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Reaching adolescents and young adults with accessible health services: Applications to HIV, contraception, and COVID-19

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Reaching adolescents and young adults with accessible health services: Applications to HIV, contraception, and COVID-19

by

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University of California, Berkeley

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Abstract

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Adolescence and emerging adulthood are critical life stages that shape the trajectory of future health. However, adolescents and young adults are underserved by existing health services, which often fail to overcome the unique barriers to care they face. Achieving universal access to healthcare requires moving beyond service availability to understand and address the myriad interconnected structural, sociocultural, and demographic factors that determine individuals' level of engagement with health services. Each chapter of this dissertation shares the unifying objective of informing real-world implementation strategies to improve access to essential health services among adolescents and young adults.

In Chapter 1, I present the preliminary impacts of a multifaceted loyalty program intervention on the provision of sexual and reproductive health products and health facility referrals to adolescent girls and young women (AGYW, ages 15-24 years) at drug shops in Tanzania. The intervention was evaluated through a 4-month randomized trial at 20 drug shops in 2019. By the end of the study, the rate of patronage by AGYW customers was four times higher at shops that implemented the intervention than comparison shops. Intervention shops also distributed more HIV self-test kits, contraceptives, and health facility referrals to AGYW than comparison shops over the study period. These results suggest that enhancing private sector drug shops with specialized programs designed around the needs and preferences of AGYW may be an effective strategy to reach them with sexual and reproductive health services.

In Chapter 2, I describe the findings of an integrated COVID-19 symptom and exposure monitoring and testing system piloted in a longitudinal cohort of 2,918 university students and employees in California in 2020. At baseline and endline, participants were tested for active SARS-CoV-2 infection via quantitative polymerase chain reaction (qPCR) test and provided blood samples for antibody testing. Throughout the study, participants who self-reported certain symptoms or exposures in daily surveys were automatically notified to return for additional qPCR testing. Analyses reveal that undergraduate students who were 18-19 years old were more likely than other

participants to be diagnosed with SARS-CoV-2 infection via qPCR test, in part due to a superspreader event identified among those living in congregate housing. Test positivity was also higher among participants who recently reported symptoms or household exposures that triggered notifications to test than those without recent symptoms or exposures. Among participants with newly developed antibodies for SARS-CoV-2 at endline, 91% had been diagnosed with incident infection via qPCR test over the study period. These results demonstrate that integrated monitoring systems can successfully identify and link at-risk students to COVID-19 testing when combined with low-barrier entry points to services.

In Chapter 3, I assess HIV knowledge and condom-related beliefs and their associations with HIV testing and condom use in a cross-sectional sample of 6,079 Rwandan secondary school students (ages 12-19 years) surveyed in 2021. Participants' level of HIV knowledge was high overall, with 74% answering at least 6 of 7 HIV knowledge questions correctly. In contrast, beliefs about condoms were mixed, with participants responding favorably to 4 of 8 condom-related statements on average. Most participants endorsed misconceptions about condoms or did not believe that condom use was appropriate in casual or serious relationships. In multivariable models, having high HIV knowledge was associated with recent HIV testing but not condom use. However, participants with supportive or middling condom beliefs were more likely to report condom use than those with prohibitive beliefs. These results motivate renewed attention to educational gaps about condoms' value in prevention and school-based interventions to create supportive social norms around condom use among youth.

In summary, this dissertation provides rigorous evidence demonstrating the benefits of tailored, multipronged approaches to reduce barriers to health services experienced by adolescents and young adults. This research also underscores the importance of epidemiologic data analysis as a tool to identify disparities, evaluate impact, and enable evidence-based decision-making to reduce inequities experienced by youth and support health and well-being across the life span.

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Introduction

In 2015, the United Nations adopted the 2030 Agenda for Sustainable Development, an ambitious set of goals and corresponding targets that represent a pathway toward a better future.[1] These targets include achieving universal health coverage and universal access to sexual and reproductive health (SRH) services.[1] In its efforts to realize this vision, the World Health Organization defines universal health coverage as the state in which every individual and community obtains "the full spectrum of essential, quality health services" without inducing financial hardship.[2,3] A necessary precondition of universal health coverage is universal access to health services.[3] Access itself is a multidimensional construct that includes physical accessibility, information accessibility, affordability, and acceptability.[3,4] Consequently, ensuring access requires moving beyond service availability to understand and address the myriad structural, sociocultural, and demographic factors that interact to determine individuals' level of engagement with health services.

Barriers to health services among adolescents and young adults

There are 1.2 billion adolescents and young adults (ages 15-24 years) globally, comprising 16% of the world's population.[5] Researchers have increasingly recognized adolescence and emerging adulthood as sensitive periods of physical, psychological, and social maturation during which individuals assume adult social roles in their communities, often through educational achievement, workforce participation, romantic partnerships, parenthood, or other milestones.[6] Accordingly, adolescence and emerging adulthood are key life stages that shape the trajectory of future health.

Adolescence is also a normative window for sexual debut, yet adolescents may have limited knowledge of HIV and pregnancy prevention and face unique barriers to SRH services.[7] For example, pervasive misconceptions about the long-term safety and efficacy of contraceptive methods reduce demand for family planning services among young women,[8] while HIV-related stigma and fear of status disclosure impede engagement with HIV testing and treatment services.[9] When youth are underequipped to protect themselves against the dual threats of HIV and unintended pregnancy, early sexual experiences can have lifelong implications for their health, educational opportunities, and personal and socioeconomic well-being.

Despite the long-term benefits of access to preventive healthcare during adolescence and young adulthood, youth remain underserved by existing health services.[10,11] Available services are rarely tailored to the complex circumstances underlying youth's health behavior. For example, youth tend to experience lower social status and are more likely to live in poverty than older adults.[12] However, health systems provide little scaffolding to support youth's transition from pediatric to adult health care.[13] Youth frequently report that concerns about privacy, confidentiality, and unfriendly or judgmental providers deter healthcare seeking, but few providers have specialized training on the provision of youth-friendly services.[14] The failure to address youth's needs may in part explain lower preventive healthcare uptake and greater reliance on

health products and services procured outside of healthcare facilities (for example, in drug shops) among youth compared to older adults.[11,15]

Thus, adolescents and young adults are important target populations for public health interventions to improve access to health services. These efforts may be especially salient for health services that have greater behavioral and motivational barriers to uptake, such as family planning and HIV testing. More recently, anticipated stigma has been identified as a potential deterrent to seeking testing for SARS-CoV-2 infection in the context of the COVID-19 pandemic.[16] However, designing effective interventions requires deeper knowledge of the contextual and individual-level factors that influence youth's health-related behaviors, including uptake of health services.

Theoretical models and frameworks guiding public health interventions

Many theoretical models have been applied to the design of public health interventions.[17–19] Table 1 summarizes four widely used models that underscore the complexity of the behaviors on which public health practitioners seek to intervene. I review these models to provide a backdrop against which to consider the interventions and analyses presented in subsequent chapters of this dissertation. In combination, these models point to many modifiable factors upon which to intervene. They also suggest that interventions that are divorced from context or only act upon one determinant of behavior are insufficient to fully address barriers to health services.

The social-ecological model describes the nested contexts in which people live, from individuals' immediate surroundings to the broader policy environment.[20] When applied to health-related behavior, this model suggests that uptake of health products and services, is determined at multiple levels and, likewise, that public health efforts can and should act upon each level. For example, HIV-related interventions may be designed to increase youth's personal HIV knowledge ('individual'), facilitate positive health communication with parents ('interpersonal'), or create supportive social norms around HIV testing in schools ('community'). At the macro-level, public health research can be applied to lobby for targeted expansion of testing services in areas with unmet need ('institutional') or evidence-based policy changes enabling underage youth to access existing services ('policy/environment').

While the social-ecological model effectively illustrates the interconnectedness of systems shaping behavior, it does not unpack the determinants of decision-making at the individual level. The three other theoretical models presented provide complementary perspectives on the interplay of forces that motivate and explain health behaviors. The health belief model, for example, emphasizes the role of individuals' health-related perceptions (i.e., regarding susceptibility to and expected severity of a disease and benefits and barriers to engaging in a health-promoting behavior) and highlights how a defined event ('cue to action') may spur health service uptake.[21] Recent iterations of this model incorporate interactions between these determinants and an individual's self-perceived ability to engage in a given behavior ('self-efficacy,' a construct adopted from social cognitive theory).[21] Although the health belief model details several key considerations guiding health-related decision-making, the

influences of other individual, social, and macro-level factors (such as those defined by the social-ecological model) are relegated to 'modifying factors' without deeper exploration.

Table 1. Theoretical models applied to health-related behavior.

Model	Determinants of behavior	Example: Determinants of HIV testing
Social-ecological model[20]	Individual factors	HIV-related knowledge and attitudes
	Interpersonal factors	Parental communication about HIV testing
	Community factors	Social norms and stigma around HIV testing
	Institutional factors	Availability of HIV testing at local health facility
	Policy/environmental factors	National policy allowing minors to consent to HIV testing
Health belief model[21]	Perceived susceptibility	Perception of HIV risk based on knowledge of transmission routes and recent behavior
	Perceived severity	Perception that HIV can be fatal if untreated
	Perceived benefits	Perception that early HIV treatment prolongs life
	Perceived barriers	Perception that healthcare providers are unfriendly
	Self-efficacy	Belief in own ability to access HIV testing
	Modifying factors	Demographic, psychosocial, and structural characteristics
	Cue to action	Partner suggests HIV testing together
Theory of planned behavior[22]	Attitudes	Belief that HIV testing is responsible
	Subjective norms	Belief that peers approve of HIV testing
	Perceived behavioral control	Belief in own ability to access HIV testing
	Intention	Intention to get tested for HIV
Information-motivation-behavioral skills model[23]	Information	HIV-related knowledge and information availability
	Motivation	Personal beliefs about HIV testing *and* perception of social support for HIV testing
	Behavioral skills	Belief in own ability to access HIV testing *and* objective ability to access HIV testing

Similar to the health belief model, the theory of planned behavior posits that an individual's supportive or prohibitive perceptions (now within the broader construct of 'attitudes') and self-efficacy (now 'perceived behavioral control') are upstream determinants of behavior, while largely ignoring macro-level determinants (e.g., structural and economic factors).[22] However, like the social-ecological model, the theory of planned behavior also asserts the importance of the sociocultural setting, specifically what an individual believes about other people's perceptions of a behavior ('subjective norms'). Notably, this model proposes that an individual's attitudes and subjective

norms directly influence their *intention* to engage in a behavior, and it is this intention that prompts action. This emphasis on intention as a proximal determinant of behavior differentiates the theory of planned behavior from other models.

In contrast, the information-motivation-behavioral skills model focuses on behavioral skills, rather than intention, as a proximal determinant of behavior.[23] The construct of 'behavioral skills' expands upon the other models' definitions of 'self-efficacy' (health-belief model) and 'perceived behavioral control' (theory of planned behavior) to comprise both self-perceived ability and *objective* ability to complete a behavior. Like the theory of planned behavior, the information-motivation-behavior skills model incorporates the roles of both individual attitudes and social norms (e.g., perceived level of social support for a behavior), which are subsumed under the construct of 'motivation.' This model contends that information (i.e., knowledge about a health behavior) and motivation shape behavior both directly and through their influence on behavioral skills.

Based on the information-motivation-behavioral-skills model, providing an individual with compelling information favoring a given behavior will not effect change if overshadowed by prohibitive motivational factors (e.g., negative peer norms) or if the behavior is infeasible due to limited behavioral skills (e.g., inability to navigate the health system). Indeed, reviews of SRH interventions for youth have documented the limitations of knowledge-based interventions in shifting behaviors such as condom use or downstream health outcomes such as unintended pregnancy and HIV/STI incidence.[24]

Beyond understanding the interplay of factors that determine behavior, effective interventions must respond to the broader societal forces that create and reinforce health inequities. Here I provide a brief overview of key concepts from four theoretical frameworks that inform equitable public health responses to challenges facing youth.

<u>The social determinants of health.</u> This framework posits that social conditions (i.e., "the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life"[25]) impact people's health and well-being and, conversely, that observed health disparities result from inequitable social conditions.[26] This perspective encourages public health action to intervene upon upstream health determinants, such as poverty and racism, and makes apparent the inadequacy of interventions that do not account for the social conditions underlying individuals' behavior.

<u>Intersectionality.</u> The intersectionality framework adds nuance to our understanding of the social determinants of health by describing how overlapping social identities (e.g., sex, gender, sexuality, race, ethnicity, nationality, socioeconomic status, disability, among others) interact to determine the matrix of privileges and disadvantages that shape an individual's life experiences.[27,28] Therefore, public health interventions cannot address social conditions in isolation but must account for the complex social identities that lead to differential impact. Likewise, the diversity of lived experiences of adolescents and young adults requires discarding "one-size-fits-all" approaches to

health promotion in favor of those designed specifically to serve and empower marginalized communities.

The life course perspective. This approach emphasizes the cumulative, compounding effects of life experiences on health and the importance of sensitive life stages, such as adolescence and emerging adulthood, in establishing long-term health trajectories.[29] Accordingly, interventions should be developmentally appropriate for their intended recipients and timed strategically. For example, SRH education programs for youth may be more impactful when implemented *before* youth become sexually active.

Reproductive justice. Created by women of color in response to the marginalization of many communities by the reproductive rights movement, this intersectional framework asserts individuals' right to "maintain personal bodily autonomy, have children, not have children, and parent the children [they] have in safe and sustainable communities."[30,31] To realize reproductive justice, public health interventions must support the full spectrum of reproductive choice. Due to age-related power imbalances, youth may be particularly vulnerable to coercive approaches that limit their personal agency in favor of achieving public health targets.[32] Thus, youth-centered interventions must actively reinforce youth's decision-making power by ensuring that a comprehensive array of health information, products, and services are readily accessible to them.

In summary, these frameworks refocus interventions on the structural causes of observed disparities, encourage practitioners to identify and correct mechanisms through which public health systems reinforce social inequities, and motivate upstream action to serve and empower marginalized people and communities.

Theory- and data-based approaches to increase access to health services

Ongoing public health initiatives draw upon many complementary, theory-informed approaches to promote, optimize, and expand the range of available health services for adolescents and young adults. One promising approach to reduce structural and social barriers to services is implementing self-care interventions that expand health services beyond formal healthcare settings and engage individuals as "active agents" in their own health management.[33,34] Another approach is strengthening partnerships with institutions outside of formal healthcare settings, such as community drug shops and schools, to enhance their capacity to provide essential health products, counseling, and referral to their clientele.[35–37] Finally, public health practitioners may integrate cross-disciplinary methods into the process of intervention design. For example, the adoption of creative design methodologies from marketing, such as human-centered design, is an increasingly popular approach to develop innovative programs and interventions that are highly-tailored to defined user segments.[38,39] Evidence-based strategies from the field of behavioral economics (e.g., setting default options, using small incentives) can also strengthen interventions by identifying opportunities to embed "nudges," or small alterations in how choices are presented, to further shape health decision-making.[40] By seeking to provide a broader array of options adapted to the diverse needs of services' intended recipients, these approaches—alone and in combination—have the potential

to increase demand and reduce cost, inconvenience, stigma, and other barriers to care experienced by youth, thereby increasing access to health services.

Epidemiologic research plays an important role in supporting these efforts. Epidemiologists harness observational data to identify populations who experience a disproportionate burden of certain adverse health outcomes, informing strategic investment and resource allocation. Similarly, analyses of observational data may elucidate which populations are underserved by available health services, motivating deeper exploration and centering of their needs and preferences in health service promotion and delivery. Observed associations between specific exposures and health outcomes may also generate hypotheses about underlying causal mechanisms and reveal potential targets for intervention. Moving beyond describing disparities and associations, epidemiologists apply experimental methodologies, such as randomized controlled trials, to rigorously evaluate programs and interventions, assessing their impact and potential for scale.

In this dissertation, I apply these epidemiologic approaches across three disparate contexts to evaluate or identify promising approaches to facilitate voluntary uptake of available health services by adolescents and young adults:

- In Chapter 1, I describe the preliminary impacts of a multifaceted loyalty program intervention on the provision of HIV self-test kits, contraception, and health facility referrals to adolescent girls and young women at drug shops in Tanzania, assessed via a randomized trial conducted in 2019.

- In Chapter 2, I examine the extent to which a low-barrier, integrated testing and monitoring system successfully detected incident SARS-CoV-2 infections in a longitudinal cohort of university students and employees in California in 2020.

- In Chapter 3, I assess HIV and condom-related knowledge and beliefs and their associations with HIV testing and condom use in a cross-sectional sample of Rwandan secondary students, surveyed in 2021.

