cluster-randomized trial of the adapted curriculum in 10 California high schools conducted immediate and one-year follow-up post-tests to evaluate the short-term and longer-term impacts.[85, 86] In the post-test immediately after the curriculum ended, researchers found that students who received the curriculum (compared to a standard sexual education curriculum) demonstrated greater knowledge of sexual health and sexual health services, more positive attitudes about sexual rights, increased communication about sex and relationships, and greater self-efficacy to manage risky situations.[85] These positive psychosocial and behavioral outcomes were maintained at the one-year follow-up.[86]

A.5. The ADAPT-ITT Model

The ADAPT-ITT model was developed by Wingood and DiClemente as a systematic approach for the adaptation of sexual health/HIV-related evidence-based interventions.[87] The ADAPT-ITT acronym stands for each of the eight phases of the model (although not all applications of the model use all phases): assessment, decision, administration, production, discussion with topical experts, integration, training, and testing. The assessment phase involves conducting needs assessments with the target population. The decision phase (which for some studies, such as the one proposed here, happens before the assessment) occurs when one chooses the evidence-based intervention(s) to be adapted. Administration involves the use of theater tests or interactive presentations with key stakeholders to determine what adaptations are needed and to ensure the intervention will be designed with end-users in mind. The revised/adapted draft of the intervention is finalized in the production and integration phases with the guidance of topical experts and information from the theater tests. Once the research team is trained in intervention delivery, the intervention can be pilot tested and results analyzed. The model explicitly includes the target population/patients/end-users and other key stakeholders in the process of intervention adaptation, enabling a participatory approach to implementation. Not all

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frameworks or models of implementation allow for this engagement,[88] which is why we have chosen the ADAPT-ITT approach. The ADAPT-ITT model has been used to adapt interventions for sexual and reproductive health,[89-96] substance use,[97, 98] mental and behavioral health,[99, 100] and chronic health issues[101, 102] in both international and domestic settings.

A.6. Preliminary studies

My previous work has contributed to key areas of this proposed K award. Previous work with AGYW and providers in Mumbai: Over the course of my graduate work, I spent over a year living and working in and around the study area to explore factors related to young women's age at marriage and SRH, as well as support STI/HIV risk reduction interventions. **Through this work, I developed working relationships with NGOs, research institutions, and healthcare providers working in the study area.** I presented my findings in discussions at community dissemination meetings (N=10 meetings averaging 15 participants per meeting), focusing on the service gaps that I identified in youth-friendly services in the study area. A recent return trip in January 2019 to the study area offered the opportunity to obtain support for this work, and talk to providers and Community Health Workers (CHWs) about the elements of the RKSK program currently being implemented. I learned that CHWs have been registering and tracking adolescents, and doing limited nutritional and hygiene health education with them, but work towards greater impact has stalled. The CHWs are responsible for leading the adolescent health clubs, but they lack training or a curriculum for the clubs. Providers currently see and refer AGYW, but feel that AGYW are not comfortable using local providers for "anything beyond colds." My previous work's promise towards research that can improve SRH for AGYW: In my K12, I have worked with adolescent girls (ages 14-18) and their providers (primarily physicians and nurse practitioners) in the U.S. to develop an electronic pre-appointment planning tool. **This work has provided insights into what patient-centered care means to youth seeking primary and SRH care, and approaches to effectively engage stakeholders** in such efforts. This work has also provided insights into provider characteristics that promote adolescent communication and uptake of services.

4. Research Plan: Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. Be sure to distinguish between standard of care vs. research procedures when applicable, and include any flowcharts of visits specifying their individual times and lengths. Describe the setting in which the research will take place.

The Pilot Intervention Model

An ecological model of youth-friendly service use posits that individual, interpersonal, community, and structural factors all impact provision and uptake.[30] The proposed integrated intervention seeks to influence individual, interpersonal, and community levels of the system (Figure 1).

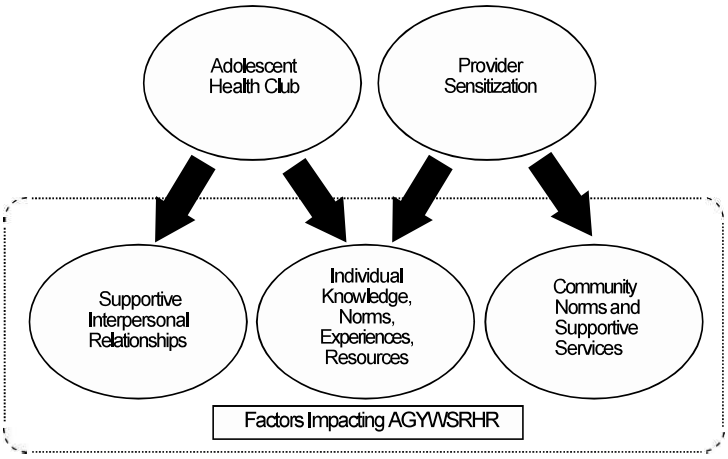

Figure 1: Ecological model of AGYW SRHR and the pilot intervention.

The Study Area

The study community is a low-income, officially-designated "slum" area in northeastern Mumbai with a diverse Hindu, Muslim, and Buddhist population of ≈700,000. Most are long-term migrants from rural areas of Maharashtra and both northern and southern states. Among neighborhood homes, 90% are one-room with a mean family size of 6.2 persons. Construction materials are varied with some houses of durable materials and many more that consist partially or primarily of found

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materials such as tarps and pieces of wood or tin. Most men are engaged in daily low-wage work, with considerable unemployment. Only 28% of women work for cash income, typically sorting and recycling in a local dumping ground or selling embroidery work. The average monthly family income is INR 5900 (approximately US $100/month). The population is young; 60.6% are under the age of 25. Among married women, 38% were married before the legal age of 18 years old, and only 5.5% of young women have studied beyond the 10th standard.[103] The Urban Health Center (UHC) in the study community is a government-funded primary care facility implemented with the Department of Preventive and Social Medicine at T.N. Medical College. The UHC, along with three smaller clinics (known as health posts), constitute the primary government healthcare for the study area. CHWs work out of the health posts and make door-to-door rounds to provide education and distribute basic interventions and medications. My mentors and I have partnered with the UHC in previous projects.[66, 104, 105] The UHC is developing an adolescent-friendly health clinic, and being expanded. Healthcare is also provided through privately-funded NGO clinics, and a wide variety of private practitioners, primarily non-allopathic (e.g., *ayurvedic, unani*, and homeopathic), with about 10% allopathic providers. The private sector has collaborated with ICRW and myself in the past, vital prior relationships that will facilitate the present K01 study. Fieldwork conducted in 2014 found relatively fewer AGYW using private providers as most private sector providers are male. However, my recent discussions and observations suggest that more private providers are expanding their practices to include female nurses and medical assistants, suggesting that more AGYW may begin seeking care in this sector. Seven NGOs work in the community, and one will collaborate with this project. *Apnalaya*, working in the area since 1975, has extensive experience in providing health and social services as well as citizenship and life skills training to youth in the study community. I have previously collaborated with *Apnalaya*. In this project, Apnalaya will be involved in two ways. First, as a key NGO working with youth in the study area, one to two members of their team will be interviewed in the key informant interviews in the assessment/formative research phase, and invited to join the community advisory board (function of board described below). Second, they will provide support in recruitment of adolescent girls in the assessment/formative research phase. They routinely hold events with AGYW and provide some health and social services to community members. They will verbally announce/advertise the study to AGYW, and refer interested AGYW to our team for further information and enrollment. Their participation will be covered by the Tata Institute and Indian Council for Medical Research IRBs.

Community advisory board

A community advisory board (CAB) will be convened for this study. Community advisory boards are considered best practice in community-academic partnerships to ensure interventions are adapted and implemented equitably, ethically, and with community needs in mind.[106, 107] Community advisory boards also typically provide input on analysis, interpretation, and dissemination of findings to ensure that outcomes can be shared with and utilized by key stakeholders in a timely manner.[108, 109] The purpose of the community advisory board in this project is to provide input from stakeholders who work with and are supportive of AGYW. The members of the CAB will include key informants (see below), and 1-2 young women (aged 18-30) not part of the intervention. The CAB will provide input on all aspects of the study, and provide a resource for community questions about the study. The CAB will be convened at least three times over the course of the study, with additional convenings as needed and requested by CAB members. The first meeting will be at the beginning of the study to discuss the roles and responsibilities of CAB members, introduce the study, and elicit input. The second meeting will be held after formative data collection is completed and before the intervention begins to elicit input on intervention adaptations and implementation. The third meeting will be held after the intervention components have been completed to discuss and interpret findings, dissemination of research findings, and areas for future research and action.

Formative Research and ADAPT-ITT Approach (Research Aim 1, Year 1)

The formative research entails a mixed methods assessment of the adolescent SRH landscape in the study area, and adaptation of the intervention components through interactive sessions, consistent with ADAPT-ITT. Unless

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otherwise stated, all consent and data collection will be handled by Dr. Brault (covered by Yale IRB) or a research assistant(s) To-Be-Named (to be listed and covered by all involved IRBs).

ADAPT-ITT Assessment Phase

Key informant interviews (KIIs): Qualitative key informant interviews (N=35-50 or until thematic saturation is reached) will be conducted with both public and private community-based health providers, NGO workers, community health workers (CHWs), and parents of young women. Interviews will also be conducted with government officials at the community and M Ward levels (wards are the smallest administrative unit of governmental ministries). These interviews will focus on qualitative mapping of adolescent health and treatment-seeking pathways and providers in the study area, and factors in the family, community, and elsewhere that influence adolescent girls' and young women's health. Interviews will also explore the impacts of the pandemic and lockdowns on adolescent girls' and families' health and well-being, and any programs or approaches used to mitigate impacts. We will also explore intentions and motivations of healthcare providers and political leaders concerning the implementation of integrated reproductive, mental, and sexual healthcare to address the impacts of COVID. The KIIs will also provide insight into aspects of the intervention and evaluation tools requiring modification. KIIs will also be invited to join a community advisory board (CAB) for the duration of the project (see description above).

In-depth interviews with adolescent girls and young women (IDIs): Qualitative in-depth interviews will be conducted with 20-70 or until thematic saturation is reached AGYW (aged 15-25 years old) to understand their experiences with healthcare in the study area, treatment-seeking patterns, and factors in the family, community and elsewhere that influence their health. Interviews will also include a section with questions about young women's experiences during COVID and associated lockdowns. Young women will also be asked to comment on the proposed intervention's feasibility and acceptability, and provide input on aspects of the intervention and evaluation tools that need modification. We will also discuss intervention components with young women, and seek to learn about sources of support/ways of coping during the pandemic that might be incorporated. Roughly equal numbers of married and unmarried young women will be recruited for participation. Young women will be recruited with assistance from the NGO programs conducted by Apnalaya (see description above), CHWs (their involvement will be covered by the Indian IRBs), and referrals from other participants.

Survey with AGYW on care-seeking patterns and perceptions of healthcare quality and quantitative analysis: A random sample of AGYW seeking care at a set of public (N=3) and private (N=3) healthcare facilities in the study area will be selected and asked to participate in a brief, 20-30 minute survey using validated measures[32, 45, 110] to discuss their patterns of healthcare-seeking (where they go for different problems, and what influences those choices), and their perceptions and experiences with adolescent healthcare. For unmarried participants under the age of 18, consent will be obtained from both a parent and the young woman. My collaborators and I have experience working in the study area and obtaining consent from parents, and we do not anticipate challenges obtaining consent. I will survey 20-25 AGYW from each facility, with a total N=100-150. Survey data will be entered into R,[111] and bivariate and multivariate analyses will be conducted to understand factors associated with AGYW treatment-seeking that may need to be addressed in the health clubs. Analyses will also explore quality of care to identify elements that may need to be incorporated into the provider sensitization. This survey will allow me to apply skills gained in Training Aim 1.

ADAPT-ITT Adaptation, Administration, and Production Phases

Theater testing with key stakeholders for intervention adaptations: Theater testing meetings will be held in which intervention sessions are presented and, in some cases, acted out to the group. Special attention will be given to adaptations needed due to COVID. Audience members' responses and post-meeting critiques of the material will be recorded and analyzed (see below). During the meetings, we will ask for both general feedback, as well as whether adolescent health club sessions need to be conducted separately with different age groups or based on marital status (married adolescents, regardless of age could have different needs than unmarried

UTHealth Houston
IRB NUMBER: HSC-SPH-21-0834
IRB APPROVAL DATE: 12/06/2022

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

adolescents). Separate meetings (up to 10 meetings total) will be held with the following stakeholder groups to present the intervention modules and elicit feedback on revisions or adaptations: 1) AGYW; 2) community members/KIIs; and 3) healthcare providers, CHVs, and NGO staff. Due to COVID, we will ensure groups remain smaller (no more than 5-10 participants) to allow adequate distancing. Additional meetings may be conducted after modifications are made to ensure agreement.

ADAPT-ITT Topical Expert, Integration, and Training Phases

Qualitative data analysis and finalization of intervention modules: Interviews and group discussions will be transcribed and translated (as needed, some KII materials will already be in English) and coded with the qualitative data analysis software, Atlas.ti.[112] Using a framework approach with codes based on key implementation and conceptual model factors of interest, data will be coded and analyzed to identify elements of the intervention and evaluation instruments needing revision, with additional codes added as novel topics/issues arise.[113-116] Coding will be conducted by myself and a research assistant, consulting with Dr. Maitra as needed. Using the formative data, and the expertise of my mentors, I will adapt the intervention modules to the context, while making sure the key evidence-based elements are not lost. As needed, additional in-depth coding of the formative qualitative data can be conducted once rapid analysis for intervention adaptation has been completed. Once the modules have been finalized, the intervention facilitators will be trained, and the intervention implemented. The facilitators for the provider/staff intervention component will be Dr. Brault (Yale and ICMR IRBs), Dr. Maitra (Tata Institute and ICMR IRBs), and Mr. Rajendra Singh (an employee of the International Center for Research on Women, an NGO with research and intervention activities throughout India; TISS and ICMR IRBs). The facilitators for the AGYW health club intervention will be Dr. Maitra, and a female research assistant To-Be-Named (Tata Institute and ICMR IRBs). A CHW may help support some sessions, and if so, their participation will be covered by the Indian IRBs).

Intervention (the "Testing" phase of ADAPT-ITT; Research Aims 2 and 3)

Intervention Eligibility: AGYW inclusion criteria: AGYW between the ages of 15-25 years old, provide consent or assent, have been living in the study area for two years or more, and if unmarried and under the age of 18, have parental consent to participate. AGYW exclusion criteria: AGYW who are unable to give consent due to psychological or mental limitations, or, if unmarried and under the age of 18 do not have parental consent to participate. Provider/staff inclusion criteria: Providers or staff who work at a public or private facility in the study area that see an average of at least five AGYW per month for the past year.

Study Design: Neither providers/staff or clinics can be randomized, as only a subset of the clinics/providers in the study area see enough AGYW to meet inclusion criteria, and some providers/staff who participate will work in the same clinics. Providers/staff will complete brief pre- and post-training surveys; however, the primary measures of their intervention will be derived from the AGYW's outcomes.