As each chapter focuses on distinct outcomes (i.e., SRH product and referral provision, SARS-CoV-2 incidence, HIV testing and condom use), populations (i.e., adolescent girls and young women in Tanzania, university students in California, secondary school students in Rwanda), and study designs (i.e., randomized trial, prospective cohort, cross-sectional survey), I present the background, methods, and strengths and limitations separately for each study. Despite the methodological and contextual dissimilarities between chapters, underlying all chapters is the unifying objective of informing strategies to improve access to essential health services among adolescents and young adults.

Chapter 1. Reaching adolescent girls and young women with HIV self-testing and contraception at girl-friendly drug shops: A randomized trial in Tanzania

1.1 Abstract

Objective: We hypothesized that an intervention designed to create girl-friendly drug shops would increase access to sexual and reproductive health products and services among adolescent girls and young women (AGYW, ages 15-24 years) in Tanzania.

Methods: We conducted a 4-month randomized trial at 20 drug shops in Shinyanga, Tanzania from August to December 2019, to determine if the *Malkia Klabu* ("Queen Club") intervention increased AGYW patronage and the provision of HIV self-testing (HIVST), contraception, and health facility referrals to AGYW. Drug shops were randomized 1:1 to the intervention or comparison arm. Both intervention and comparison shops were provided with OraQuick HIVST kits to give AGYW customers for free. Intervention shops also implemented *Malkia Klabu*, a loyalty program for AGYW created using human-centered design through which AGYW could access free contraception. We compared outcomes in intention-to-treat analyses using shop observations and shopkeeper records.

Results: By endline, shops implementing *Malkia Klabu* had higher AGYW patronage than comparison shops (rate ratio: 4.4; 95% confidence interval: 2.0, 9.8). Over the study period, intervention shops distributed more HIVST kits (median per shop: 130.5 vs. 58.5, p=.02) and contraceptives (325.5 vs. 7.0, p<.01) to AGYW and provided more referrals for HIV, family planning, or pregnancy services combined (3.5 vs. 0.5, p=.02) than comparison shops. No adverse events were reported.

Conclusions: The *Malkia Klabu* intervention increased AGYW patronage and the provision of HIVST kits, contraception, and referrals to AGYW at drug shops, despite HIVST kits being freely available at all participating shops. Enhancing drug shops with girl-friendly services may be an effective strategy to reach AGYW with sexual and reproductive health services.

1.2 Introduction

Adolescent girls and young women (AGYW; ages 15-24 years) in Tanzania experience barriers to sexual and reproductive health (SRH) services that may compromise their long-term health and well-being.[41] Although young women bear a disproportionate burden of HIV infection and unintended pregnancy,[42,43] stigma related to young women's sexual behavior, misinformation about contraception, prohibitive transportation costs, long wait times at clinics, and concern about unfriendly health providers may constrain young women's demand for SRH services.[41,44,45] While no government policies directly prohibit the provision of family planning services to adolescents, some healthcare providers may believe minors are ineligible or require parental consent to receive contraception.[46–48] HIV testing is freely available at public health facilities in Tanzania, yet nearly half of HIV-positive young women remain undiagnosed.[49] To accelerate progress toward ending the HIV/AIDS epidemic, Tanzania lowered the age of consent for HIV testing to 15 years and legalized HIV self-testing (HIVST) in 2019.[50] Evidence from other countries in sub-Saharan Africa demonstrates that HIVST is highly acceptable to youth, who value the increased convenience and confidentiality it affords,[51–53] but little is known about how to ensure that young women will be able to access HIVST kits once they are widely available.

Community drug shops may be one effective distribution channel through which to reach young women with SRH services, including HIVST and contraception.[54,55] In Tanzania, privately-owned drug shops called Accredited Drug Dispensing Outlets (ADDOs) greatly outnumber health facilities and pharmacies, are ubiquitous in many communities, and enable widespread access to quality-assured pharmaceuticals.[56–58] These small businesses, often operated by women, are authorized to dispense certain essential prescription medicines (e.g., common antimicrobials), as defined by a government list.[56] Alongside other medicines and health products, many ADDOs provide SRH products and services such as contraceptives (i.e., combined oral contraception, levonorgestrel oral emergency contraception, condoms), pregnancy tests, informal counseling, and health facility referrals. Notably, although contraceptive services are free at public health facilities, 21% of women in Tanzania obtained their most recent contraceptive method from private sector drug shops,[59] and young women were more likely than older women to rely on private sector method providers.[15]

For these reasons, expanding and improving the delivery of SRH services offered by drug shops in Tanzania may mitigate some barriers to access among young women. However, demand for SRH services at drug shops among young women may be stymied by fear of discriminatory treatment by shopkeepers, lack of awareness of and/or misconceptions about available SRH products, and pervasive social norms regarding the (in)appropriateness of SRH products for unmarried young women.[60,61] Thus, novel demand-creation strategies may be necessary to amplify young women's access to SRH services at drug shops.

We employed the established, iterative process of human-centered design (HCD) to develop *Malkia Klabu* ("Queen Club"), a comprehensive loyalty program intervention to motivate young women to obtain HIVST kits and other SRH services at ADDOs while

simultaneously meeting the professional and financial needs of drug shopkeepers.[60] To test the feasibility of our intervention as a precursor to a larger trial, we conducted a 4-month pilot randomized trial at privately-owned drug shops in Tanzania through which we newly introduced HIVST kits in ADDOs. We hypothesized that enhancing drug shops with the *Malkia Klabu* intervention would increase AGYW patronage and the provision and uptake of HIVST kits, contraception, and health facility referrals for AGYW.

1.3 Methods

Study design and setting

We conducted a parallel arm randomized controlled trial at 20 ADDOs (drug shops) in Shinyanga, Tanzania, a resource-limited, semi-rural region where we introduced OraQuick HIVST kits in ADDOs. OraQuick, the first HIVST kit to be prequalified by the World Health Organization, is an oral fluid screening test that displays high accuracy in the hands of lay users.[62] Although HIVST was legalized in Tanzania in 2019, HIVST kits are not yet registered or widely available outside of research settings.[50] In Shinyanga, the HIV prevalence is 5.1% among young women, more than twice the prevalence among young men (2.0%), and 34% of women aged 15-19 have begun childbearing,[59,63] underscoring the importance of tailored approaches to improve young women's access to HIV and SRH services.

The trial was pre-registered (clinicaltrials.gov: *NCT04045912*). We report the findings according to the Consolidated Standards of Reporting Trials (CONSORT) Statement checklist.[64]

Participant recruitment and eligibility

We randomly selected drug shops from four administrative wards in the Shinyanga Region using a registry of ADDOs provided by the Municipal Pharmacist. The Municipal Pharmacist contacted shop owners using phone numbers from the registry and informed them that they would be invited to participate in a study. After this first contact, research staff called drug shop owners to provide information about the study and, if interested, arrange to meet to obtain informed consent. Owners from all participating drug shops provided written informed consent.

The inclusion criteria for drug shop owners were: (1) at least 18 years of age, (2) owns an ADDO, (3) willing to offer HIVST kits and AGYW-friendly services at their shop, and (4) provides written informed consent for the study. The exclusion criteria were: (1) less than 18 years of age, (2) owns a drug shop that is not government-accredited, (3) unwilling to offer HIVST kits and/or AGYW-friendly services at their drug shop, (4) does not provide informed consent. As participating shops were selected from four neighboring wards within a small geographic area, there was potential for overlap in the communities they served.

Formal power calculations were not performed for this feasibility trial. We ceased recruitment upon reaching the desired sample size of 20 drug shops.

Randomization and blinding

Drug shops were randomly assigned 1:1 to the intervention or comparison arm through a participatory randomization process intended to increase study engagement. Specifically, at an HIVST training which representatives from all shops attended, each shopkeeper drew a colored ball from an opaque bag in front of all attendees to obtain their study arm assignment. Randomization was stratified by administrative ward. Due to the nature of the intervention, it was not feasible to blind participants or researchers implementing the intervention or assessing the outcomes.

Outcomes

Our study had four primary outcomes:

1. AGYW patronage: the number and proportion of AGYW customers observed by research staff during shop observations.

2. Contraceptive distribution: the number and type of contraceptive products (i.e., condoms, oral contraception, emergency contraception) that shopkeepers reported distributing to AGYW customers during the study period.

3. Health facility referrals: the number of referrals for SRH services (i.e., family planning, pregnancy, and HIV testing/treatment services) that shopkeepers reported providing to AGYW customers during the study period.

4. HIVST kit uptake: the number of HIVST kits that shopkeepers reported distributing to AGYW customers during the study period.

Additionally, access to pregnancy tests emerged as an important feature of “girl-friendly” drug shops among AGYW during the design process for the intervention. Thus, although not preregistered, we assessed pregnancy test distribution via shopkeepers’ report as a secondary outcome.

Participants were encouraged to contact the research team if any adverse events occurred (e.g., social harms consequent to HIVST). Research assistants also asked about adverse events as part of study close-out procedures.

Procedures

Upon recruitment, shopkeepers completed surveys about shop operations, their sociodemographic characteristics, and their attitudes toward providing SRH services to young women. For shops where the owner was not involved in day-to-day shop operations, we obtained written informed consent from the shop’s primary employee to complete the survey.

Regardless of study arm, all participating drug shops completed a half-day group training on HIVST, in which local health officials reviewed HIV/AIDS information; explained the purpose of HIVST; led a hands-on demonstration of the OraQuick HIVST kit; and guided shopkeepers through interactive discussions (e.g., brainstorming ways to prevent social harms among customers), roleplays (e.g., pairing up to practice explaining test results to a customer), and quizzes. Shopkeepers received an HIV referral plan for customers who required linkage to confirmatory testing or treatment. Throughout the 4-month intervention period, all shops were freely supplied with OraQuick HIVST kits by the study to provide to AGYW for free and a separate supply of HIVST kits that they could sell to non-AGYW customers (not included in the present analysis).[65] As distribution was restricted to research settings, OraQuick HIVST kits were only locally available at participating study shops during the study period.

Additionally, drug shops assigned to the intervention arm implemented a multifaceted loyalty program, *Malkia Klabu* ("Queen Club"), designed for AGYW using HCD and motivational strategies based on behavioral economics (Figure S1.1, design process described elsewhere).[60] In brief, participating intervention shops invited AGYW customers to join the *Malkia Klabu* loyalty program to earn mystery prizes (e.g., lotion, menstrual pads) through repeat purchases. At any time, program members could point to symbols on the back of the loyalty card to discreetly request free SRH products (i.e., HIVST kits, condoms, oral contraception, emergency contraception, and pregnancy tests) without hassle or fear of denial (Figure S1.2). Intervention shops were also given an SRH display containing sample products, contraceptive method informational cards, and a computer tablet with SRH videos for interested customers to watch (i.e., a video on how to use the HIVST kit and videos of young Tanzanian women discussing their preferred contraceptive methods). Intervention shopkeepers completed a half-day group training on contraceptive counseling for AGYW facilitated by local health officials, which reviewed modern contraceptive methods and principles of adolescent-friendly service provision. Shopkeepers were reimbursed weekly for contraceptives and pregnancy tests provided to AGYW at pre-specified fixed amounts reflective of typical local retail prices (i.e., 1,500 TSh [$0.65] for three condoms; 2,000 TSh [$0.86] for oral contraception; 6,000 TSh [$2.58] for emergency contraception; and 1,000 TSh [$0.43] for pregnancy tests). Unlike HIVST kits, shops were not directly stocked with these products by the study.

Throughout the study, research staff visited all shops weekly to count and restock HIVST kits (both arms) and *Malkia Klabu* supplies (intervention arm only). Additional visits were conducted whenever shops contacted the research team to request restocking.

We relied upon three sources of data to evaluate the *Malkia Klabu* intervention:

1. Shop observations: Research staff conducted shop observations at baseline (before randomization), midline (after 2-3 months), and endline (after 3-4 months) to assess AGYW patronage in participating drug shops. Each observation period entailed a 3-hour continuous time block during which research staff documented all customers entering the shop, including their apparent sex and age and

products/referrals received. We randomly sampled five observation day/time blocks (e.g., Wednesday from 10 am to 1 pm) per shop per time point, corresponding to up to 15 observations per shop across the study period (Figure S1.3). The sampling algorithm required that each set of five day/time blocks included at least one weekend, weekday, morning, and afternoon observation to increase comparability between shops. If a shop was closed during a scheduled observation, the observation was attempted on the same day/time block in the subsequent week(s).

2. Customer logs: Participating shopkeepers were trained to fill standardized customer logs provided by the study that tracked transactions with female customers who appeared to be aged 15-24 years (i.e., AGYW), including the provision of HIVST kits; other SRH products (i.e., oral contraception, condoms, emergency contraception, and pregnancy tests); and health facility referrals for HIV, family planning, and/or pregnancy services. Research staff reviewed and collected completed logs during weekly restocking visits.

3. Administrative stocking records: Research staff maintained administrative records of HIVST kits stocked in each shop and counted remaining HIVST kits during weekly restocking visits; these records were used to validate shopkeepers' logs of HIVST kit distribution.

Statistical analyses

Data from all participating drug shops were included in intention-to-treat analyses. We conducted two types of analyses to estimate the effects of the intervention on the primary and secondary outcomes. First, we used negative binomial regression to estimate rate ratios comparing the rate of AGYW patronage between study arms via a difference-in-differences approach.[66] Models were adjusted for administrative ward to account for stratified randomization and included shops as random effects to account for clustering of observations by shop and log-duration of observation as an offset term.[67] To assess the robustness of our modeling approach, we also ran alternative models (1) using shop fixed effects in lieu of random effects and (2) using zero-inflated negative binomial regression. Our findings remained consistent and, thus, we present only the first approach.

Second, we compared the mean and median number of HIVST kits, contraceptives, pregnancy tests, and SRH referrals provided over the study period per shop by study arm using t-tests and Kruskal-Wallis tests.[68] We also present several post-hoc secondary analyses conducted to examine the stability of our findings. Specifically, we reran all analyses of SRH product and referral provision excluding one outlier (an intervention shop that accounted for 51% of SRH products and referrals provided in the intervention arm) and reran analyses of HIVST kit provision using administrative stocking records, rather than customer logs. Finally, we calculated descriptive statistics for SRH products and referrals provided to AGYW during post-randomization (midline and endline) shop observations by study arm. While shop observations were not a primary source of data on product/referral provision (due to the low number of SRH-

related customer interactions expected to take place during observation windows), these data were used to assess whether trends observed in shopkeeper-reported customer logs are supported by direct observations made by research staff.

Analyses were conducted in R, version 4.1.0.[69]

Ethical approvals

This study was approved by the National Institute of Medical Research in Tanzania and the Human Research Protection Program at the University of California, San Francisco with the University of California, Berkeley Committee for Protection of Human Subjects in reliance.

1.4 Results

We randomly selected 41 drug shops, of which 34% were ineligible (all of which were either no longer open or not an ADDO) and 15% could not be contacted (Figure 1.1). Of the 21 shops that were eligible and could be contacted between July 22 and August 14, 2019, 20 (95%) consented to participate; 10 were randomized to each arm. All completed the study through the predetermined date of December 31, 2019 (four months after implementation) and were included in analyses.

Shops were 1.4 kilometers apart on average (range: 0.04 kilometers to 3.7 kilometers). Three-quarters of participating shopkeepers were female (Table 1.1). Many shopkeepers (60%) had medical training outside of their role at the shop, primarily in nursing or midwifery, and most participating drug shops (85%) were staffed by only one person. At the time of recruitment, most shops sold daily oral contraception (75%) and condoms (80%), but only 20% of shops sold emergency contraception.

In baseline shop observations conducted *before* randomization, drug shops averaged one AGYW customer per 3-hour observation with no differences in AGYW patronage by study arm (Figure 1.2, Table 1.2, Figure S1.4). At midline, intervention drug shops implementing *Malkia Klabu* had somewhat higher AGYW patronage relative to comparison shops (rate ratio [RR]: 1.5; 95% confidence interval [CI]: 0.7, 3.3). By endline, the rate of AGYW patronage at intervention shops was 4.4 times that of comparison shops (95% CI: 2.0, 9.8). In contrast, trends in patronage by non-AGYW customers over the study period did not differ by study arm. Thus, the proportion of AGYW customers in intervention shops increased over the study period (17% at baseline vs. 39% at endline), while the proportion of AGYW customers in comparison shops remained steady (12% at baseline vs. 11% at endline).

Based on shopkeeper-completed customer logs, the 10 intervention shops distributed more HIVST kits (1,456 vs. 596), contraceptives (6,649 vs. 199 products), and pregnancy tests (1,822 vs. 281) and made more referrals for SRH services (661 vs. 67) to AGYW during the study period than the 10 comparison arm shops (Figures 1.3, S1.5). The mean and median number of SRH products and referrals provided to AGYW

per shop over the 4-month study period were higher among intervention shops than comparison shops (Table 1.3).