For the adolescent health club component, the pilot study employs a waitlisted control group design[117, 118] (Figure 2). In this modified version of the stepped wedge design,[119] all groups receive the intervention, and participants serve as their own controls. This design utilizes a smaller sample size of AGYW and fewer facilitators, making it more feasible for a K award, while still enabling all participants to participate in the intervention. The waitlisted control design also avoids some of the

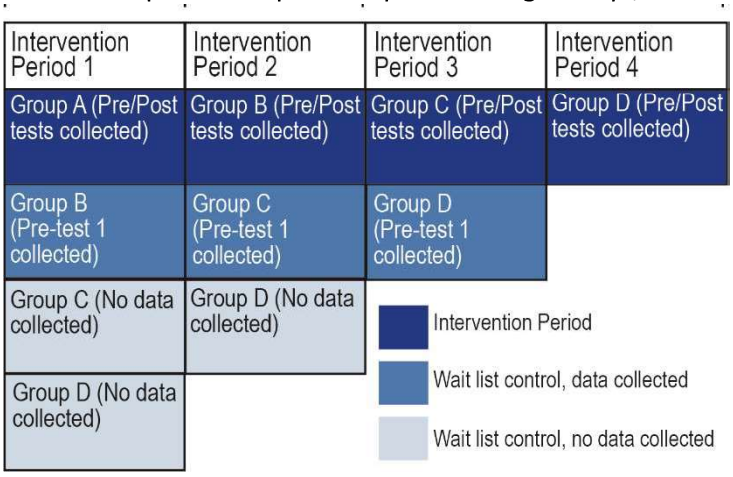

Figure 2: Wait-list design for four adolescent health club groups.

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challenges associated with carryover effect that can occur in other crossover designs, as participants move unidirectionally from control to intervention.[117, 118, 120] The adolescent health club curriculum (which takes approximately 2.5 months to complete) will be sequentially administered to four groups, each with a waitlisted control group. Individuals can be compared to themselves, and the other groups. Sequentially administering the intervention will be more feasible than administering the intervention simultaneously to separate neighborhood clusters, limiting the number of facilitators needed.

***Provider Sensitization Component and Evaluation*:** Providers and clinic staff at the public UHC and health posts, as well as from private clinics known to provide care for adolescents will be screened to determine if they meet eligibility criteria, and if they do, then they will be invited to participate in the sensitization workshop. There will be two workshop groups with 20 participants each, and one workshop group with no more than 20 Community Health Workers (also referred to as Community Health Volunteers or CHVs). All participants will complete pre/post intervention surveys, primarily focused on feasibility and acceptability of the intervention, using previously validated measures.[121, 122] After each session, the facilitator will complete a log to code activities as implemented fully, implemented partially or modified significantly and describe any changes. The log will also include a section to document any unusual events associated with any of the sessions, and the effect of these events on implementation, acceptability, or feasibility. Every other session will be observed and documented in fieldnotes that will be analyzed to contribute to process evaluation (see analysis details below). The log and observations will enable a qualitative assessment of intervention fidelity. A subset will be selected for exit interviews to contextualize the quantitative measures, and learn about participants' perspectives on feasibility and acceptability.

Adolescent Health Club Component and Evaluation: Households with AGYW ages 15 to 25 will be identified by community health workers from randomly selected block sectors of the study area. Clubs will be conducted in separate neighborhood sectors, to limit contamination. Conducting club meetings near to the lanes adolescent girls live in will make it easier for them to attend. To further assess and address potential contamination, we will ask individuals to verify the adolescent health club they attended in the post-intervention survey, whether they attended an additional health club outside our intervention (such as, in school). If any contamination is evident based on this question, then we will model it. AGYW and their mothers (if unmarried and under the age of 18) will be approached by a member of the research team and the adolescent health club intervention will be explained. If consent is obtained, the AGYW will be enrolled, and randomized to either participate or join the wait-list. AGYW will complete the pre-intervention evaluation instrument upon enrollment. In addition to the activities in the "It's All One" Curriculum spread over eight modules, providers from the sensitization component will attend one meeting to discuss services available in the adolescent-friendly clinics, and hear young women's previous experiences accessing care. Similar to the process for the provider sensitization component, the facilitator will complete a log after each session to code activities as implemented fully, implemented partially or modified significantly and describe any changes. The log will also include a section to document any unusual events associated with any of the sessions, and the effect of these events on implementation, acceptability, or feasibility. Every other session will be observed and documented in fieldnotes that will be analyzed to contribute to process evaluation (see analysis details below). As with the provider component, the log and fieldnotes will enable a qualitative assessment of intervention fidelity. When young women complete the curriculum, they will also complete the post-intervention evaluation instrument. A sub-sample of young women (N=15) will be asked to participate in a focus group discussion to reflect on the club's impact and acceptability. Domains measured by previously validated instruments[32, 48, 66, 123-126] to be covered in the pre- and post-intervention surveys are shown in Table 3. There are relatively few validated quantitative measures of implementation outcomes,[127, 128] and none in Hindi, thus the measure we have chosen[129] will have to be translated and back-translated to ensure comprehension.

Table 1: Domains to be covered in AGYW pre- and post-intervention surveys.

Pre-Intervention Survey Domains	Post-Intervention Survey Domains

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

Demographics	Demographics
Clinic service uptake/use	Clinic service uptake/use[32, 130]
SRHR knowledge	SRHR knowledge[123, 131]
Violence and safety	Violence and safety[124, 125]
Gender norms	Gender norms[48, 132]
Agency	Agency[66, 133]
Mental health	Mental health[126]
	Intervention acceptability[129]
	Satisfaction with intervention/services[128]
	Feasibility[128]

***Intervention Power Calculation and Sample Size Considerations*:** Power calculations and sample size for the adolescent health club component are determined based on the SRH knowledge measure.[123] With 85% power, in a two-arm comparison design (similar to round one in Figure 2 above), and based on data from a previous intervention study[131] in which the investigators found a pre/post intervention difference of 1.3 and a standard deviation of 3, we will need 50 pairs or 100 participants in the adolescent clubs total. Broken into four groups, I plan for each group to be 25 participants. As this calculation does not take into consideration within-group analysis, it is a ≈20% overestimate, which allows for 20% loss to follow-up, or participant drop-out without loss of statistical power. However, to minimize bias, I am targeting 95% follow-up. 95% follow-up is based on our team's procedures for tracking and retaining adolescent health club participants. Specifically, we will make clear the participation expectations upon recruitment, consent, and the initial health club meeting. We will follow-up with participants who miss club sessions via cell phone and home visits as needed. These methods have been used by the research team in previous studies in the study area.

Implementation and Intervention Data Analysis

Qualitative analysis: The observations and interviews conducted during and after the intervention will be transcribed, translated into English (as needed), and entered into the qualitative software analysis program Atlas.ti (v.8.1).[112] A modified framework approach[113, 115, 134] to coding will be used in which deductive themes will be developed *a priori* based on the study's conceptual framework and implementation indicators, and inductive codes will be developed and applied iteratively based on review of the transcribed documents. Text will then be reviewed for patterns of consistency, variation, relationships between themes and exemplary cases or quotations. Qualitative data will also be merged with the quantitative findings to triangulate results and further contextualize the quantitative indicators, in keeping with a parallel mixed methods design.[114, 116, 135]

Quantitative analysis: I will use R to analyze the data. Descriptive statistics will be obtained for continuous and categorical variables. The health outcome scales to be used in this study are well-validated (in contrast to the implementation outcome scales), and can be assumed to have approximate normal distributions, although these assumptions will be checked. This study will conduct both within and between-group analyses for the adolescent club component. All subjects will have pre- and post-treatment within-subject measures, and these comparisons can be preliminarily analyzed with paired t-tests. Primary analyses will focus on using repeated measures general linear mixed models to examine comparisons across recruitment cohorts. We will also be able to compare the treated participants from group 1 with the untreated participants in group 2, followed by the group 2 treated participants with the untreated group 3 participants, and finally the group 3 treated participants with the untreated group 4 participants, and can use repeated general linear mixed models for this unbalanced design.

5. Genetic Testing N/A ☒
   A. Describe

UTHealth Houston IRB NUMBER: HSC-SPH-21-0834
IRB APPROVAL DATE: 12/06/2022

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

i. the types of future research to be conducted using the materials, specifying if immortalization of cell lines, whole exome or genome sequencing, genome wide association studies, or animal studies are planned *Write here*

ii. the plan for the collection of material or the conditions under which material will be received *Write here*

iii. the types of information about the donor/individual contributors that will be entered into a database *Write here*

iv. the methods to uphold confidentiality *Write here*

B. What are the conditions or procedures for sharing of materials and/or distributing for future research projects? *Write here*

C. Is widespread sharing of materials planned? *Write here*

D. When and under what conditions will materials be stripped of all identifiers? *Write here*

E. Can donor-subjects withdraw their materials at any time, and/or withdraw the identifiers that connect them to their materials? *Write here*

i. How will requests to withdraw materials be handled (e.g., material no longer identified: that is, anonymized) or material destroyed)? *Write here*

F. Describe the provisions for protection of participant privacy *Write here*

G. Describe the methods for the security of storage and sharing of materials *Write here*

6. **Subject Population:** Provide a detailed description of the types of human subjects who will be recruited into this study.

Qualitative data collection will be collected from the following individuals:

Key informant interviews (KII) (N=35-50 or until thematic saturation is reached) will be conducted with both public and private community-based health providers, NGO workers, community health workers (CHWs), and parents of young women. Interviews will also be conducted with government officials at the community and M Ward levels (wards are the smallest administrative unit of governmental ministries). KIIs will also be invited to join a community advisory board (CAB) for the duration of the project.

Adolescent girls and young women (N=20-70 or until thematic saturation is reached) between the ages of 15-25 years old living in the study area. Consent will be obtained from the individual and her mother (if the participant is unmarried and under the age of 18). Participants over the age of 18 are considered adults, and can provide consent for themselves. Participants married and under the age of 18 are considered emancipated minors, and as such, can also provide consent for themselves. Roughly equal numbers of married and unmarried young women will be recruited for participation.

Theater testing meetings (up to 10 with 5-10 participants per group) will be held in which intervention sessions are presented and, in some cases, acted out to the group. Separate meetings will be held with the following stakeholder groups to present the intervention modules and elicit feedback on revisions or adaptations: 1) AGYW; 2) community members/KIIs; and 3) healthcare providers, CHVs, and NGO staff. Additional meetings may be conducted after modifications are made to ensure agreement.

Quantitative data will also be collected from adolescent girls and young women between the ages of 15-25 years old living in the study area, and seeking healthcare from public (N=3) and private (N=3 clinics). Inclusion criteria will be the same as for the qualitative in-depth interviews. The brief survey will include validated measures to understand AGYW's patterns of healthcare-seeking (where they go for different problems, and what influences

UTHealth Houston
IRB NUMBER: HSC-SPH-21-0834
IRB APPROVAL DATE: 12/06/2022

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

those choices), and their perceptions and experiences with adolescent healthcare. Twenty-five AGYW will be surveyed from each facility, with a total N=100-150.

The intervention will include two different sets of subjects:

Adolescent girls and young women. AGYW inclusion criteria include AGYW between the ages of 15-25 years old, provide consent or assent, have been living in the study area for two years or more, and if unmarried and under the age of 18, have parental consent to participate. AGYW exclusion criteria include AGYW who are unable to give consent due to psychological or mental limitations, or, if unmarried and under the age of 18 do not have parental consent to participate.

Healthcare providers/staff. Provider/staff working at a public or private healthcare facility in the study area that sees an average of at least five AGYW per month for the past year.

7. **Subject classification:** Check off all classifications of subjects that will be specifically recruited for enrollment in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement.

☒Children	☒ Healthy	☐Fetal material, placenta, or dead fetus
☒Non-English Speaking	☐ Prisoners	☒Economically disadvantaged persons
☐Decisionally Impaired	☐ Employees	☒Pregnant women and/or fetuses
☐Yale Students	☒ Females of childbearing potential	

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects?
Yes ☐ No ☒

8. **Inclusion/Exclusion Criteria:** What are the criteria used to determine subject inclusion or exclusion?

Adolescent girls and young women inclusion criteria: AGYW between the ages of 15-25 years old, provide consent or assent, have been living in the study area for one year or more, and if unmarried and under the age of 18, have parental consent to participate. Married AGYW and/or those age 18 or over will be recruited if they meet inclusion criteria and provide informed consent. Unmarried AGYW under the age of 18 will also need consent from a parent.

Adolescent girls and young women exclusion criteria: AGYW who are unable to give consent due to psychological or mental limitations, or, if unmarried and under the age of 18 do not have parental consent to participate.

Healthcare providers/staff inclusion criteria: Providers or staff who provide consent and work at a public or private facility in the study area that see an average of at least five AGYW per month for the past year.

9. How will **eligibility** be determined, and by whom?

Participant eligibility will be determined by asking potential participants prior to consent. If participants indicate their eligibility, then they will be consented into the study. Eligibility will be further assessed during the process of consent, by affirming their understanding of the purpose of the study and the voluntary nature of their participation in the study. Eligibility will be determined by the PI and/or trained, Hindi and Marathi-speaking research assistants to be named.

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

10. **Risks:** Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.

The primary foreseeable risks to key informants are loss of confidentiality regarding information they share during the interviews.

The primary foreseeable risks to adolescent girls and young women who participate in any of the study components (qualitative data collection, quantitative data collection, or the intervention) are:

a) Loss of confidentiality regarding sensitive information (e.g. SRH problems, mental illness, experiences of violence)
b) Any emotional consequences of an individual recognizing that they have experienced health problems or gender inequity.
c) Loss of confidentiality regarding sensitive information revealed during small-group intervention sessions

The primary foreseeable risks to healthcare providers/staff who participate in their intervention are:

a) Loss of confidentiality regarding provider biases towards adolescents and young adults
b) Loss of confidentiality of personal information shared during small-group intervention sessions.

We understand that there may be a risk that young women disclose that they were married under the legal age of 18, and would therefore be admitting to participating in an illegal activity. However, we have outlined approaches to minimizing the risk of breach of confidentiality below. **Further, although the legal age of marriage for women in India is 18, underage marriage is rarely reported to the authorities, and the law against early marriage is rarely enforced. According to figures from India's National Crime Records Bureau, there was 1 case of underage marriage reported in Mumbai and 13 reported cases in Maharashtra (the state where Mumbai is located) in 2018, which is the most recent year for which data is available. Further, there were only 2 convictions for underage marriage in all of India in 2018.[136] We will not ask young women to discuss their age at marriage in group settings, and will encourage group participants to maintain confidentiality. In other places in this protocol, we have also outlined the various ways in which we will maintain confidentiality and data privacy for participants. We thus believe it is unlikely underage marriage data will be breached, or reported to police.**

11. **Minimizing Risks:** Describe the manner in which the above-mentioned risks will be minimized.

To avoid risks associated with the disclosure of sensitive information, every effort will be made to ensure participant confidentiality. Confidentiality of collected materials will be maintained via a numbered reference system maintained by Dr. Brault and her research collaborators at ICRW. A waiver of written consent is requested to minimize risk of loss of confidentiality. Names will not appear in any publication and data will be reported in aggregate form only. Access to computer files containing participant data will be password protected and all personal identifiers (except study ID) will be removed from analytic files. Completed instruments and other hard copy study results will be kept locked in a dedicated storage facility, and access to these will be limited to key personnel.

Despite the intent of myself and my collaborating partners to maintain confidentiality of information, participants may share personal information with others during the intervention components. Since the project will not be able to ensure the confidentiality of participant's responses, members of the group will be reminded of the confidential nature of the discussion and will be cautioned not to discuss any conversations or individual responses outside of the group. **We will not ask young women to discuss their age at marriage in group settings.**

All research personnel working with study participants or study data will have completed training in the protection of human subjects per the guidelines issued by the U.S. Department of Health and Human Services, as

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

well as the Office of Human Research Protections, before contacting prospective participants or working with study data. All Apnalaya field staff who will be involved in recruitment or initiation of consent have completed training in the protection of human subjects.

To avoid participant discomfort, all team members involved in data collection will ask questions and promote participant discussion about sensitive issues in a sensitive and empathetic manner. All AGYW participating will be closely monitored for any distress or severe health problems throughout their study participation. Any participants expressing safety concerns or distress will be referred to the appropriate services, either within or outside the community. All such referrals will be followed up by Dr. Brault and her collaborators in India to ensure that the participant received appropriate care. Any such event will be considered a severe adverse event (SAE) and will be reported to all regulatory agencies following the SAE reporting protocol in the mandatory time period.