Notably, emergency contraception comprised 69% of contraception that shopkeepers reported providing to AGYW by intervention shops, compared to 20% of contraception provided to AGYW by comparison shops. This was partially attributable to one outlying shop, which accounted for 65% of emergency contraception and 55% of all contraception distributed in the intervention arm (Figure S1.6). Counterintuitively, the increase in variance caused by this positive outlier reduced the significance of t-tests comparing mean contraceptive product distribution by study arm (Table 1.3). In post-hoc secondary analyses excluding this shop, HIVST kit and contraceptive distribution remained higher in the intervention arm, with all mean comparisons reaching statistical significance due to reduced variance (Table S1.1). However, this shop accounted for 77% of SRH referrals in the intervention arm, and when excluded, differences in SRH referral by study arm were attenuated.

In secondary analyses, differences in HIVST kit distribution were similar when using data from administrative stocking records, rather than shopkeepers' logs (Table S1.2), and during post-randomization shop observations, more contraceptives were provided to AGYW in intervention shops than comparison shops (26 vs. 2), although referrals were similar (4 vs. 3) (Table S1.3).

No adverse events were reported over the study period.

1.5 Discussion

The *Malkia Klabu* intervention was associated with increased distribution of HIVST kits, contraceptives, and health facility referrals to young women in drug shops. In the absence of the intervention*,* comparison shops distributed nearly 600 HIVST kits to young women over the study period, suggesting that free provision of HIVST kits in drug shops may lead to uptake even when young women are not otherwise incentivized to access SRH services. However, drug shops that offered *Malkia Klabu* distributed more than twice as many HIVST kits and 33 times as many contraceptive products as comparison shops during the study, demonstrating the potential value of comprehensive interventions to create girl-friendly drug shop environments.

Malkia Klabu drew upon myriad complementary approaches to promote, optimize, and expand the range of SRH products and services available to AGYW. The intervention was designed to act upon both demand-side *and* supply-side barriers to services (e.g., by normalizing SRH product provision to AGYW among participating shopkeepers). Several intervention components were specific to contraception, such as additional training for shopkeepers on AGYW-friendly contraceptive service provision, free contraceptive products for AGYW club members, non-verbal pathways through which AGYW could discreetly request contraceptive products, and hands-on contraceptive displays with informational videos. However, unlike HIVST kits (which were free in both

study arms), it is not possible to disentangle the effect of contraceptive subsidies from the other intervention components. Regardless, the dramatic increase in contraceptive distribution at intervention shops suggests that implementing programs that are tailored to young women in drug shops may be an effective strategy through which to reach them with contraceptive products.

Notably, emergency contraception accounted for most of the contraceptive products distributed to young women at intervention shops. This finding aligns with existing research suggesting that emergency contraception is especially desirable to young women, who may prefer methods that can be used post-coitally or on an as-needed basis.[70,71] The high demand for emergency contraception observed among young women in drug shops may offer the opportunity to build upon these shop interactions by integrating timely HIV-related interventions (e.g., bundling emergency contraception with condoms, post-exposure prophylaxis [PEP], and/or an HIVST kit). Fostering trusted relationships between young women and shopkeepers may also pave the way for shopkeepers to link AGYW to more proactive methods for HIV prevention, such as pre-exposure prophylaxis (PrEP), and health facilities that offer an expanded selection of contraceptive options, including long-acting reversible contraception.

When designing *Malkia Klabu*, we sought to move beyond surface-level service availability to understand and address the complex structural and sociocultural factors that interact to determine young women's engagement with health services. There has been increasing interest by the global health community in applying human-centered design to solve public health challenges, including SRH challenges faced by young women in sub-Saharan Africa. Despite HCD's growing use as a tool for global health,[38] few HCD-derived programs have been formally evaluated, a gap we aimed to address through the present study. This study's rigor is bolstered by random selection of drug shops from government registries, high participation rates among contacted shops, randomization of shops into study arms, and no loss to follow-up among participating shops. Although only shops that were willing to offer AGYW-friendly services were eligible to participate, all but one shop that met the other eligibility criteria and could be contacted enrolled in the study, limiting potential bias due to self-selection. In combination, these strengths increase the likelihood that the drug shops included in each study arm are representative of drug shops within the targeted communities. Additionally, HIVST kits were free to AGYW in *both* study arms, allowing for direct comparison of HIVST kit distribution between study arms. Finally, data on AGYW patronage were collected via repeated, systematic observations by research staff at randomly determined times, reducing information bias.

One potential limitation of the study is our reliance on visual assessment of customer age by both research staff conducting shop observations and shopkeepers completing customer logs. As the study was designed to reduce hassle and stigma experienced by AGYW at drug shops, this approach was chosen to avoid potentially intrusive questioning of AGYW customers. However, this increases the potential for misclassification of AGYW customers. The use of shopkeeper-completed customer logs to assess the distribution of HIVST kits, other SRH products, and health facility referrals raises other limitations. Shopkeepers' record-keeping is of uncertain and likely variable

quality, and because shopkeepers were not blinded, measurement error may be differential by study arm. For example, shopkeepers in the intervention arm, who received more products and reimbursements via the study, may have been more motivated to record product distribution and referrals to AGYW, biasing the results in favor of the intervention. However, because research staff provided all participating shops with HIVST kits, we were able to triangulate research staff's own administrative records on HIVST kits stocked at shops during weekly stocking visits with shopkeepers' customer logs to evaluate the degree to which their record-keeping aligned with our own; we found high concordance. Nevertheless, our reliance on shopkeeper customer logs to measure other SRH product distribution and referrals remains a limitation. We did not collect data on customers' use of HIVST or contraception after leaving the shop or their uptake of shopkeeper referrals for confirmatory HIV testing or other facility-based services. Thus, we cannot ascertain the effect of the intervention on HIV diagnoses or other downstream SRH outcomes among AGYW.

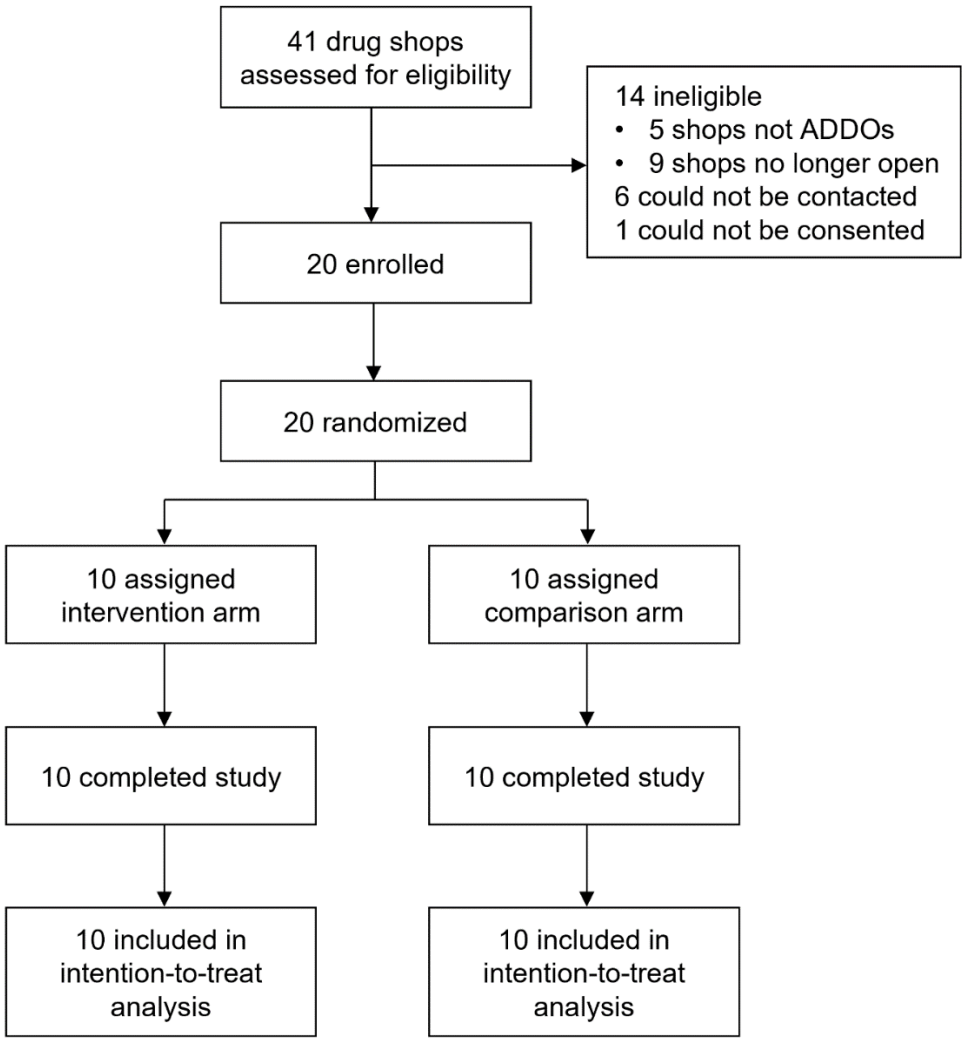
To contextualize the findings of this trial, we conducted a mixed-methods evaluation to better understand various stakeholders' experiences with the intervention. Through in-depth interviews with AGYW customers, shopkeepers, and HIV referral counselors, we found high acceptability of HIVST provision at drug shops and evidence that multiple intervention features drawn from behavioral economics worked in concert to motivate AGYW and shopkeepers' engagement with *Malkia Klabu*.[72,73] Future studies are needed to evaluate the performance of this intervention in other settings and to develop strategies to efficiently tailor the intervention to local contexts during broader implementation. This pilot trial included only 10 intervention shops, all located within the specific context in which the intervention was designed. We noted significant heterogeneity in intervention shops' performance in the present study, with several shops standing out as high and low responders. While we can qualitatively describe preliminary characteristics associated with performance level in this limited sample (e.g., a high-performing shop was located near a secondary school and had an enthusiastic shopkeeper), larger-scale implementation is necessary to quantitatively evaluate which factors are most predictive of performance. Such data could inform targeted implementation of the intervention in drug shops and settings in which it is most likely to be impactful. The small size of this study made it possible to provide shops with extensive support while they implemented the multifaceted intervention components. However, scaling *Malkia Klabu* will likely require streamlining the intervention to the core components determined to be most critical to its success and identifying the minimum levels of support and product subsidies necessary for shops to effectively implement and sustain it.

Although this pilot provides strong preliminary evidence of the *Malkia Klabu* intervention's feasibility and acceptability, additional research is necessary to understand its adaptability, scalability, and down-stream impacts. Accordingly, our next step is to conduct a 5-year cluster randomized trial and mixed-method implementation science study among drug shops in two regions of Tanzania (*NCT05357144*). Through this larger scale implementation, we will evaluate *Malkia Klabu*'s effects on the number of HIV diagnoses and antenatal care registrations (i.e., as a proxy for pregnancies) among AGYW at the population level, link these outcomes to demand-side pathways

leading to impact (e.g., recent HIV testing, met need for contraception), and identify supply-side factors influencing effectiveness (e.g., shop implementation models).

1.6 Tables and Figures

Figure 1.1 Trial profile for the randomized trial evaluating the Malkia Klabu intervention.



ADDOs: Accredited Drug Dispensing Outlets.

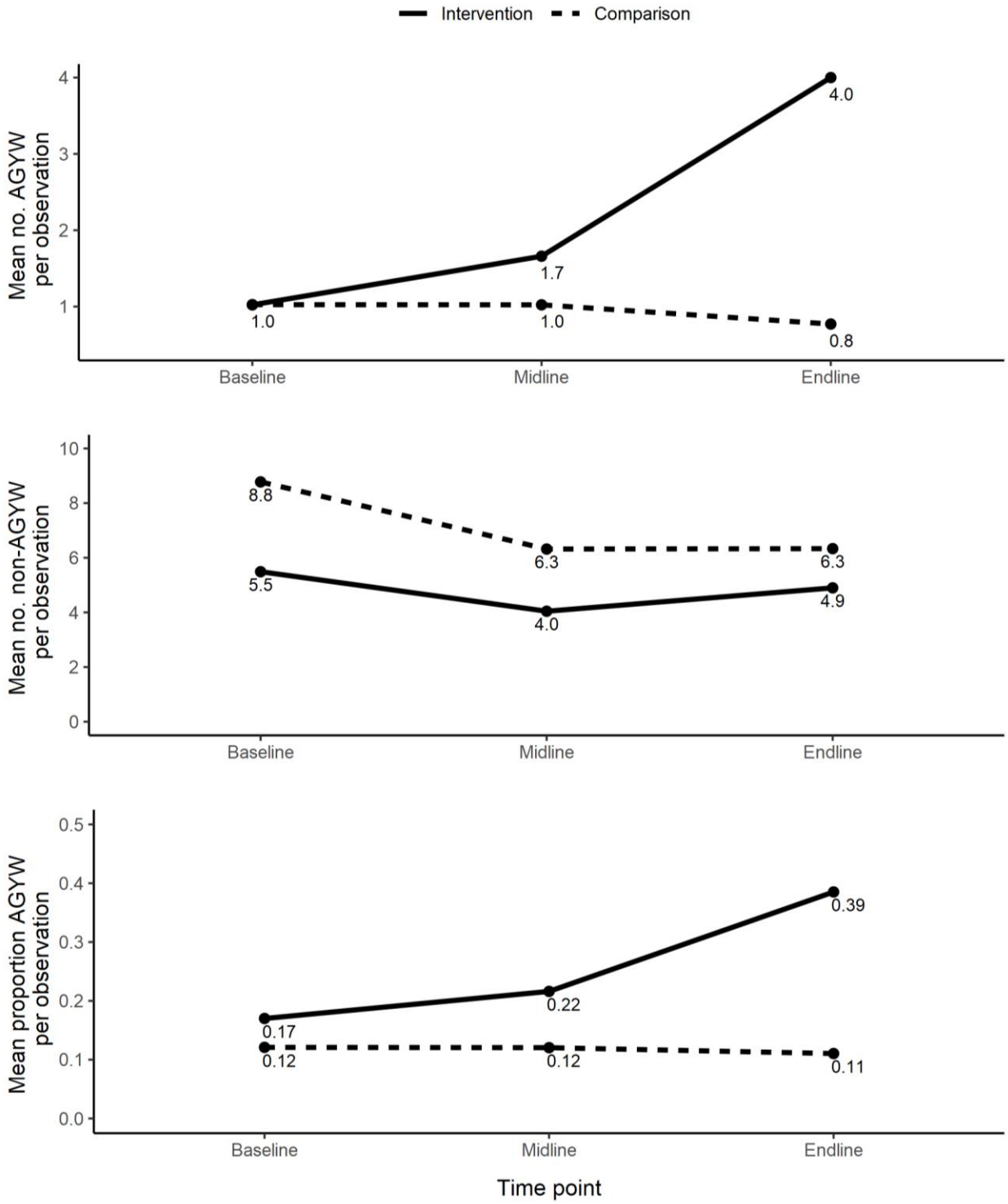
Table 1.1 Baseline characteristics of 20 shopkeepers and drug shops participating in the randomized trial evaluating the Malkia Klabu intervention.

	Comparison arm (n=10)	Intervention arm (n=10)	Combined arms (n=20)
Sex, n (%)			
Female	8 (80)	7 (70)	15 (75)
Male	2 (20)	3 (30)	5 (25)
Age (years), mean (SD)	38.7 (15.7)	48.5 (15.3)	43.6 (15.9)
Education, n (%)			
Primary school	2 (20)	1 (10)	3 (15)
Any secondary school	4 (40)	3 (30)	7 (35)
Diploma course	1 (10)	4 (40)	5 (25)
Other certificate	3 (30)	2 (20)	5 (25)
Years worked in a drug shop, mean (SD)	9.0 (6.2)	14.7 (13.6)	11.8 (10.7)
Medical training beyond shop, n (%)			
Doctor	0 (0)	1 (10)	1 (5)
Nurse or professional midwife	4 (40)	4 (40)	8 (40)
Other	2 (20)	1 (10)	3 (15)
None	4 (40)	4 (40)	8 (40)
Owns participating shop, n (%)	4 (40)	8 (80)	12 (60)
Response to: “Unmarried women should be ashamed to ask their provider for contraceptives,” n (%)			
Strongly agree or agree	3 (30)	2 (20)	5 (25)
Undecided	1 (10)	0 (0)	1 (5)
Disagree or strongly disagree	6 (60)	8 (80)	14 (70)
Response to: “Unmarried women should not be given contraceptives because they should not be having sex,” n (%)			
Strongly agree or agree	2 (20)	2 (20)	4 (20)
Undecided	1 (10)	1 (10)	2 (10)
Disagree or strongly disagree	7 (70)	7 (70)	14 (70)
Location of shop,† n (%)			
Ward 1	3 (30)	3 (30)	6 (30)
Ward 2	3 (30)	3 (30)	6 (30)
Ward 3	2 (20)	2 (20)	4 (20)
Ward 4	2 (20)	2 (20)	4 (20)
No. people who work in shop, n (%)			
1 person	10 (100)	7 (70)	17 (85)
2 people	0 (0)	2 (20)	2 (10)
3 people	0 (0)	1 (10)	1 (5)
Years shop in business*, mean (SD)	8.2 (8.1)	9.0 (7.7)	8.6 (7.7)
Shop sells condoms, n (%)	10 (100)	6 (60)	16 (80)
Shop sells oral contraception, n (%)	9 (90)	6 (60)	15 (75)

Shop sells emergency contraception, n (%)	1 (10)	3 (30)	40 (20)
No. customers last work shift**, mean (SD)	27.7 (15.2)	20.0 (11.5)	24.1 (13.8)
No. AGYW customers last work shift, mean (SD)	7.7 (4.8)	7.5 (7.5)	7.6 (6.1)

SD: standard deviation, No.: number, AGYW: adolescent girls and young women (ages 15-24).
†Randomization stratified by administrative ward.
*Missing: 2 drug shops in comparison arm.
**Missing: 1 drug shop in intervention arm.