12. **Data and Safety Monitoring Plan:** Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.)
    a. What is the investigator's assessment of the overall risk level for subjects participating in this study?
    The overall risk to participants is expected to be minimal. The intention of the study is to adapt and pilot an integrated community/clinic intervention to improve the SRH of adolescent girls and young women in a low-income community in Mumbai, India.

    b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study?
    There will be young, unmarried women under the age of 18 participating in this study, however, as described above, the overall risk is expected to be minimal.

    c. Include an appropriate Data and Safety Monitoring Plan. Examples of DSMPs are available here http://your.yale.edu/policies-procedures/forms/420-fr-01-data-and-safety-monitoring-plans-templates for
        i. Minimal risk

Minimal Risk DSMP

The principal investigator is responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews quarterly. During the review process the principal investigator will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment. In addition, although we feel that the activities associated with this study are low-risk, we will assemble a Data Safety Monitoring Committee. This committee will be assembled given the ages of the AGYW involved. The members of the monitoring committee will be: Marie Brault (PI), the PI's primary mentors (Sten Vermund at YSPH and Shubhada Maitra at the Tata Institute for Social Sciences in Mumbai), Leslie Curry (YSPH), Deepa Camenga (Yale School of Medicine, Adolescent Medicine specialist), and a community representative to be named. This Data Safety Monitoring Committee will meet once her year (or more if needed) over the course of the study to systematically review the safety record related to subject participation during all phases of the project. The committee will review any adverse events, confirm that all study procedures are being followed per the protocol and monitor other aspects of the study (e.g. drop-out rates and reasons). A written report of the committee members will be prepared and submitted to the IRBs on record.

The principal investigator, the Institutional Review Board (IRB) or the Data Safety Monitoring Committee have the authority to stop or suspend the study or require modifications.

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

This protocol presents minimal risks to the subjects and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs), including adverse events, are not anticipated. In the unlikely event that such events occur, Reportable Events (which are events that are serious or life-threatening and unanticipated (or anticipated but occurring with a greater frequency than expected) and possibly, probably, or definitely related) or Unanticipated Problems Involving Risks to Subjects or Others that may require a temporary or permanent interruption of study activities will be reported immediately (if possible), followed by a written report within 5 calendar days of the Principal Investigator becoming aware of the event to the IRB (using the appropriate forms from the website) and any appropriate funding and regulatory agencies. The investigator will apprise fellow investigators and study personnel of all UPIRSOs and adverse events that occur during the conduct of this research project via email as they are reviewed by the principal investigator. The protocol's research monitor(s), e.g., Safety Monitoring Committee (DSMC), DSMBs, study sponsors, funding and regulatory agencies, and regulatory and decision-making bodies will be informed of breach of confidentiality or mental discomfort-related adverse events within 5 days of the event becoming known to the principal investigator.

ii. Greater than minimal

d. For multi-site studies for which the Yale PI serves as the lead investigator: Not applicable
   i. How will adverse events and unanticipated problems involving risks to subjects or others be reported, reviewed and managed? *Write here*
   ii. What provisions are in place for management of interim results? *Write here*
   iii. What will the multi-site process be for protocol modifications? N/A

13. **Statistical Considerations:** Describe the statistical analyses that support the study design.
    Statistical considerations for the intervention
    Neither providers/staff or clinics can be randomized, as only a subset of the clinics/providers in the study area see enough AGYW to meet inclusion criteria, and some providers/staff who participate will work in the same clinics. Providers/staff will complete brief pre- and post-training surveys; however, the primary measures of their intervention will be derived from the AGYW's outcomes.
    For the adolescent health club component, the pilot study employs a waitlisted control group design. In this modified version of the stepped wedge design, all groups receive the intervention, and participants serve as their own controls. This design utilizes a smaller sample size of AGYW and fewer facilitators, making it more feasible for a K award, while still enabling all participants to participate in the intervention. The waitlisted control design also avoids some of the challenges associated with carryover effect that can occur in other crossover designs, as participants move unidirectionally from control to intervention. The adolescent health club curriculum (which takes approximately 2.5 months to complete) will be sequentially administered to four groups, each with a waitlisted control group. Individuals can be compared to themselves, and the other groups. Sequentially administering the intervention will be more feasible than administering the intervention simultaneously to separate neighborhood clusters, limiting the number of facilitators needed. Power calculations and sample size for the adolescent health club component are determined based on the SRHR knowledge measure. With 85% power, in a two-arm comparison design, and based on data from a previous intervention study in which the investigators found a pre/post intervention difference of 1.3 and a standard deviation of 3, we will need 50 pairs or 100 participants in the adolescent clubs total. Broken into four groups, this means that we will plan for each group to be 25 participants. As this calculation does not take into consideration within-group analysis, it is a slight overestimate, which allows for some attrition.

SECTION II: RESEARCH INVOLVING DRUGS, BIOLOGICS, RADIOTRACERS, PLACEBOS AND

If this section (or one of its parts, A or B) is not applicable, check off N/A and delete the rest of the section.

A. RADIOTRACERS ☒N/A

1. Name of the radiotracer: *Write here*

2. Is the radiotracer FDA approved? ☐YES ☐NO

If NO, an FDA issued IND is required for the investigational use unless RDRC assumes oversight.

3. Check one: ☐IND# *Write here* or ☐RDRC oversight (RDRC approval will be required prior to use)

4. **Background Information:** Provide a description of previous human use, known risks, and data addressing dosage(s), interval(s), route(s) of administration, and any other factors that might influence risks. If this is the first time this radiotracer is being administered to humans, include relevant data on animal models.
Write here

4. **Source:** Identify the source of the radiotracer to be used. *Write here*

5. **Storage, Preparation and Use:** Describe the method of storage, preparation, stability information, method of sterilization and method of testing sterility and pyrogenicity.
Write here

B. DRUGS/BIOLOGICS ☒N/A

1. If an **exemption from IND filing requirements is** sought for a clinical investigation of a drug product that is lawfully marketed in the United States, review the following categories and complete the category that applies (*and delete the inapplicable categories)*:

Exempt Category 1: The clinical investigation of a drug product that is lawfully marketed in the United States can be exempt from IND regulations if all of the following are yes:	
1. The intention of the investigation is NOT to report to the FDA as a well-controlled study in support of a new indication for use or to be used to support any other significant change in the labeling for the drug.	☐
2. The drug that is undergoing investigation is lawfully marketed as a prescription drug product, and the intention of the investigation is NOT to support a significant change in the advertising for the product.	☐
3. The investigation does NOT involve a route of administration or dosage level or use in populations or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product	☐
4. The investigation will be conducted in compliance with the requirements for institutional (HIC) review and with the requirements for informed consent of the FDA regulations (21 CFR Part 50 and 21 CFR Part 56).	☐
5. The investigation will be conducted in compliance with the requirements regarding promotion and	☐

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

charging for investigational drugs.	

Exempt Category 2 (all items i, ii, and iii must be checked to grant a category 2 exemption)

☐i. The clinical investigation is for an *in vitro* diagnostic biological product that involves one or more of the following (check all that apply):

- ☐ Blood grouping serum
- ☐ Reagent red blood cells
- ☐ Anti-human globulin

☐ii. The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product orprocedure; and

☐iii. The diagnostic test is shipped in compliance with 21 CFR §312.160.

Exempt Category 3

☐ The drug is intended solely for tests in vitro or in laboratory research animals if shipped in accordance with 21 CFR 312.60

Exempt Category 4

☐ A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND.

2. **Background Information:** Provide a description of previous human use, known risks, and data addressing dosage(s), interval(s), route(s) of administration, and any other factors that might influence risks. If this is the first time this drug is being administered to humans, include relevant data on animal models.
Write here

3. **Source:** Identify the source of the drug or biologic to be used. *Write here*

a) Is the drug provided free of charge to subjects? ☐YES ☐NO
If yes, by whom? *Write here*

4. **Storage, Preparation and Use:** Describe the method of storage, preparation, stability information, and for parenteral products, method of sterilization and method of testing sterility and pyrogenicity.
Write here

UTHealth Houston
IRB NUMBER: HSC-SPH-21-0834
IRB APPROVAL DATE: 12/06/2022

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

Check applicable Investigational Drug Service utilized:

☐ YNHH IDS ☐ CMHC Pharmacy ☐ West Haven VA
☐ PET Center ☐ None
☐ Other:

Note: *If the YNHH IDS (or comparable service at CMHC or WHVA) will not be utilized, explain in detail how the PI will oversee these aspects of drug accountability, storage, and preparation.*

5. Use of Placebo: ☒Not applicable to this research project

If use of a placebo is planned, provide a justification which addresses the following:

a) Describe the safety and efficacy of other available therapies. If there are no other available therapies, state this. *Write here*

b) State the maximum total length of time a participant may receive placebo while on the study. *Write here*
c) Address the greatest potential harm that may come to a participant as a result of receiving placebo. *Write here*
d) Describe the procedures that are in place to safeguard participants receiving placebo. *Write here*

6. Continuation of Drug Therapy After Study Closure ☒Not applicable to this project

Are subjects provided the opportunity to continue to receive the study drug(s) after the study has ended?

☐ **Yes** If yes, describe the conditions under which continued access to study drug(s) may apply as well as conditions for termination of such access. *Write here*

☐ **NO** If no, explain why this is acceptable. *Write here*

B. DEVICES ☒N/A

1. Are there any investigational devices used or investigational procedures performed at Yale-New Haven Hospital (YNHH) (e.g., in the YNHH Operating Room or YNHH Heart and Vascular Center)? ☐Yes ☐No

If Yes, please be aware of the following requirements:

A YNHH New Product/Trial Request Form must be completed via EPIC: **Pull down the Tools tab in the EPIC Banner, Click on Lawson, Click on "Add new" under the New Technology Request Summary and fill out the forms requested including the "Initial Request Form," "Clinical Evidence Summary", and attach any other pertinent documents. Then select "save and submit" to submit your request**; AND

Your request must be reviewed and approved **in writing** by the appropriate YNHH committee before patients/subjects may be scheduled to receive the investigational device or investigational procedure.

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

2. **Background Information:** Provide a description of previous human use, known risks, and any other factors that might influence risks. If this is the first time this device is being used in humans, include relevant data on animal models.
   Write here
3. **Source:**
   a) Identify the source of the device to be used. *Write here*
   b) Is the device provided free of charge to subjects? ☐Yes ☐No

4. **Investigational device accountability**: State how the PI, or named designee, ensures that an investigational device is used only in accordance with the research protocol approved by the HIC, and maintains control of the investigational device as follows:

   a) Maintains appropriate records, including receipt of shipment, inventory at the site, dispensation or use by each participant, and final disposition and/or the return of the investigational device (or other disposal if applicable): *Write here*

   b) Documents pertinent information assigned to the investigational device (e.g., date, quantity, batch or serial number, expiration date if applicable, and unique code number): *Write here*

   c) Stores the investigational device according to the manufacturer's recommendations with respect to temperature, humidity, lighting, and other environmental considerations: *Write here*

   d) Ensures that the device is stored in a secure area with limited access in accordance with applicable regulatory requirements: *Write here*

   e) Distributes the investigational device to subjects enrolled in the IRB-approved protocol: *Write here*

SECTION III: RECRUITMENT/CONSENT AND ASSENT

1. **Targeted Enrollment: Give the number of subjects:**
   a. Targeted for enrollment at Yale for this protocol: No Yale subjects are being recruited. All participants will be recruited and participate in one study area in Mumbai, India.
   b. If this is a multi-site study, give the total number of subjects targeted across all sites: There is only one site in Mumbai, India.

   The enrollments by population and phase is as follows:

Phase 1 Key informants recruited for qualitative interviews: N=35-50 individuals or until thematic saturation is reached
Phase 1 AGYW recruited for qualitative interviews: N=20-70 or until thematic saturation is reached
Phase 1 AGYW recruited for quantitative survey: N=150
Phase 1 Theater testing groups (includes adults and AGYW in separate groups): up to 10 groups with 5-10 participants per group
Phase 2 Providers/clinic staff/CHVs:
N=60
Phase 2 AGYW: N=100
Total N's across all groups and phases: N= no more than 525

2. **Indicate recruitment methods below.** Attach copies of any recruitment materials that will be used.

☒ Flyers	☐ Internet/web postings	☐ Radio
☐ Posters	☐ Mass email solicitation	☐ Telephone
☐ Letter	☐ Departmental/Center website	☐ Television

UTHealth Houston
IRB NUMBER: HSC-SPH-21-0834
IRB APPROVAL DATE: 12/06/2022

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

☐ Medical record review* ☐ Departmental/Center research boards ☐ Newspaper

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

☐ Departmental/Center newsletters ☐ Web-based clinical trial registries ☐ Clinicaltrails.gov
☐ YCCI Recruitment database ☐ Social Media (Twitter/Facebook):
☒ Other: In person, through referrals with face-to-face or email introductions

* **Requests for medical records should be made through JDAT as described at** http://medicine.yale.edu/ycci/oncore/availableservices/datarequests/datarequests.aspx

3. Recruitment Procedures:

a. Describe how potential subjects will be identified.

The participants for the formative qualitative research (both key informants and young women) will be recruited primarily from Apnalaya's (community-based organization partnering on this study) established networks in the community over their 45 year-long work in the study area. As needed, additional recruitment will be from established networks of community leaders, NGO directors and staff, religious leaders, community health workers, and female community mobilizers. These networks have been established through the PI's previous work in the study area. Based on our previous work, we anticipate that these sources will easily yield the numbers of key informants (N=35-50) and adolescent girls and young women (N=20-70) required for the qualitative data collection in the formative stage. Mothers of girls interviewed will be asked to also participate in separate key informant interviews and theater testing groups, facilitating recruitment of this group.

For the quantitative portion of the formative research, a random sample of adolescent girls and young women (AGYW; ages 15-25 years old) seeking care at a set of public (N=3) and private (N=3) healthcare facilities in the study area will be referred by their healthcare provider and/or Apnalaya's health projects and asked to participate in a brief survey using validated measures to discuss their patterns of healthcare-seeking (where they go for different problems, and what influences those choices), and their perceptions and experiences with adolescent healthcare. Twenty to twenty- five AGYW will be surveyed from each facility, with a total N=150. Based on recent estimates of service usage, clinics in the study area see approximately 80-100 young women in the age range of 15-25 years old per month. Thus, we do not anticipate any challenges recruiting the sample size required for this quantitative survey.

Theater-testing group participants will be recruited similarly to the qualitative interviews above, and participants from the surveys may also be invited to join the theater-testing groups.

For the provider/staff sensitization component, a total of N=60 providers and staff will be recruited from the public and private clinics where AGYW were recruited for the formative quantitative survey. There will be two separate groups of 20 people each who undergo the sensitization workshop. The workshop will take place over four days. In previous work in the study area, retaining providers for a short intervention such as the one described in this proposal has not been a challenge and therefore we anticipate no challenges in recruiting the required sample size.