Figure 1.2 Patronage of adolescent girls and young women compared to other customers at 20 drug shops during multiple 3-hour shop observations per shop, by time point and study arm.



No.: number, AGYW: adolescent girls and young women (ages 15-24).

Table 1.2 Patronage of adolescent girls and young women compared to other customers at 20 drug shops during 3-hour shop observations by time point and study arm.

	Baseline	Midline	Endline	Midline/endline combined
Total no. observations (range per shop)				
Comparison arm	40 (2-5)	44 (3-5)	48 (4-5)	92 (8-10)
Intervention arm	45 (3-5)	47 (4-5)	49 (4-5)	96 (9-10)
Mean no. AGYW per observation (SD)				
Comparison arm	1.03 (1.14)	1.02 (1.27)	0.77 (1.22)	0.89 (1.24)
Intervention arm	1.02 (1.22)	1.66 (2.87)	4.00 (5.24)	2.85 (4.39)
Mean no. non-AGYW per observation (SD)				
Comparison arm	8.78 (8.00)	6.32 (4.71)	6.33 (5.77)	6.33 (5.26)
Intervention arm	5.49 (3.50)	4.04 (3.50)	4.90 (3.86)	4.48 (3.69)
Mean proportion AGYW per observation† (SD)				
Comparison arm	0.12 (0.13)	0.12 (0.12)	0.11 (0.21)	0.12 (0.17)
Intervention arm	0.17 (0.19)	0.22 (0.28)	0.39 (0.31)	0.31 (0.31)
RR (95% CI)*: No. AGYW				
Comparison arm	Reference	Reference	Reference	Reference
Intervention arm	1.03 (0.50, 2.13)	1.47 (0.65, 3.32)	4.38 (1.96, 9.77)	2.81 (1.34, 5.91)
RR (95% CI)*: No. non-AGYW				
Comparison arm	Reference	Reference	Reference	Reference
Intervention arm	0.74 (0.47, 1.15)	0.99 (0.70, 1.41)	1.09 (0.77, 1.53)	1.04 (0.77, 1.41)

No.: number, SD: standard deviation, AGYW: adolescent girls and young women (ages 15-24), RR: rate ratio, CI: confidence interval.
†Number of AGYW customers ÷ total number of customers, excluding 12 observations with 0 customers.
*Estimated via difference-in-differences approach using negative binomial regression models adjusted for ward with random effects for shops and log-duration of observation as an offset term.

Figure 1.3 Total number of sexual and reproductive health products and health facility referrals provided to adolescent girls and young women by 20 drug shops during the 4-month study period by study arm.

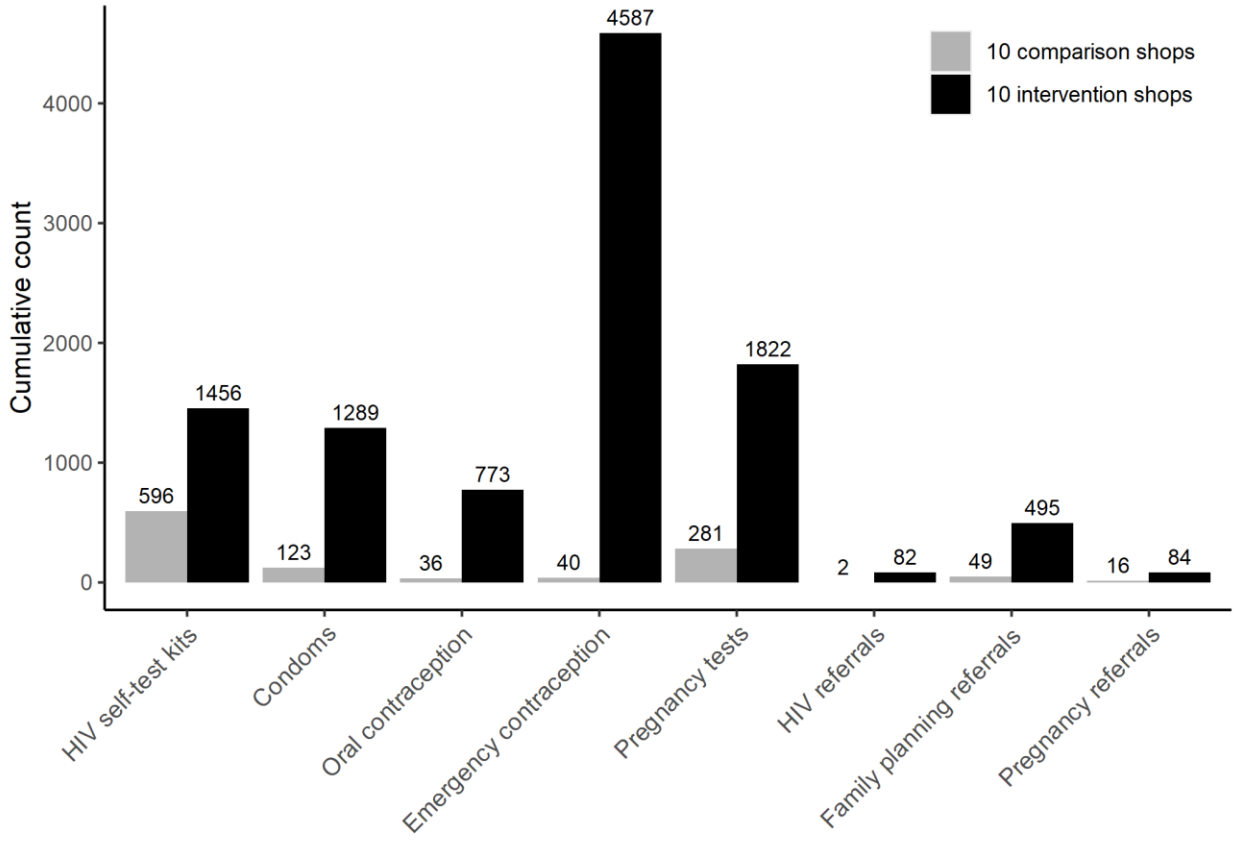


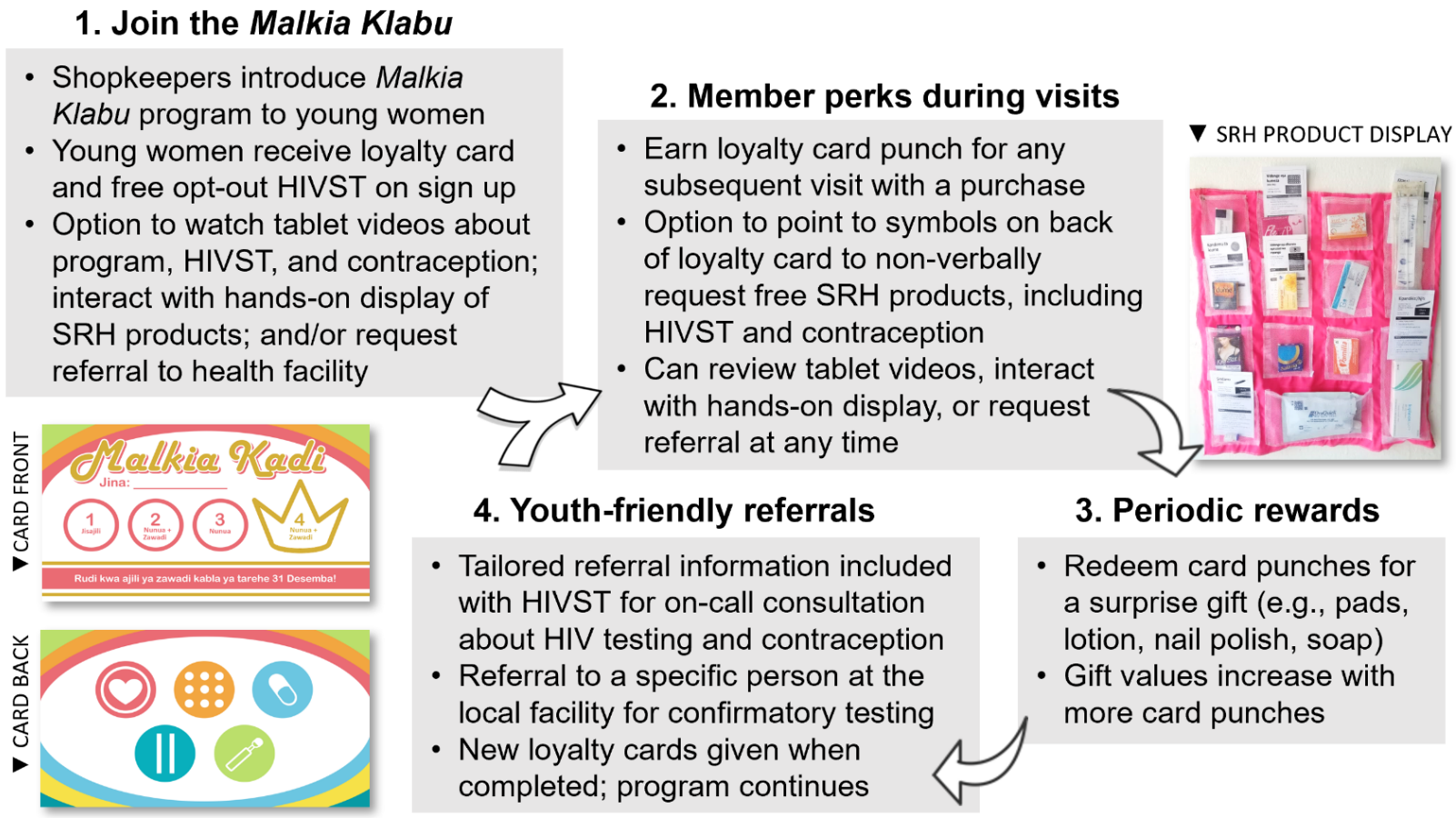
Table 1.3 Number of sexual and reproductive health products and health facility referrals provided to adolescent girls and young women by study arm.

	Comparison arm shops (n=10)	Intervention arm shops (n=10)	P-value*
HIV self-test kits			
Total	596	1,456	-
Mean per shop (SD)	59.6 (30.4)	145.6 (107.6)	.03
Median per shop (Q1, Q3)	58.5 (43.8, 70.0)	130.5 (97.0, 166.2)	.02
Condoms			
Total	123	1,289	-
Mean per shop (SD)	12.3 (25.8)	128.9 (142.7)	.03
Median per shop (Q1, Q3)	1.0 (0.0, 7.8)	92.5 (58.2, 111.8)	<.01
Daily oral contraception			
Total	36	773	-
Mean per shop (SD)	3.6 (5.3)	77.3 (60.5)	<.01
Median per shop (Q1, Q3)	1.0 (0.2, 5.5)	74.0 (31.0, 128.8)	<.01
Emergency contraception			
Total	40	4,587	-
Mean per shop (SD)	4.0 (4.9)	458.7 (904.4)	.14
Median per shop (Q1, Q3)	1.0 (0.0, 6.5)	148.5 (72.0, 332.2)	<.01
Contraception (all)			
Total	199	6,649	-
Mean per shop (SD)	19.9 (27.4)	664.9 (1,073.5)	.09
Median per shop (Q1, Q3)	7.0 (1.0, 33.0)	325.5 (210.5, 539.0)	<.01
Pregnancy tests			
Total	281	1,822	-
Mean per shop (SD)	28.1 (29.0)	182.2 (236.0)	.07
Median per shop (Q1, Q3)	16.5 (5.8, 43.0)	136.0 (87.7, 164.3)	<.01
HIV referrals			
Total	2	82	-
Mean per shop (SD)	0.2 (0.4)	8.2 (20.0)	.23
Median per shop (Q1, Q3)	0 (0.0, 0.0)	0 (0.0, 3.5)	.19
Family planning referrals			
Total	49	495	-
Mean per shop (SD)	4.9 (15.1)	49.5 (120.0)	.27
Median per shop (Q1, Q3)	0.0 (0.0, 0.0)	2.0 (0.2, 19.2)	.03
Pregnancy referrals			
Total	16	84	-
Mean per shop (SD)	1.6 (4.0)	8.4 (17.8)	.27
Median per shop (Q1, Q3)	0.0 (0.0, 1.0)	1.0 (0.2, 3.2)	.14
Referrals (all)			
Total	67	661	-
Mean per shop (SD)	6.7 (19.1)	66.1 (157.5)	.27
Median per shop (Q1, Q3)	0.5 (0.0, 1.8)	3.5 (1.0, 23.8)	.02

SD: standard deviation, Q1: first quartile, Q3: third quartile.
*P-value for comparison of means by Welch's two-sample t-test, for comparison of medians Kruskal-Wallis rank sum test.

1.7 Supplementary Materials

Figure S1.1 Components of the integrated Malkia Klabu intervention developed through a human-centered design process.



HIVST: HIV self-test kit, SRH: sexual and reproductive health.

Figure S1.2 Malkia Klabu ("Queen Club") membership card.

FRONT: LOYALTY CARD

Loyalty program steps in English: (1) Sign up, (2) Purchase + gift, (3) Purchase, (4) Purchase + gift.

BACK: SYMBOL CARD

Symbol meanings clockwise from top left: condoms (red), oral contraception (orange), emergency contraception (blue), HIV self-test kit (green), pregnancy test (turquoise).

Figure S1.3 Date, time of day, and day of the week of drug shop observations across three time points by study arm.

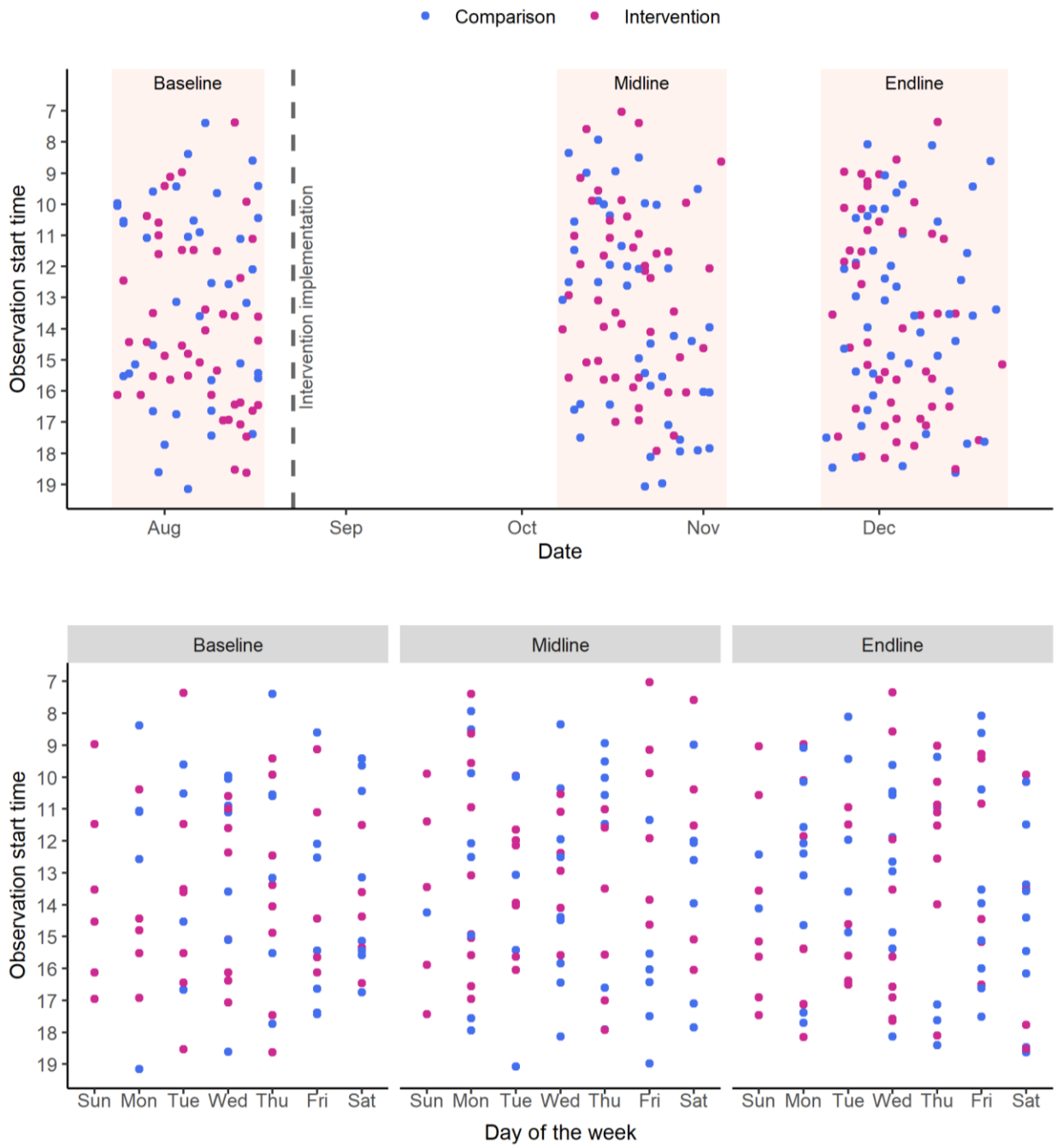
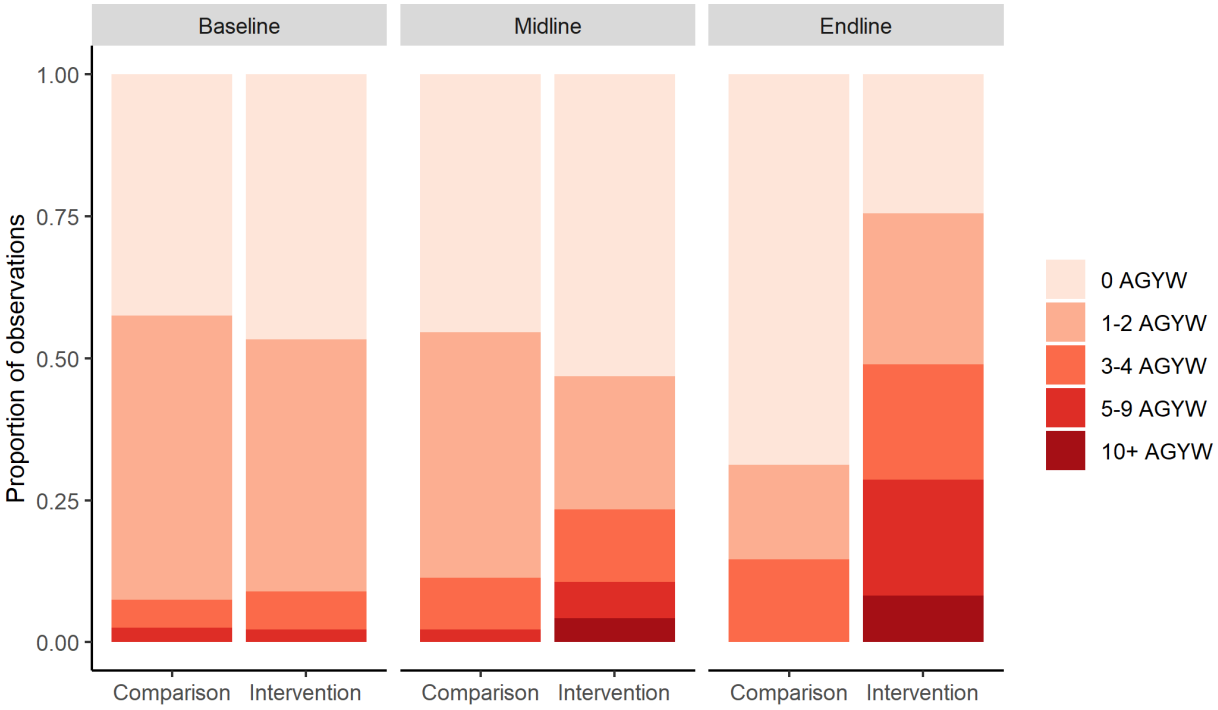
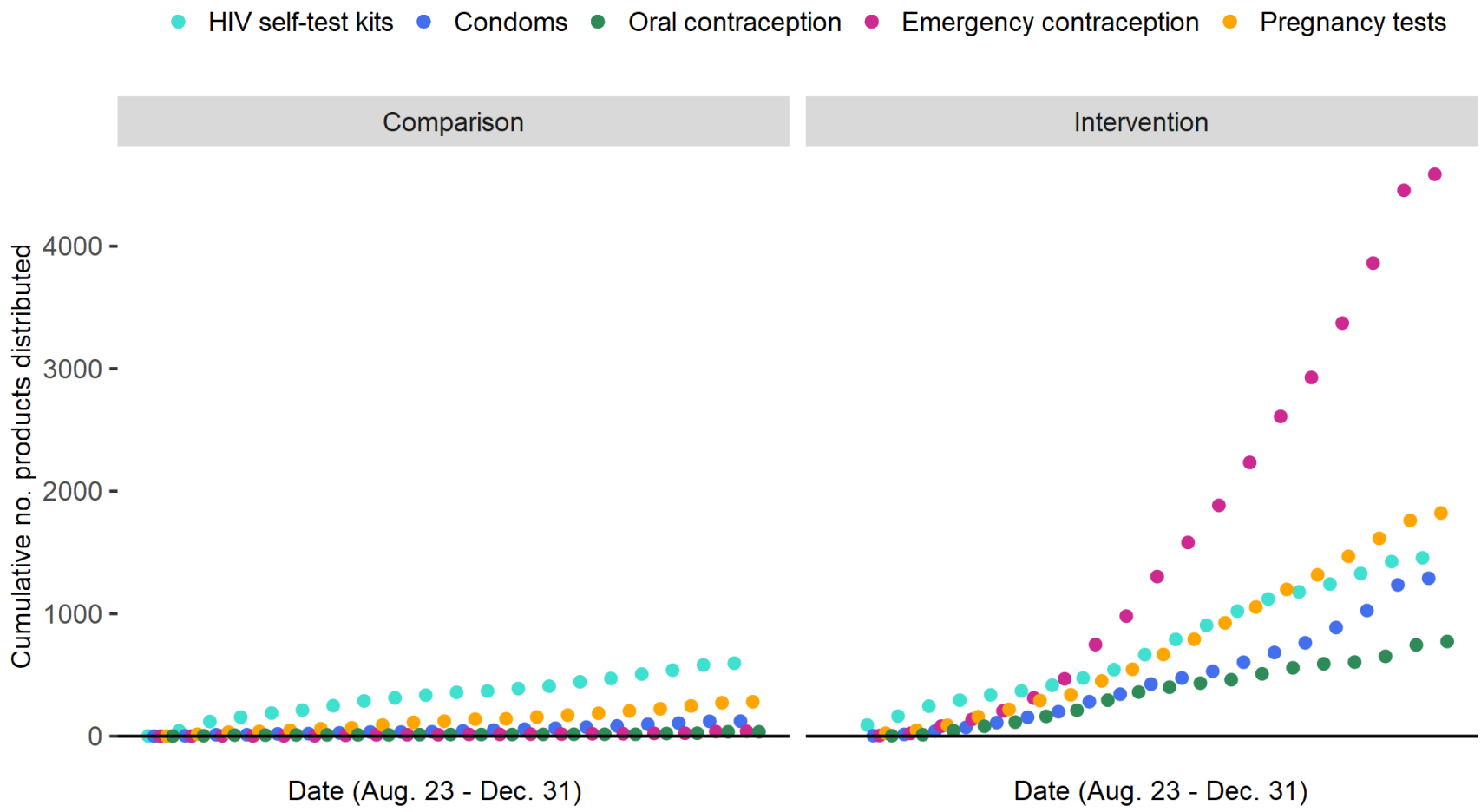


Figure S1.4 Number of adolescent girls and young women observed per 3-hour drug shop observation by time point and study arm.



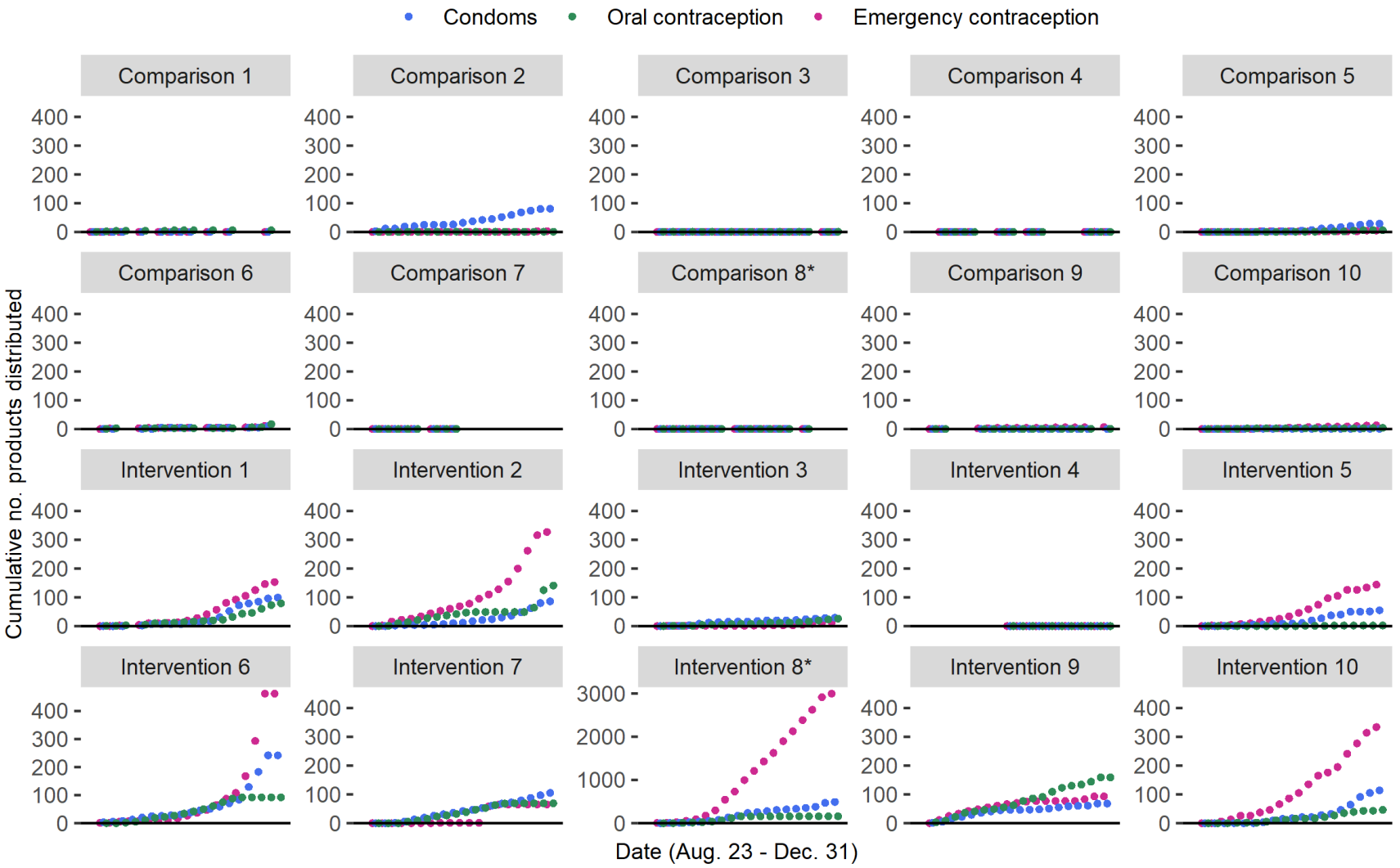
AGYW: adolescent girls and young women (ages 15-24).

Figure S1.5 Sexual and reproductive health products provided to adolescent girls and young women during the 4-month study period by study arm.



No.: number.

Figure S1.6 Contraceptive products provided to adolescent girls and young women by each participating drug shop during the 4-month study period.



No.: number.
*Intervention 8 plot has rescaled Y-axis.

Table S1.1 Number of sexual and reproductive health products and health facility referrals provided to adolescent girls and young women excluding Intervention Shop 8.

	Comparison arm shops (n=10)	Intervention arm shops* (n=9)	P-value**
HIV self-test kits			
Total	596	1,052	-
Mean per shop (SD)	59.6 (30.4)	116.9 (125.0)	.03
Median per shop (Q1, Q3)	58.5 (43.8, 70.0)	125.0 (93.0, 137.0)	.04
Condoms			
Total	123	798	-
Mean per shop (SD)	12.3 (25.8)	88.67 (68.5)	.01
Median per shop (Q1, Q3)	1.0 (0.0, 7.8)	86.0 (55.0, 105.0)	.01
Oral contraception			
Total	36	614	-
Mean per shop (SD)	3.6 (5.3)	68.2 (56.5)	.01
Median per shop (Q1, Q3)	1.0 (0.2, 5.5)	69.0 (26.0, 92.0)	.01
Emergency contraception			
Total	40	1,591	-
Mean per shop (SD)	4.0 (4.9)	176.8 (161.2)	.01
Median per shop (Q1, Q3)	1.0 (0.0, 6.5)	144.0 (65.0, 327.0)	<.01
Contraception (all)			
Total	199	3,003	-
Mean per shop (SD)	19.9 (27.4)	333.7 (249.2)	<.01
Median per shop (Q1, Q3)	7.0 (1.0, 33.0)	320.0 (201.0, 494.0)	<.01
Pregnancy tests			
Total	281	990	-
Mean per shop (SD)	28.1 (29.0)	110.0 (63.5)	<.01
Median per shop (Q1, Q3)	16.5 (5.8, 43.0)	136.0 (79.0, 153.0)	.01
HIV referrals			
Total	2	18	-
Mean per shop (SD)	0.2 (0.4)	2.0 (4.0)	.22
Median per shop (Q1, Q3)	0.0 (0.0, 0.0)	0.0 (0.0, 2.0)	.34
Family planning referrals			
Total	49	109	-
Mean per shop (SD)	4.9 (15.1)	12.1 (22.0)	.42
Median per shop (Q1, Q3)	0.0 (0.0, 0.0)	1.0 (0.0, 17.0)	.06
Pregnancy referrals			
Total	16	28	-
Mean per shop (SD)	1.6 (4.0)	3.1 (6.5)	.56
Median per shop (Q1, Q3)	0.0 (0.0, 1.0)	1.0 (0.0, 1.0)	.25
Referrals (all)			
Total	67	155	-
Mean per shop (SD)	6.7 (19.1)	17.2 (32.0)	.41
Median per shop (Q1, Q3)	0.5 (0.0, 1.8)	2.0 (1.0, 20.0)	.04

SD: standard deviation, Q1: first quartile, Q3: third quartile.
*Excluding Intervention Shop 8. **P-value for comparison of means by Welch's two-sample t-test, for comparison of medians Kruskal-Wallis rank sum test.

Table S1.2 Number of HIV self-test kits provided to adolescent girls and young women during the 4-month study period based on shopkeeper-completed customer logs vs. administrative stocking records.

	Comparison arm shops (n=10)	Intervention arm shops (n=10)	P-value*
Shopkeeper customer logs			
Total	596	1,456	-
Mean per shop (SD)	59.6 (30.4)	145.6 (107.6)	.03
Median per shop (Q1, Q3)	58.5 (43.8, 70.0)	130.5 (97.0, 166.2)	.02
Administrative stocking records			
Total	552	1,402	-
Mean per shop (SD)	55.2 (31.1)	140.2 (96.8)	.02
Median per shop (Q1, Q3)	53.5 (40.0, 65.0)	132.5 (98.5, 153.0)	.02

SD: standard deviation, Q1: first quartile, Q3: third quartile.
*P-value for comparison of means by Welch's two-sample t-test, for comparison of medians Kruskal-Wallis rank sum test.

Table S1.3 Number of sexual and reproductive health products and health facility referrals provided to adolescent girls and young women during 3-hour shop observations by time point and study arm.