For the adolescent health club component, households with AGYW between the ages of 15 and 25 will be identified by Apnalaya's field team from randomly selected block sectors of the study area. AGYW and their mothers (if unmarried and under the age of 18) will be approached by a member of the research team and the adolescent health club intervention will be explained. If consent is obtained, the AGYW will be enrolled to either participate in the health club immediately or join the wait-list. An initial sample of 50 AGYW will be recruited (one group of 25 to begin intervention immediately, and one wait-list group). After the first intervention group has completed the health club curriculum, the wait-listed group will begin the intervention, and another 25 AGYW will be recruited for a wait-list. This will continue until four groups of 20-25 AGYW complete the health club intervention. Factoring in an attrition rate of 20%, the expected N at endpoint is 80. AGYW will complete the pre-intervention evaluation instrument upon enrollment. When young women complete the health club curriculum, they will also complete the post-intervention evaluation instrument. A sub-sample of young women will be asked

UTHealth Houston
IRB NUMBER: HSC-SPH-21-0834
IRB APPROVAL DATE: 12/06/2022

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

to participate in a focus group discussion to reflect on the club's impact and acceptability. To limit differences in

UTHealth Houston
IRB NUMBER: HSC-SPH-21-0834
IRB APPROVAL DATE: 12/06/2022

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

the time needed to assemble the health club groups, we will avoid recruiting during busy religious festivals/holidays (such as Ramadan) or vacation periods.

b. Describe how potential subjects are contacted.
Key informants and healthcare providers/staff for all phases will be contacted in the following ways: through in-person meetings, and snowball referrals/introductions via email (email recruitment template is attached) or cell phone.
AGYW for the qualitative data collection will be contacted primarily through Apnalaya's outreach activities, and through snowball referrals/introductions either in person or through cell phone. For the quantitative portion of the formative research, a random sample of adolescent girls and young women (AGYW; ages 15-25 years old) seeking care at a set of public (N=3) and private (N=3) healthcare facilities in the study area will be referred by their healthcare provider/Apnalaya health promotion team member to me or my research assistant and asked to participate in a brief survey.
For the adolescent health club component, households with AGYW between the ages of 15 and 25 will be identified by Apnalaya's field team from randomly selected block sectors of the study area. AGYW and their mothers (if unmarried and under the age of 18) will be approached by a member of the research team and the adolescent health club intervention will be explained. If consent is obtained, the AGYW will be enrolled to either participate in the health club immediately or join the wait-list.

c. Who is recruiting potential subjects?
Subjects will be recruited by the 3-4 members of Apnalaya's adolescent outreach team.

4. Assessment of Current Health Provider Relationship for HIPAA Consideration:
Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?
☐ Yes, all subjects
☐ Yes, some of the subjects
☒ No

If yes, describe the nature of this relationship.
None of the members of the research team will have a direct existing clinical relationship with any potential subjects, however, healthcare providers and Apnalaya staff may tell potential subjects about the study, and refer them to me or my research assistant.

5. Request for waiver of HIPAA authorization: (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.)
Choose one:
☐ For entire study
☐ For recruitment/screening purposes only
☐ For inclusion of non-English speaking subject if short form is being used and there is no translated HIPAA research authorization form available on the University's HIPAA website at hipaa.yale.edu.

i. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data: *Write here*

ii. If requesting a waiver of **signed** authorization, describe why it would be impracticable to obtain the subject's signed authorization for use/disclosure of this data: *Write here*

UTHealth Houston
IRB NUMBER: HSC-SPH-21-0834
IRB APPROVAL DATE: 12/06/2022

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

The investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

6. Process of Consent/Assent: Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.
   Formative phase of the research: Verbal consent for all adult (18 years or older, and under the age of 18 but married and therefore emancipated) participants will be obtained directly from the participant prior to the beginning of any study procedures. All qualitative interviews and the quantitative survey in the first formative research phase of the study will be conducted in a private room, and consent will also be obtained in this private, confidential space. For participants who are minors (unmarried and under the age of 18), verbal consent will first be obtained from a parent or guardian, and verbal assent will be obtained from the participant. The parent/guardian will be asked to step out of the room for the interview/survey, and the participant will again be asked if they assent to participating in the study. The second assent will be done to ensure the subject is independently choosing to participate.
   For the AGYW health club, AGYW and their mothers (if unmarried and under the age of 18) will be approached by a member of the research team either at home or at a location convenient to them (NGO, clinic, community center) and the adolescent health club intervention will be explained. Parental verbal consent will be obtained from the parent and verbal assent will be obtained from the adolescent. At the time of the pre-intervention evaluation (which will be conducted in a private space upon enrollment into the study), the adolescent will be asked to provide assent a second time to ensure they are independently choosing to participate. For all participants and all study components, we recognize that consent is a continuous process, and we will remind participants that they are free to withdraw their consent and cease participation at any point in time. The Apnalaya field team member who is involved in recruitment will initiate the consent process during recruitment and referral to the PI, and the PI and her research assistant (Ms. Vaishali Jagtap) will continue the consent process by re-assessing comprehension concerning the study activities, and re-affirming consent.

7. Evaluation of Subject(s) Capacity to Provide Informed Consent/Assent: Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.
   Capacity to consent will be dependent on the following:
   1. Ability to understand the purpose of the study and the voluntary nature of the individual's participation in the study.
   2. Ability to retain and relay the above information.
   3. Ability to provide verbal consent.

8. Non-English Speaking Subjects: Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. If enrollment of these subjects is anticipated, translated copies of all consent materials must be submitted for approval prior to use.
   My research assistant and the Apnalaya outreach staff will be fluent in the local languages of Hindi and English. All health care providers, some key informants, and some AGYW will be fluent in English, but other key informants and AGYW may not be. Thus, information sheets (we are requesting a waiver of written

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

consent) will be translated into Hindi. My research assistant(s) will be able to assess comprehension in Hindi, as they will have experience in enrolling and consenting participants in Hindi.

UTHealth Houston
IRB NUMBER: HSC-SPH-21-0834
IRB APPROVAL DATE: 12/06/2022

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

As a limited alternative to the above requirement, will you use the short form* for consenting process if you unexpectedly encounter a non-English speaking individual interested in study participation and the translation of the long form is not possible prior to intended enrollment? YES ☐ NO ☒

Note* If more than 2 study participants are enrolled using a short form translated into the same language, then the full consent form should be translated into that language for use the next time a subject speaking that language is to be enrolled.

Several translated short form templates are available on the HRPP website (yale.edu/hrpp) and translated HIPAA Research Authorization Forms are available on the HIPAA website (hipaa.yale.edu). If the translation of the short form is not available on our website, then the translated short form needs to be submitted to the IRB office for approval via modification prior to enrolling the subject. ***Please review the guidance and presentation on use of the short form available on the HRPP website.***

If using a short form without a translated HIPAA Research Authorization Form, please request a HIPAA waiver in the section above.

9. Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed consent, or a full waiver of consent, depending on the study. If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.

☐Not Requesting any consent waivers

☒Requesting a waiver of signed consent:

☒ Recruitment/Screening only *(if for recruitment, the questions in the box below will apply to recruitment activities only)*

☒ Entire Study (Note that an information sheet may be required.)

For a waiver of signed consent, address the following:

- Would the signed consent form be the only record linking the subject and the research? YES ☒ NO ☐
- Does a breach of confidentiality constitute the principal risk to subjects? YES ☒ NO ☐

OR

- Does the research pose greater than minimal risk? YES ☐ NO☒
- Does the research include any activities that would require signed consent in a non-research context? YES ☐ NO ☒

☐ Requesting a waiver of consent:

☐ Recruitment/Screening only *(if for recruitment, the questions in the box below will apply to recruitment activities only)*

☐ Entire Study

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

For a full waiver of consent, please address all of the following:

- Does the research pose greater than minimal risk to subjects?
  ☐ Yes ***If you answered yes, stop. A waiver cannot be granted.***
  ☐ No
- Will the waiver adversely affect subjects' rights and welfare? YES ☐ NO☐
- Why would the research be impracticable to conduct without the waiver? *Write here*
- Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date? *Write here*

SECTION IV: PROTECTION OF RESEARCH SUBJECTS

Confidentiality & Security of Data:

1. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research?

   During the formative data collection, no names will be collected. Email addresses and/or cell phone numbers may be collected and used to facilitate recruitment and interview/survey data collection. After the interview or survey is completed, any cell phone or email information collected will be destroyed. Contact information will not be linked to phase 1 interview or survey responses.

   During the intervention phase (both the facility-based and adolescent/community-based intervention), cell phone numbers may be collected and used to: facilitate recruitment, notify participants about intervention session scheduling, and/or follow-up with intervention participants who miss a session. After a participant's participation in the intervention is completed, any email or cell phone information collected will be destroyed. The PI will review intervention survey data within 48 hours from the time it is collected to determine if there are any immediate mental health concerns (i.e., a high score on a mental health measure indicating severe psychological distress), and if needed link the participant with additional services.