	Baseline (Pre-randomization)		Midline/endline combined	
	Comparison arm shops	Intervention arm shops	Comparison arm shops	Intervention arm shops
Observations				
Total no. observations	40	45	92	96
Mean no. per shop	4.0	4.5	9.2	9.6
HIV self-test kits*				
Total no. provided	-	-	12	40
Mean per observation (SD)	-	-	0.13 (0.40)	0.42 (1.0)
Condoms				
Total no. provided	0	0	0	4
Mean per observation (SD)	0 (0)	0 (0)	0 (0)	0.04 (0.32)
Daily oral contraception				
Total no. provided	1	0	1	1
Mean per observation (SD)	0.03 (0.16)	0 (0)	0.01 (0.10)	0.01 (0.10)
Emergency contraception				
Total no. provided	1	0	1	21
Mean per observation (SD)	0.03 (0.16)	0 (0)	0.01 (0.10)	0.22 (0.62)
Contraception (all)				
Total no. provided	2	0	2	26
Mean per observation (SD)	0.05 (0.22)	0 (0)	0.02 (0.15)	0.27 (0.70)
Pregnancy tests				
Total no. provided	3	3	5	9
Mean per observation (SD)	0.08 (0.27)	0.07 (0.25)	0.05 (0.23)	0.09 (0.36)
HIV referrals				
Total no. provided	1	0	3	1
Mean per observation (SD)	0.03 (0.16)	0 (0)	0.03 (0.23)	0.01 (0.10)
Family planning referrals				
Total no. provided	0	0	0	1
Mean per observation (SD)	0 (0)	0 (0)	0 (0)	0.01 (0.10)
Pregnancy referrals				
Total no. provided	1	0	0	2
Mean per observation (SD)	0.03 (0.16)	0 (0)	0 (0)	0.02 (0.14)
Referrals (all)				
Total no. provided	2	0	3	4
Mean per observation (SD)	0.05 (0.22)	0 (0)	0.03 (0.23)	0.04 (0.20)

No.: number, SD: standard deviation.
*HIV self-test kits were not sold at participating shops before randomization.

Chapter 2. Monitoring SARS-CoV-2 incidence and seroconversion in a university cohort in California, June to August 2020

2.1 Abstract

Objective: To inform effective SARS-CoV-2 mitigation strategies in university settings, we piloted an integrated symptom and exposure monitoring and testing system among a cohort of university students and employees.

Methods: We aimed to identify incident SARS-CoV-2 infections in a longitudinal cohort of 2,180 students and 738 employees of a public university in California from June to August 2020. At baseline and endline, we tested participants for active SARS-CoV-2 infection via quantitative polymerase chain reaction (qPCR) test and collected blood samples for antibody testing. Participants received notifications to complete additional qPCR tests throughout the study if they reported symptoms or exposures in daily surveys or were selected for surveillance testing. Viral whole genome sequencing was performed on positive qPCR samples, and phylogenetic trees were constructed with these genomes and external genomes retrieved using GISAID and UShER.

Results: Over the study period, 57 students (2.6%) and 3 employees (0.4%) were diagnosed with SARS-CoV-2 infection via qPCR test. Phylogenetic analyses revealed that a superspreader event among undergraduates in congregate housing accounted for at least 48% of cases but did not spread beyond campus. Test positivity was higher among participants who self-reported symptoms (incidence rate ratio [IRR]: 12.4; 95% confidence interval [CI]: 7.3, 21.3) or had household exposures (IRR: 12.3; 95% CI: 5.6, 26.9) that triggered notifications to test. Most (91%) participants with newly identified antibodies at endline had been diagnosed with incident infection via qPCR test during the study.

Conclusions: Our findings suggest that integrated monitoring systems can successfully identify and link at-risk students to SARS-CoV-2 testing. Building upon such systems may prove key in the next stage of the pandemic, as universities grapple with highly transmissible variants, incomplete vaccine coverage and breakthrough infections, and reduced reliance on prevention strategies such as masking and remote learning.

2.2 Introduction

Universities have been identified as hotspots for SARS-CoV-2 transmission in the United States,[74] where SARS-CoV-2 incidence is highest among young adults.[75] Young adults may be less likely to adhere to social distancing guidelines and more likely to experience workplace exposure (for example, at food service or retail jobs).[75] Their risk may be heightened in university settings where many live in congregate housing, interact with wide social networks, or attend large gatherings.[76] Although young adults are at low risk of serious acute illness or death from COVID-19 (the disease caused by SARS-CoV-2),[77] the higher likelihood of asymptomatic or mildly symptomatic infection in this age group makes young adults a key population through which SARS-CoV-2 may spread to other, more vulnerable groups.[75,78] Indeed, there is evidence that transmission among university students may lead to increased COVID-19-related mortality in the surrounding counties.[79–81] Although widespread vaccination has enabled most campuses to return to in-person activities, the elimination of SARS-CoV-2 transmission in campus populations may be stymied by vaccine hesitancy among students and employees and breakthrough infection and subsequent transmission by vaccinated persons, particularly in the context of waning immunity, low booster uptake, and viral variants that reduce vaccine efficacy.[82,83] Therefore, rapid and resource-efficient identification of incident cases in university populations is a critical first step of outbreak investigation and control, followed by isolation, case investigation, and contact tracing, to minimize transmission within campus and to the broader community.

Universities have adopted a wide range of approaches for testing and outbreak mitigation.[84–86] While a number of well-resourced universities have scaled up testing capacity to frequently test all students and employees accessing campus or living in university-affiliated housing,[86] many other universities do not have well-defined testing strategies or restrict testing to those with symptoms or known exposure.[85] In addition to testing programs, some universities have sought to reduce on-campus transmission by mandating the completion of self-administered symptom screening tools by students and employees. However, such tools have primarily been used to regulate daily access to campus (i.e., deny entry to those who report COVID-19-like symptoms), rather than to detect emergent outbreaks among university populations. As universities resume normal operations and discontinue mitigation strategies such as masking, non-punitive, resource-efficient strategies that can both identify those who are at highest risk of infection *and* expediently link them to low-barrier testing services may play a key role in transitioning from a “one-size-fits-all” approach of uniform testing to a sustainable monitoring paradigm.

In 2020, we piloted an integrated symptom and exposure monitoring and testing system designed to identify incident SARS-CoV-2 infections among a cohort of university students and employees.[87] Here we describe the incidence and seroprevalence of SARS-CoV-2 infection within this cohort to evaluate the extent to which incident infections were successfully detected and contained over the study period, identify sociodemographic factors associated with incident infection, and ascertain which self-reported symptoms and exposures tracked by the monitoring system were predictive of

test positivity, with the ultimate objective of informing monitoring and testing strategies in university settings.

2.3 Methods

Study design and setting

The study comprised three prospective cohorts of University of California, Berkeley affiliates followed from June to August 2020: students, essential workers (i.e., employees working on campus in health, facilities, or student services), and other employees (hereafter, "faculty/staff"). We report the findings according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for cohort studies.[88]

Throughout the study period, UC Berkeley did not offer in-person classes, and on-campus work was restricted to essential workers and a small subset of faculty, staff, and student researchers. Although few students were living in on-campus residence halls, many students continued to live in congregate living settings off campus, such as fraternities, sororities, and co-operative housing.

Participant recruitment and eligibility

The study was promoted through targeted messages from university officials to campus email listservs and social media platforms from early June to mid-July 2020. To increase reach to students expected to be at higher risk of COVID-19, we also placed flyers in congregate living settings and conducted in-person recruitment for student athletes who had resumed training on campus. Participants were eligible to enroll in the study if they were at least 18 years of age, were a current student or employee at UC Berkeley, and planned to live in or near Berkeley during the summer of 2020. Specific eligibility criteria and enrollment windows varied by cohort (Table S2.1, Figure S2.1).

Upon enrollment, participants were linked to an online baseline survey that collected sociodemographic data and information about their COVID-19-related health history. Participants were then referred to a baseline testing appointment at University Health Services (UHS) that included a SARS-CoV-2 quantitative polymerase chain reaction (qPCR) test and blood sample collection for antibody testing (procedures described below). To facilitate daily temperature monitoring, study staff also provided participants with free oral thermometers upon request at testing appointments. Participants who completed this appointment or a non-study qPCR test at UHS by July 20 were eligible to remain in the study (Figure S2.1). We pre-specified a maximum sample size of 4,000 participants across cohorts but did not reach this limit before the final day of baseline data collection.

Symptom and exposure surveys

Participants received daily text messages or emails, depending on their preference specified in the baseline survey, which linked to short symptom surveys through which they reported their body temperature and any symptoms of illness. Once per week, the daily survey included a longer exposure module, which asked about recent symptoms of illness among their household member(s), potential exposure(s) to COVID-19, and activities related to potential COVID-19 risk. All surveys were administered via REDCap.[89,90]

Endline survey and testing

In early August, participants were sent an endline survey that collected updated information on their COVID-19 history to identify any diagnoses outside of the study. Participants in the student and essential worker cohorts were also invited to complete endline testing appointments by August 18, including a final qPCR test and blood collection.

qPCR testing

Mid-turbinate nasal and oral swabs were collected by UHS clinical staff and tested for SARS-CoV-2 by qPCR at the Innovative Genomics Institute (IGI).[91] qPCR tests were performed at baseline for all three cohorts and at endline for the student and essential worker cohorts. Between baseline and endline testing, additional qPCR tests were performed for the following reasons:

- Symptom- or exposure-based tests triggered based on participants' responses in daily surveys: Participants who reported COVID-19-like signs or symptoms[1] in themselves (daily) or in household member(s) (weekly) or who reported a suspected or confirmed COVID-19 case in their household (weekly) were automatically notified to sign up for a qPCR test.

- Random surveillance testing: A subset of participants in the student and faculty/staff cohorts who had not had a qPCR test within a week were randomly selected and emailed notifications to come in for surveillance testing in July.

- Address-based surveillance testing: Participants who lived at the same address as another participant who tested positive for SARS-CoV-2 were immediately emailed surveillance testing notifications. Following an outbreak among group-housed students in early July, surveillance testing notifications were also emailed to all participants who had not been tested within the week and who reported living in fraternities, sororities, or co-operative housing.

[1] Signs or symptoms that triggered a testing notification when reported were: temperature of ≥100.4°F, dry cough (without mucus), coughing up mucus, feeling feverish, unusual pain or pressure in the chest, difficulty breathing, shortness of breath, unexplained trouble thinking or concentrating, loss of sense of taste, and loss of sense of smell.

- Participant-initiated testing: Participants could self-schedule study testing appointments on demand, with or without consulting a healthcare provider and regardless of exposure history.

Participants with positive qPCR test results were informed by phone by UHS clinical staff, who provided guidance on isolation and performed case investigation to identify potential contacts. Participants with negative qPCR test results were informed of their results via the UHS online patient portal.

Viral whole genome sequencing was performed on a set of positive samples at the IGI, using previously described procedures.[92] IGI then processed the genomes through the Nextstrain Auger pipeline with external genomes to place them in larger phylogenetic trees: a tree with all IGI genomes sequenced at the time of analysis (356 genomes); a tree containing 7,091 genomes subsampled from the worldwide genomes in GISAID at the time (approximately 200,000 genomes as of October 2020); and a tree containing 500 genomes (from 1 million genomes as of April 2021) using UShER.[93–95]

Antibody testing

Up to 10 mL of blood was collected by phlebotomists via venipuncture at baseline from participants in all three cohorts and again at endline from participants in the student and essential worker cohorts. Blood was centrifuged and serum was stored at -20°C for 2 to 4 months before being tested at Vitalant Research Institute using the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack, which detects IgA, IgG, and IgM antibodies and has an estimated clinical specificity of 100% and unreported sensitivity.[96]

Participant compensation

Participants in the student cohort received a $50 gift card after completing baseline testing and 10 daily surveys; this incentive was conditional on daily survey completion to encourage early habit formation.[97] Student participants received a second $50 gift card at their endline testing appointment. To facilitate travel to and from UHS for testing appointments, student participants were also offered pre-paid car rides via a ride-sharing app.

Participants in the essential worker cohort received a gift card worth $1 per daily survey completed (to a maximum of $70) after the study ended. Participants in the faculty/staff cohort were not compensated.

Statistical analyses

To identify sociodemographic factors associated with incident infection, we used Poisson regression to estimate unadjusted incidence rate ratios (IRRs) for SARS-CoV-2 infection by study cohort and within strata of sociodemographic variables self-reported in the baseline survey (e.g., age, gender, housing type), setting person-months of enrollment as an offset term to account for differing lengths of follow-up.

We also calculated IRRs comparing test positivity by recent signs/symptoms, exposures, and activities reported in the daily and weekly surveys. We estimated IRRs for several temperature thresholds (i.e., ≥100.4°F, ≥100.0°F, ≥99.0°F) to compare to symptom-specific IRRs; however, continuous associations between temperature and positivity have been previously explored in this cohort.[98] We accounted for clustered observations due to repeated tests per participant using a generalized estimating equation approach with Huber-White standard error estimates and an exchangeable working correlation structure.[99]

Finally, to assess the extent to which the testing and monitoring system captured incident infections, we identified participants who seroconverted from having non-reactive (no antibodies detected) to reactive (antibodies detected) blood samples between baseline and endline and calculated the proportion of these participants who were also diagnosed with incident SARS-CoV-2 infection via positive qPCR test during the study period.

Analyses were conducted in R, version 4.0.4.[69]

Ethical approvals

All study activities were approved by the University of California, Berkeley Committee for the Protection of Human Subjects.

2.4 Results

Participant recruitment and retention

Between June 1 and July 20, 2020, we enrolled 2,180 students, 268 essential workers, and 470 faculty/staff who completed at least one qPCR test or antibody test (Table 2.1, Figure S2.1). The student cohort was split between undergraduate (52%) and graduate (48%) students. Nearly half (44%) of essential workers worked in health services (i.e., providing clinical care to students). While 85% of essential workers were working on campus at the time of enrollment, most (81%) faculty/staff were working entirely remotely. At the time of enrollment, only 12 (0.4%) participants reported a previous COVID-19 diagnosis.

Participants provided a total of 5,545 person-months of follow-up from enrollment to the end of the study (mean person-days per participant: 57, range: 32-78). Participants completed a mean of 40 daily symptom surveys and 6 weekly exposure surveys over the study period, for a total of 117,235 symptom and 17,172 exposure surveys. A subset of participants did not complete any daily symptom surveys (1.7%) or weekly exposure surveys (4.2%).

SARS-CoV-2 incidence

During the study period, participants underwent 7,638 qPCR tests for active SARS-CoV-2 infection, with a mean of 2.6 tests per participant (range: 0-9). Almost all (99.9%) participants completed at least one qPCR test. Overall, 60 participants (2.0%) tested positive: 57 students, 2 essential workers, and 1 faculty/staff.

Among cohorts, students were at highest risk of incident infection over the study period (IRR students vs. faculty/staff: 5.8; 95% confidence interval [CI]: 1.3, 103.0). Due to the low number of cases outside of the student cohort, we examined additional risk factors for infections among students only (Table 2.2), finding higher rates of infection among students who were 18-19 years old (IRR vs. students ≥22 years: 8.3; 95% CI: 4.2, 17.5) and undergraduates (IRR vs. graduate students: 4.1; 95% CI: 2.2, 8.7). We also observed a higher incidence among white students (IRR: 2.8 vs. non-white students; 95% CI: 1.5, 5.5). These associations were largely driven by an outbreak among participants living in fraternities or sororities. Nearly one-quarter of participants living in fraternities or sororities were infected with SARS-CoV-2 during the study period (IRR vs. other students: 20.9; 95% CI: 12.3, 35.5), and these participants accounted for 49% of cases observed among student participants.

IGI retrieved whole viral genome sequences for 35 of the 60 positive cases from this study, 29 (83%) of which were found to be part of a campus superspreader event involving a total of 57 campus-affiliated individuals with samples sequenced by IGI. Most (69%) study participants within this cluster lived at one of two residences, with likely a single participant originating the superspreader event based on phylogenetic analyses. When the rare trio of mutations that defined the genomes in this cluster was searched in a phylogeny constructed from over 1.2 million genomes worldwide in April 2021,[95] no descendent leaves were found in the tree under the cluster, indicating that the lineage likely died out after the superspreader event.

Factors associated with test positivity

At least one symptom survey was completed in the 7 days before sample collection for 90% of tests (n=6,864), including 72% of tests (n=5,469) that had symptom data from the day of sample collection. Of the 54 cases who completed at least one survey during the week before their positive sample was collected (mean: 4 surveys), 23 cases (43%) had reported at least one of the nine COVID-19 symptoms that triggered a notification for them to test. Test positivity was 12.4 times higher among participants who had a recent symptom-triggered notification than participants who did not (95% CI: 7.3, 21.3) (Table 2.3). Notification-triggering symptoms most strongly associated with test positivity included loss of sense of taste or smell and feeling feverish. Weakness, sweats or chills, and swollen glands were the non-triggering symptoms most strongly associated with test positivity.

Participants completed at least one weekly exposure survey in the 14 days before sample collection for 61% of tests (n=4,678). Of the 31 cases who had recently completed an exposure survey at the time of sample collection, 9 (29%) reported a

potential household exposure that triggered a notification for them to test (Table 2.3). Test positivity was 12.3 times higher among participants who had a recent exposure-triggered notification than participants who did not (95% CI: 5.6, 26.9). Test positivity was also significantly higher among participants who reported recent engagement in 'higher risk' social activities, most notably attending a gathering of more than 10 people (IRR: 9.0; 95% CI: 4.4, 18.1).

SARS-CoV-2 seroprevalence

Only 18 (0.6%) of 2,877 participants who provided blood samples at baseline had SARS-CoV-2 antibodies (Table 2.4), all but one of them students. Most participants with antibodies at baseline either suspected past infection (28%), had been previously diagnosed (22%), or had a positive qPCR test the day blood was drawn (11%). Most (85%) participants in the student and essential worker cohorts provided blood samples at both baseline and endline (mean interval between samples: 48 days). Among 2,076 participants with baseline and endline blood samples, 33 (1.6%) seroconverted from non-reactive at baseline to reactive at endline, 30 of whom (91%) were also diagnosed via qPCR test during the study. Of the three participants who seroconverted without a positive qPCR test, two self-reported suspected past infection (one before baseline, one during the study period), while the third did not suspect past infection and had four negative qPCR tests over 40 days of study participation.

Of the 60 participants with incident SARS-CoV-2 infection during the study period, 41 (68%) provided an endline blood sample at least one week after the date of their first positive qPCR test (mean time between positive qPCR test and blood sample: 36 days; range: 13-52 days). Of these, 34 (83%) were reactive (Table 2.4).

2.5 Discussion

This study provides a model of a voluntary, incentivized system to identify and link at-risk students to SARS-CoV-2 testing. While the incidence and seroprevalence of SARS-CoV-2 were generally low in this cohort of university students and employees in the summer of 2020, we observed the highest incidence among undergraduate students living in congregate settings, with nearly half of cases found to be associated with a superspreader event.

Within this cohort, we previously demonstrated the acceptability of our low-barrier SARS-CoV-2 mitigation approach and the limitations of temperature monitoring as a tool for case identification.[87,98] The present analysis builds upon these contributions by triangulating prospective qPCR testing data with phylogenetic analyses of positive samples and serial antibody testing to evaluate whether case identification and containment were achieved. In doing so, we found evidence that the system successfully identified a high proportion of incident SARS-CoV-2 cases among participants and may have mitigated community transmission after an outbreak. Specifically, 91% of participants with newly identified antibodies for SARS-CoV-2 at the

end of the study had also been diagnosed with incident infection via qPCR test during the study period. While a sizeable cluster of cases among participants was traced to a single superspreader event, phylogenetic analyses demonstrated that the cluster was contained without spreading beyond campus; its rare phylogenetic signature was not observed in any genomes from samples in the surrounding communities or California state in the months following the superspreader event. As the outbreak unfolded, the system also allowed for rapid real-time response (i.e., surveillance testing notifications to students living in congregate housing) and offered a readily accessible, incentivized entry point for testing for students concerned about potential exposure.

Although some universities have adopted punitive measures intended to prevent transmission by controlling student behavior (for example, suspending students for hosting gatherings),[100–102] this approach has been criticized for its potential to reduce students' trust and cooperation.[103–105] Instead of punishing or shaming students who fail to adhere to public health guidance, some epidemiologists have called for a harm-reduction approach that supports and engages students as part of the solution.[103–105] The present study reinforces the potential to integrate voluntary testing and risk monitoring systems to support targeted case identification, as evidenced by the significantly higher positivity rates found among participants whose self-reported symptoms and exposures triggered notifications to test. Our findings also support increased outreach to groups of students at highest risk, particularly younger students in congregate housed settings such as fraternities and sororities.

This study is strengthened by rich longitudinal data, including symptom and exposure tracking, qPCR testing, and seroprevalence data from more than 2,000 participants. The study population comprised of a broad sample of university affiliates, both students and employees, with strong representation of university subpopulations perceived to be at higher risk of infection (e.g., undergraduates, essential healthcare workers). As on-campus activities were severely restricted throughout the study period (all classes were held online, and few students were living in residence halls), this study cannot provide insight into SARS-CoV-2 transmission risks related to on-campus student activities. Nevertheless, as 73% of UC Berkeley undergraduate students lived off campus *before* the pandemic,[106] systems to detect off-campus (i.e., community and household) transmission remain important for SARS-CoV-2 monitoring efforts among students. Additionally, all participants in the essential workers cohort and a subset of participants in the faculty/cohort were working on campus during the study period, further motivating efforts to monitor incidence in this population.

There remain several limitations. We observed relatively few SARS-CoV-2 cases during the study period, which took place before the development of highly transmissible variants, such as Delta and Omicron, and before vaccine rollout. Further research is necessary to adapt and evaluate similar systems in the context of both heightened transmissibility and more prevalent natural and vaccine-induced immunity. Observed associations between symptoms and positivity may also differ among those who have been infected by more recent variants and/or vaccinated. Additionally, a high proportion of identified cases were traced to one outbreak, limiting the generalizability of our exploratory assessment of risk factors for incident infection. There was also anecdotal

evidence that the outbreak prompted exposed students to enroll as study participants.[87] While this self-referral into the study is likely to increase selection bias, it also illustrates the utility of implementing non-stigmatizing, incentivized testing approaches to increase testing uptake among at-risk students. Finally, our identification of participants who seroconverted between baseline and endline may be incomplete due to loss to follow-up and imperfect sensitivity of SARS-CoV-2 antibody testing.

By integrating symptom and exposure monitoring systems with low-barrier testing, we identified incident SARS-CoV-2 infections to reduce transmission within a university setting. While there have been seismic shifts in the SARS-CoV-2 pandemic since 2020, universities continue to grapple with how best to mitigate on-campus spread in the face of emerging variants, incomplete vaccination coverage, breakthrough infections, and decreased reliance on other mitigation strategies (e.g., masking, remote learning).[107,108] The lessons learned through this study may inform the design of future adaptive strategies, ideally building beyond symptom/exposure monitoring and qPCR testing to integrate complementary interventions such as rapid antigen self-testing and vaccination and booster promotion.

2.6 Tables and Figures

Table 2.1 Baseline characteristics of participants in the Berkeley COVID-19 Safe Campus Initiative by study cohort, June–August 2020.

	All	Students	Essential Workers	Faculty/Staff
N (row %)	2,918 (100)	2,180 (74.7)	268 (9.2)	470 (16.1)
Age, mean ± SD	29.4 ± 11.6	24.3 ± 5.4	42.5 ± 12.3	45.2 ± 12.3
Gender, n (column %)				
Man	1,177 (40.3)	911 (41.8)	103 (38.4)	163 (34.7)
Woman	1,653 (56.6)	1,187 (54.4)	164 (61.2)	302 (64.3)
Non-binary/other	51 (1.7)	46 (2.1)	1 (0.4)	4 (0.9)
Race/ethnicity, n (column %)*				
American Indian/Alaska Native	39 (1.3)	29 (1.3)	2 (0.7)	8 (1.7)
Asian/Pacific Islander	833 (28.5)	703 (32.2)	66 (24.6)	64 (13.6)
Black/African American	103 (3.5)	83 (3.8)	16 (6.0)	4 (0.9)
Hispanic/Latine/Spanish origin	420 (14.4)	346 (15.9)	39 (14.6)	35 (7.4)
White	1,814 (62.2)	1,261 (57.8)	160 (59.7)	393 (83.6)
Other	280 (9.6)	223 (10.2)	31 (11.6)	26 (5.5)
Program level, n (column %)				
Undergraduate	-	1,114 (51.7)	-	-
Graduate	-	1,039 (48.2)	-	-
Living at fraternity/sorority, n (column %)	-	125 (5.7%)	-	-
Education, n (column %)				
High school diploma/GED	-	-	6 (2.2)	0 (0)
Some college or trade school	-	-	59 (22.0)	13 (2.8)
Bachelor's degree	-	-	78 (29.1)	119 (25.3)
Graduate/professional degree	-	-	121 (45.1)	337 (71.7)
Department, n (column %)				
Health services	-	-	129 (48.1)	-
Facilities/building services	-	-	61 (22.8)	-
Student services/other	-	-	77 (28.7)	-
Job title, n (column %)				
Faculty	-	-	-	110 (23.4)
Staff	-	-	-	311 (66.2)
Postdoctoral scholar/other	-	-	-	49 (10.4)
Currently working outside the home, n (column %)	748 (25.6)	418 (19.2)	228 (85.1)	102 (21.7)
Pre-enrollment COVID-19 diagnosis, n (column %)	12 (0.4)	8 (0.4)	1 (0.4)	3 (0.6)

*****Categories not mutually exclusive.

Table 2.2 Bivariate associations between sociodemographic characteristics and SARS-CoV-2 incidence among student participants in the Safe Campus Initiative, June–August 2020.

	Cases, N (row %)	Non-Cases, N (row %)	IRR (95% CI)
Overall*	57 (2.6)	2,120 (97.4)	-
Age			
18-19 years	21 (8.0)	243 (92.0)	8.34 (4.17, 17.48)
20-21 years	24 (3.8)	607 (96.2)	4.15 (2.11, 8.58)
≥22 years	12 (0.9)	1,270 (99.1)	Reference
Gender			
Woman	37 (3.1)	1,147 (96.9)	1.45 (0.85, 2.58)
Man	19 (2.1)	892 (97.9)	Reference
Non-binary/other	0 (0)	46 (100)	-
Race/ethnicity**			
American Indian/Alaska Native	0 (0)	29 (100)	-
Asian/Pacific Islander	11 (1.6)	691 (98.4)	0.49 (0.24, 0.91)
Black/African American	1 (1.2)	82 (98.8)	0.45 (0.03, 2.03)
Hispanic/Latine/Spanish origin	8 (2.3)	337 (97.7)	0.88 (0.39, 1.76)
White	45 (3.6)	1,216 (96.4)	2.80 (1.53, 5.54)
Other	4 (1.8)	217 (98.2)	0.65 (0.20, 1.58)
Program level			
Undergraduate	46 (4.1)	1,067 (95.9)	4.12 (2.17, 8.66)
Graduate	10 (1.0)	1,027 (99.0)	Reference
Living at fraternity/sorority	28 (22.4)	97 (77.6)	20.86 (12.27, 35.54)
Currently working outside the home	6 (1.4)	410 (98.6)	0.51 (0.20, 1.11)

IRR: incidence rate ratio, CI: confidence interval.
*N=2,177 students with at least one qPCR test for SARS-CoV-2 during the study period.
**Not mutually exclusive; all participants not included in specified racial/ethnic category served as reference for each comparison.

Table 2.3 Bivariate associations between prospectively monitored symptoms and exposures and SARS-CoV-2 qPCR test positivity among participants in the Safe Campus Initiative, June–August 2020.

	Test Positivity, % (+ Tests / All Tests)	IRR (95% CI)
Overall*	0.8 (60 / 7,629)	-
Signs/symptoms within 7 days of test		
No	0.4 (21 / 5,704)	Reference
Yes (any)	3.2 (31 / 971)	8.6 (5.0, 14.9)
- Temperature ≥100.4°F †	0.0 (0 / 8)	0.0 (0.0, 0.0)
- Temperature ≥100.0°F	11.8 (2 / 17)	15.6 (4.1, 60.4)
- Temperature ≥99.0°F	2.6 (9 / 346)	4.1 (1.9, 8.7)
- Feeling feverish †	14.9 (11 / 74)	23.7 (12.7, 44.3)
- Dry cough †	5.5 (7 / 128)	7.9 (3.6, 17.2)
- Coughing up mucus †	5.5 (5 / 91)	7.6 (3.1, 18.8)
- Unusual chest pain or pressure †	9.7 (6 / 62)	13.8 (6.1, 31.1)
- Difficulty breathing †	5.6 (1 / 18)	7.2 (1.1, 48.7)
- Shortness of breath †	8.7 (4 / 46)	11.9 (4.4, 31.9)
- Trouble thinking/concentrating †	7.6 (5 / 66)	10.6 (4.3, 25.7)
- Loss of sense of taste †	42.9 (3 / 7)	57.6 (23.5, 141)
- Loss of sense of smell †	33.3 (4 / 12)	45.8 (19.0, 110)
- Any notification-triggering symptom †	5.8 (23 / 397)	12.4 (7.3, 21.3)
- Loss of appetite	10.0 (6 / 60)	14.3 (6.3, 32.5)
- Fatigue	3.5 (13 / 373)	5.6 (3.0, 10.4)
- Trouble sleeping	5.1 (7 / 137)	7.4 (3.4, 16.1)
- Headache	4.6 (14 / 302)	7.7 (4.2, 14.1)
- Runny, blocked, or painful sinuses	5.2 (14 / 268)	8.8 (4.8, 16.0)
- Sneezing	1.9 (2 / 104)	2.5 (0.6, 10.0)
- Swollen, red, or painful eyes	8.6 (5 / 53)	12.1 (4.9, 29.7)
- Sore throat	3.1 (8 / 259)	4.5 (2.1, 9.4)
- Stomach pain	5.8 (5 / 86)	8.1 (3.3, 19.8)
- Diarrhea	4.8 (4 / 83)	6.6 (2.4, 17.8)
- Nausea or vomiting	3.3 (3 / 92)	4.4 (1.4, 13.6)
- Body aches or muscle pain	8.1 (12 / 149)	13.0 (7.0, 24.4)
- Sweats or chills	11.3 (10 / 89)	17.5 (9.0, 34.0)
- Swollen glands	11.9 (5 / 42)	16.6 (7.0, 39.7)
- Weakness	13.2 (10 / 76)	20.5 (10.6, 39.4)
Exposures within 14 days before test		
No	0.3 (14 / 4,179)	Reference
Yes (any)	3.4 (17 / 499)	10.1 (5.0, 20.4)
- Suspected or confirmed COVID-19 case in household †	6.7 (6 / 89)	14.7 (6.0, 35.9)
- Close contact with suspected or confirmed case outside household	2.9 (4 / 138)	6.3 (2.2, 18.2)
- Household member with new COVID-19-like symptoms †	4.4 (5 / 114)	7.6 (3.0, 19.6)
- Household member with any new symptoms of illness	2.4 (8 / 336)	4.7 (2.1, 10.4)

- Any notification-triggering exposure †	5.2 (9 / 173)	12.3 (5.6, 26.9)
Activities within 14 days before test		
No	0.5 (3 / 630)	Reference
Yes (any)	0.7 (29 / 4,142)	1.5 (0.5, 4.8)
- Spent time at another residence	1.1 (26 / 2,330)	4.6 (1.9, 11.1)
- Had visitors at own residence	1.0 (22 / 2,203)	2.5 (1.2, 5.4)
- Attended gathering of >10 people	2.8 (19 / 672)	9.0 (4.4, 18.1)
- Worked outside the home	0.5 (10 / 2,132)	0.6 (0.3, 1.2)
- Used public restroom	0.7 (12 / 1,830)	1.0 (0.5, 2.0)
- Used public transportation	0.6 (5 / 695)	0.8 (0.3, 2.3)
- Participated in group sports	1.6 (4 / 255)	2.6 (0.9, 7.3)

qPCR: quantitative polymerase chain reaction, IRR: incidence rate ratio, CI: confidence interval.
*Excluding resamples and repeated positives; includes N=2,914 participants with at least one qPCR test for SARS-CoV-2 during the study period.
† Reporting triggered notification to test.

Table 2.4 Seroprevalence of SARS-CoV-2 antibodies among participants in the Safe Campus Initiative, June–August 2020.