Due to the group nature of the intervention components, participants will meet each other in person, and may disclose identifiable information to other participants. Since the project will not be able to ensure the confidentiality of participant's responses, members of the group will be reminded of the confidential nature of the discussion and will be cautioned not to discuss any conversations or individual responses outside of the group. A unique numerical code will be assigned to intervention participants and used to link their pre- and post- intervention information. Contact information will not be linked with pre- and post-intervention surveys.

2. How will the research data be collected, recorded and stored?

   Data will be collected and recorded using pen and paper (fieldnotes and observations and hard copies of survey/evaluation instruments if tablets are not available), digital audio-recorder (to record qualitative interviews for transcription and analysis), and tablets (for survey/evaluation instruments). Data will be stored on Dr. Brault's Yale-managed and encrypted laptop and backed up to a password-protected hard drive and the Yale secure Box. De-identified transcripts of the qualitative interviews may also be stored for analysis on a Yale desktop/laptop to allow research assistants to assist with qualitative analysis.

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

3. How will the digital data be stored? ☐CD ☐DVD ☐Flash Drive ☒Portable Hard Drive ☒Secured Server ☒Laptop Computer ☐Desktop Computer ☐Other

4. What methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the subject's participation in the study?

   Identifiable data (email addresses and phone numbers) will be stored on Dr. Brault's Yale-managed and encrypted laptop, and not be retained any longer than necessary. Audio-recordings will be uploaded to the transcription (Landmark, which has been used by other Yale PIs) company's secure website for transcription. Landmark destroys the audio-recording from their site after they complete the transcript. Audio-recordings belonging to the PI will be permanently destroyed after a complete transcript of the recording is completed (typical turnaround time for transcription is approximately two weeks), and double-checked for accuracy (typical amount of time required for double-checking a transcript is two days). All data will be stored on Yale-managed and encrypted devices to further safeguard the confidentiality and security of all data.

All portable devices must contain encryption software, per University Policy 5100. If there is a technical reason a device cannot be encrypted please submit an exception request to the Information Security, Policy and Compliance Office by clicking on url http://its.yale.edu/egrc or email it.compliance@yale.edu

5. What will be done with the data when the research is completed? Are there plans to destroy the identifiable data? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured.

   Identifiable data (email addresses and/or cell phone numbers) will be destroyed by Dr. Brault after the participant has completed study activities or when requested by the participant (whichever occurs first).

6. If appropriate, has a Certificate of Confidentiality been obtained?
   Yes, as this application is pending NIH funding.

SECTION V: POTENTIAL BENEFITS

Potential Benefits: Identify any benefits that may be reasonably expected to result from the research, either to the subject(s) or to society at large. (Payment of subjects is not considered a benefit in this context of the risk benefit assessment.)

The benefits to providers/health staff is developing better skills and techniques for working with AGYW and implementing better patient care practices. The benefits to AGYW are learning about their health and rights, coping skills, developing empowerment/agency with respect to SRH, and external resources over the course of the health club intervention. They also have the opportunity to contribute to improvements in community healthcare and other resources for AGYW in the community.

SECTION VI: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. **Alternatives:** What other alternatives are available to the study subjects outside of the research?

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

Participants are free to decline to participate, or may end their participation at any point in time. Adolescent girls and young women may decline to participate, and it will not affect their access to services or standard of care in the community.

2. Payments for Participation (Economic Considerations): Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.

   AGYW will receive a small payment for their participation. For qualitative interviews and the quantitative survey in the formative phase, participants will receive 200 Indian rupees (approximately equivalent to $2.80USD) for their time spent in the interview (estimated to last 30 minutes to an hour). These payments will be provided at the conclusion of the interview/survey. For participation in the intervention session, participants will receive 200 rupees for each session they attend, to be paid at the end of each session.

   Key informants who are in management positions, are healthcare providers, and/or work for the government will not receive a payment. Frontline key informants (community health workers, NGO field staff, daycare/childcare workers) and parents will receive the same payment as AGYW (200 INR or approximately $2.80 USD) for their time in the key informant interviews. Lunch/snack will be provided to the healthcare providers and staff who attend the facility-based intervention, as well as KIIs who attend the theatre testing group sessions.

   For physicians who participate in the facility-based intervention, they will receive 5,000 INR (approx. $60 USD) upon completion of the intervention, or a portion of that depending on how many sessions they attend. CHVs will receive 1000 INR (approx. $12 USD) upon completion of their intervention sessions, or a portion of that depending on how many sessions they attend. These amounts are to compensate them for their time, defray transportation expenses, and are based on recommendations of Indian colleagues who have conducted similar interventions with health providers in the past.

3. Costs for Participation (Economic Considerations): Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.

   The only potential costs associated with participation are participants' time, and possibly the cost of transportation to reach the intervention sessions. Efforts will be made to conduct intervention sessions at centrally located venues, and/or venues the participants already go to (such as the Urban Health Center). In addition, adolescent girls and young women will receive a small payment for their time (between 2-16 USD depending on the time and extent of participation), which will help defray the costs of transportation.

4. In Case of Injury: This section is required for any research involving more than minimal risk, and for minimal risk research that presents the potential for physical harm (e.g., research involving blood draws).

   N/A

   a. Will medical treatment be available if research-related injury occurs? *Write here*

   b. Where and from whom may treatment be obtained? *Write here*
   c. Are there any limits to the treatment being provided? *Write here*
   d. Who will pay for this treatment? *Write here*
   e. How will the medical treatment be accessed by subjects? *Write here*

UTHealth Houston
IRB NUMBER: HSC-SPH-21-0834
IRB APPROVAL DATE: 12/06/2022

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

IMPORTANT REMINDERS

Will this study have a billable service? **Yes** ☐ **No**☒

A billable service is defined as any service rendered to a study subject that, if he/she was not on a study, would normally generate a bill from either Yale-New Haven Hospital or Yale Medical Group to the patient or the patient's insurer. The service may or may not be performed by the research staff on your study, but may be provided by professionals within either Yale-New Haven Hospital or Yale Medical Group (examples include x-rays, MRIs, CT

APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

scans, specimens sent to central labs, or specimens sent to pathology). Notes: 1. There is no distinction made whether the service is paid for by the subject or their insurance (Standard of Care) or by the study's funding mechanism (Research Sponsored). 2. This generally includes new services or orders placed in EPIC for research subjects.

If answered, "yes", this study will need to be set up in OnCore, Yale's clinical research management system, for Epic to appropriately route research related charges. Please contact oncore.support@yale.edu

Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities?
Yes ☐ No ☒

If Yes, please answer questions a through c and note instructions below.

a. Does your YNHH privilege delineation currently include the **specific procedure** that you will perform? **Yes ☐ No ☐**

b. Will you be using any new equipment or equipment that you have not used in the past for this procedure? **Yes ☐ No ☐**

c. Will a novel approach using existing equipment be applied? **Yes ☐ No ☐**

If you answered "no" to question 4a, or "yes" to question 4b or c, please contact the YNHH Department of Physician Services (688-2615) for prior approval before commencing with your research protocol.

IMPORTANT REMINDER ABOUT RESEARCH AT YNHH

Please note that if this protocol includes Yale-New Haven Hospital patients, including patients at the HRU, the Principal Investigator and any co-investigators who are physicians or mid-level practitioners (includes PAs, APRNs, psychologists and speech pathologists) who may have direct patient contact with patients on YNHH premises must have medical staff appointment and appropriate clinical privileges at YNHH. If you are uncertain whether the study personnel meet the criteria, please telephone the Physician Services Department at 203-688-2615. **By submitting this protocol as a PI, you attest that you and any co-investigator who may have patient contact has a medical staff appointment and appropriate clinical privileges at YNHH.**

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APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

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APPROVED BY THE YALE UNIVERSITY IRB 8/12/2021

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UTHealth Houston
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