	Baseline, N (%)	Endline, N (%)	Both, N (%)
Serostatus – Cross-sectional*			
Reactive	18 (0.6)	48 (2.3)	-
Non-reactive	2,859 (99.4)	2,039 (97.7)	-
Serostatus – Longitudinal**			
Non-Reactive → Non-Reactive	-	-	2,029 (97.7)
Non-Reactive → Reactive	-	-	33 (1.6)
Reactive → Non-Reactive	-	-	0 (0)
Reactive → Reactive	-	-	14 (0.7)
Serostatus – Previous qPCR Positive†			
Reactive	-	34 (82.9)	-
Non-reactive	-	7 (17.1)	-

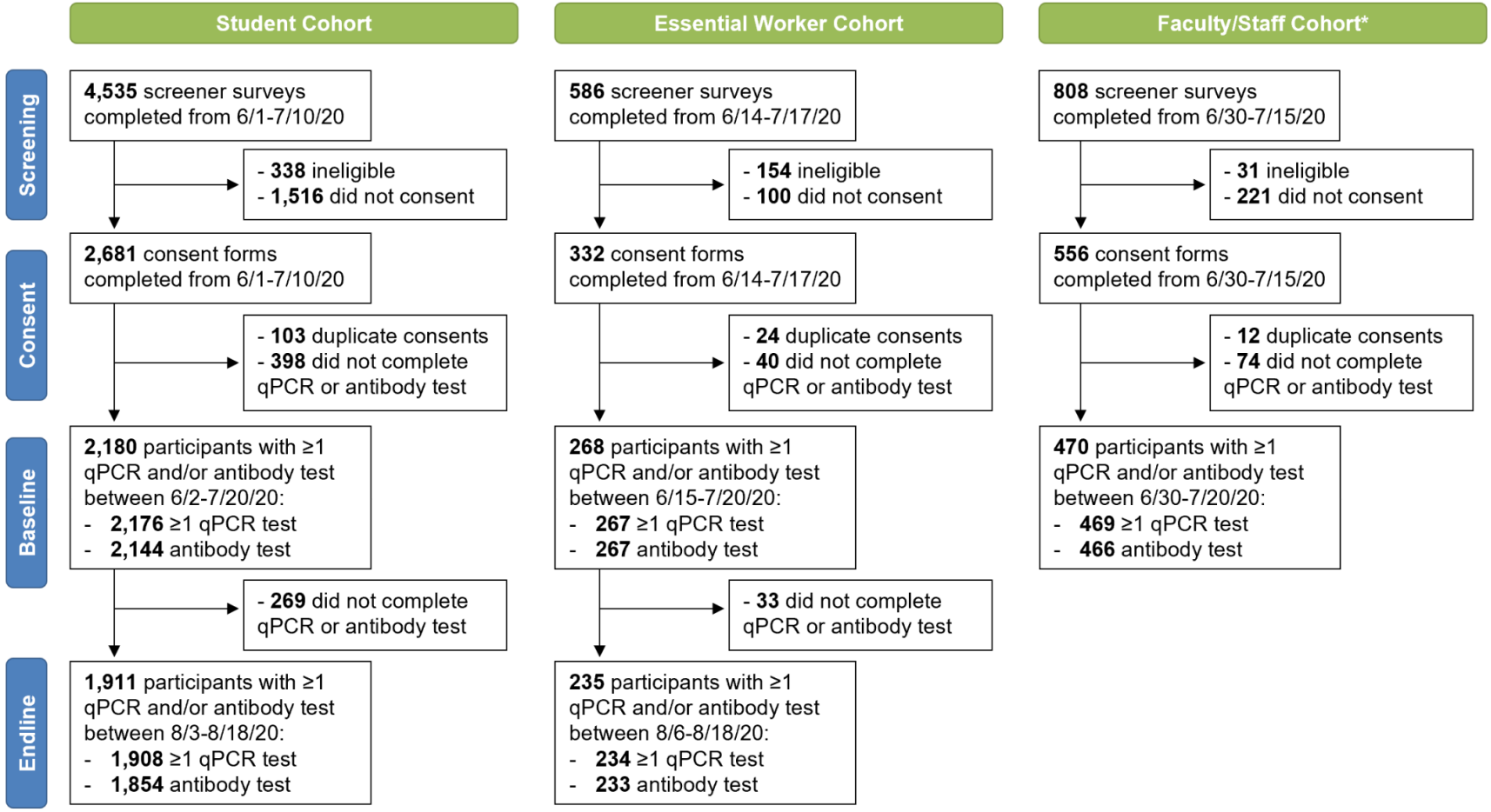
qPCR: quantitative polymerase chain reaction.
*N=2,888 participants who provided at least one blood sample.
**N=2,076 participants who provided blood samples at baseline and endline.
†N=41 participants who provided an endline blood sample ≥7 days *after* infection with SARS-CoV-2 identified via positive qPCR test.

2.7 Supplementary Materials

Table S2.1 Eligibility criteria across the Berkeley COVID-19 Safe Campus Study cohorts.

	Student Cohort	**Essential Worker Cohort**	**Faculty/Staff Cohort**
Eligibility Criteria	- At least 18 years of age	- At least 18 years of age	- At least 18 years of age
	- Currently enrolled as an undergraduate or graduate student at UC Berkeley (i.e., not graduated in Spring 2020 or incoming for Fall 2020)	- Currently employed in one of the following departments at UC Berkeley: health services, police, facility services or other building management, environmental health and safety, laboratory animal care, athletics, dining, childcare, other residential or student services - Currently working on campus at UC Berkeley *or* expected to return to work during June 2020	- Currently employed as a faculty member, staff member, or postdoctoral scholar at UC Berkeley - Not already enrolled in the essential workers cohort
	- Primarily residing in Alameda County or Contra Costa Country between 6/1/20-8/31/20	N/A	- Primarily residing in Alameda County or Contra Costa Country between 6/1/20-8/31/20
	- Willing to sign release of information for COVID-19-related medical records	- Willing to sign release of information for COVID-19-related medical records	- Willing to sign release of information for COVID-19-related medical records

Figure S2.1 Flow diagram for the Berkeley COVID-19 Safe Campus Study cohorts.



qPCR: quantitative polymerase chain reaction.
*Faculty/staff cohort not invited for endline testing appointments but could complete follow-up qPCR tests through 8/18/20.

Chapter 3. HIV and condom-related knowledge and beliefs, HIV testing, and condom use in a school-based cross-sectional survey of 6,000 Rwandan adolescents

3.1 Abstract

Objective: Comprehensive sex education was added to Rwanda's national school curriculum in 2016. We evaluated HIV and condom-related knowledge/beliefs and their associations with HIV testing and condom use in a school-based sample of Rwandan adolescents to identify enduring gaps in HIV and family planning education.

Methods: From February to May 2021, we surveyed 6,079 students ages 12-19 years (median: 15 years; 51% female) from 60 secondary schools in eight Rwandan districts about their sexual health knowledge and behavior. We consolidated responses to seven true-or-false questions testing HIV knowledge and eight statements encoding condom beliefs to classify level of HIV knowledge (high, medium, low) and favorability of condom beliefs (prohibitive, middling, supportive). We estimated adjusted prevalence ratios (aPRs) to assess whether HIV knowledge and condom beliefs were associated with HIV testing and condom use.

Results: HIV knowledge was high overall, with 74% answering at least 6 of 7 HIV knowledge questions correctly. In contrast, beliefs about condoms were mixed, with participants indicating favorable attitudes in response to 4 of 8 condom-related statements on average. Many believed condoms could disappear inside the body (64%), were not suitable for casual (50%) or steady (40%) relationships, or were too embarrassing to buy (37%). One third (38%) of participants reported previous HIV testing, of whom half (20%) had tested within the past year. Among the 28% of participants who reported having ever had sex, 50% reported currently using condoms, although only 38% used a condom at last sex. Participants with high HIV knowledge were more likely than those with low knowledge to have HIV tested in the past year (aPR high vs. low: 1.3; 95% confidence interval [CI]: 1.1, 1.6). HIV knowledge was not associated with condom use among sexually experienced participants, but participants with supportive or middling condom beliefs were more likely to report current condom use than those with prohibitive beliefs (aPR supportive vs. prohibitive: 1.5; 95% CI: 1.3, 1.8; aPR middling vs. prohibitive: 1.3; 95% CI: 1.1, 1.6).

Conclusion: Despite high HIV knowledge, HIV and pregnancy prevention among Rwandan youth may be stymied by prohibitive beliefs and misconceptions about condoms. The association between condom beliefs and condom use warrants renewed attention to educational gaps about condoms' value in prevention and motivates school-based interventions to create supportive social norms around condom use among youth.

3.2 Introduction

Over the past two decades, there have been great strides toward ensuring widespread access to HIV and family planning services in Rwanda. Notable achievements include linking 97% of adults diagnosed with HIV to antiretroviral treatment and investing in a successful voluntary family planning program that reduced socioeconomic disparities in modern contraceptive use.[109–111] However, there remain lingering challenges for adolescent sexual and reproductive health (SRH). While HIV prevalence is less than 1% among Rwandan adolescents, 28% of adolescents ages 15-19 with HIV are unaware of their status.[109] Young women have twice the HIV prevalence of young men.[112] Despite a five-fold increase in met need for contraception among young women between 2000 and 2015,[15] 59% of unmarried sexually active women ages 15-19 had unmet need for family planning in 2019-20.[113]

Although adolescence is a normative developmental window for sexual exploration, early sexual experiences among Rwandan youth may take place in contexts with heightened risk for HIV transmission and unintended pregnancy.[114,115] In a nationally-representative 2018-2019 survey, 10% of Rwandan adolescents reported early sexual debut (before age 15),[109] which is associated with increased HIV risk among young women in sub-Saharan Africa.[116] A qualitative study of Rwandan secondary school students described two common types of sexual experiences: experimental sex with same-age peers, which was often unprotected due to its unplanned nature, and transactional sex with older partners,[114] which may increase risk of HIV exposure and decrease relational power to enforce condom use.[117,118]

In 2018, Rwanda's Ministry of Health committed to a strategic plan to achieve universal access to high-quality integrated family planning and SRH services among Rwandan adolescents, primarily by increasing awareness, availability, and accessibility of youth-friendly SRH services through education and training initiatives.[119] While SRH services are increasingly available to Rwandan adolescents, most are not tailored to their needs.[111,115,120,121] For example, even when health facilities are geographically accessible and provide free contraceptives, they may not offer youth-friendly hours (e.g., weekends or evenings) or private waiting areas,[115] and most healthcare providers have limited or no specialized training in the provision of adolescent SRH services.[120] Although national policy allows minors to consent to HIV testing,[122,123] a parent or guardian must be present to receive results, and parental permission may be required for minors accessing family planning services.[121,123,124] All of these and other structural and policy-level factors may impede access to or stigmatize use of existing services.

Theoretical models applied to SRH, such as the theory of planned behavior, suggest that SRH knowledge, norms, and attitudes are also important upstream determinants of uptake of HIV and family planning services and condom use.[18,125–128] For example, sexually active youth may not perceive themselves as being at risk of HIV or understand modes of transmission, discouraging testing.[129] Youth may hold negative misconceptions and social norms about condoms that deter use.[115,130–132] Thus, even when health services are accessible, low availability of reliable sources of SRH

information and corresponding knowledge deficits pose a barrier to service uptake for adolescents.

Alongside other initiatives to promote youth SRH,[119] comprehensive sex education was added to Rwanda's national curriculum for primary and secondary schools in 2016.[133–135] While there is evidence that comprehensive sex education is an effective model to increase knowledge and positively shape attitudes and behaviors when well-implemented,[24] research on comprehensive sex education elsewhere in sub-Saharan Africa has noted varying levels of implementation fidelity.[136–138] Rwanda's curriculum seeks to address a broad range of SRH topics, including the prevention of HIV/STI and unwanted pregnancy, through a human rights-based approach, but as yet, there is little publicly-available information regarding its implementation coverage and fidelity as well as associated successes and challenges.

In the context of Rwanda's adoption of comprehensive sex education over the past five years, we aimed to: (a) evaluate adolescent Rwandan students' HIV knowledge and beliefs around condoms to identify educational gaps and (b) estimate associations between these knowledge/beliefs and health-promoting behaviors (i.e., HIV testing, condom use) to better understand whether school-based educational interventions have potential to improve downstream SRH outcomes. These aims are facilitated by a sizable and unique cross-sectional data set comprising more than 6,000 Rwandan secondary school students surveyed in 2021.

3.3 Methods

Study design and setting

We conducted a cross-sectional analysis using baseline data from the cluster-randomized trial to evaluate *CyberRwanda*, a digital platform to connect Rwandan adolescents with youth-friendly family planning and reproductive health information and services. The trial protocol has been previously published.[139] We report the findings according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for cross-sectional studies.[88]

In brief, from February to May 2021, we recruited and surveyed 6,079 students ages 12-19 years from 60 secondary schools in eight Rwandan districts about their sexual health knowledge and behavior. Secondary schools in these districts were eligible to participate if they: (1) had school leadership who were willing to participate, (2) were located within 4.5 kilometers of a participating *CyberRwanda* pharmacy, (3) were located at least 1.5 kilometers from another secondary school, (4) were attended by at least 150 students, and (5) were day schools (i.e., did not board any students). Of 61 eligible schools, 60 were randomly selected to participate. Officials at participating schools completed surveys about school characteristics, including whether their curriculum covers SRH topics.

Participant recruitment and eligibility

We aimed to enroll 50 female students and 50 male students per school to reach the pre-specified sample size of 6,000 participants.[139] Students were eligible to participate if they: (1) were attending grades Secondary 1 or Secondary 2 at a participating school, (2) were 12 to 19 years old, (3) provided consent (if 18 or 19 years old) or assent (if less than 18 years old) to participate, (4) provided parental consent (if less than 18 years old) to participate, and (5) were willing to provide contact information for study follow-up.

Participating schools sent parental consent forms home with all Secondary 1 and Secondary 2 students who were less than 18 years old. We created a sampling frame of all students who returned parental consent forms *or* were listed as 18 or 19 years old in school enrollment records, randomly sampling students by sex until reaching the desired sample size of 50 students per sex per school (Figure S3.1).

Selected students were invited to data collection events held at their schools during non-school hours (primarily weekends), where they were assessed for eligibility and, if eligible, provided informed consent or assent to participate. Participants were compensated 3,000 RWF (~$3 USD) to cover transportation fees.

Survey procedures

Participants were administered a Qualtrics-based survey in Kinyarwanda by trained Rwandan interviewers from YLabs. Using tablet computers, interviewers read surveys aloud and entered participants' responses. For potentially sensitive questions about sexual behavior, interviewers read the response options before turning the tablet to participants to privately enter their responses.

The survey averaged one hour to complete and included questions about participants' sociodemographic characteristics; HIV and family planning knowledge, beliefs, norms, and self-efficacy; and sexual history. Participants who indicated they had never had sex during the first half of the survey were asked a confirmatory question later in the survey to reduce potential misclassification. Participants who reported ever having had sex were asked about their contraceptive use and reproductive autonomy.

HIV knowledge and condom beliefs

We consolidated participants' responses to questions about HIV knowledge and statements encoding condom beliefs that may facilitate or demotivate use to classify their level of HIV knowledge and favorability of condom beliefs.

HIV knowledge was measured using seven fact-based questions, six of which were adapted from the Rwandan Demographic and Health Survey (DHS) and one additional question about whether circumcision affects men's risk of HIV infection.[140] The questions centered on HIV prevention (e.g., "Can a person reduce the risk of getting HIV/AIDS by having sex with only one uninfected partner who has no other partners?") and common misconceptions (e.g., "Can a person get the HIV/AIDS virus by sharing food with someone who is infected?"). Responses were scored based on accuracy, with

each correct response receiving one point and each incorrect or uncertain response receiving zero, and then summed to create an HIV knowledge score ranging from 0 to 7 (Table S3.1).

To compare HIV knowledge in our sample to youth surveyed in the 2019-2020 Rwandan DHS, we also created an indicator of comprehensive knowledge of HIV. Following the DHS definition, participants were classified as having comprehensive knowledge if they correctly responded to a specific subset of five questions.[113]

Condom beliefs were assessed by asking participants who had seen or heard of condoms (>99%) for their opinions on eight statements about condoms, adapted from an adolescent health questionnaire used by the World Health Organization.[141] The statements included perceptions of efficacy (e.g., “Condoms are an effective way of preventing pregnancy”), subjective social norms (e.g., “Condoms are suitable for casual relationships”), and other concerns (e.g., “Condoms can slip off the man and disappear inside the woman’s body”). Each response that was favorable toward condom use was scored as one (e.g., disagreeing with the statement “It would be embarrassing for someone like me to buy or obtain condoms”), and each response that could be prohibitive of condom use was scored as zero (e.g., agreeing with or indicating uncertainty in response to the statement “If a girl suggested using condoms to her partner, it would mean that she didn’t trust him”) (Table S3.2). Responses were summed to create a condom beliefs score ranging from 0 to 8 with higher scores indicating more favorable attitudes.

Each summed score was then categorized using ad hoc cut points intended to capture qualitatively meaningful differences in knowledge/beliefs (Figure S3.2). Participants’ level of HIV knowledge was classified as low (0-4 correct statements), medium (5-6 correct statements), or high (7 correct statements, perfect score), while their condom beliefs were classified as prohibitive (0-3 supportive responses), middling (4-5 supportive responses), or supportive (6-8 supportive responses).

HIV testing and condom use

Participants were asked whether they had ever HIV tested and, if so, how many months it had been since their most recent HIV test. In primary analyses, we classified participants based on whether they reported HIV testing in the past year to approximate current testing behavior. As 9% of participants who had previously HIV tested did not recall the timing of their most recent test, we also assessed ever HIV testing as a secondary outcome.

Participants who reported ever having had sex were asked about their current contraceptive method(s) and contraceptive method(s) used at last sex, including male and female condoms. In primary analyses, we classified participants based on whether they reported currently using condoms. However, as classification of contraceptive use is likely to differ based on the time-frame of assessment (e.g., ‘current’ use may undercount coital-dependent methods),[130,142] we examined condom use at last sex as a secondary outcome.

Covariates

The survey collected sociodemographic information, including age, sex, school grade, and district. Participants were asked their relationship status, and those that reported having a boyfriend, girlfriend, or spouse were classified as partnered. Socioeconomic status was assessed by constructing a household assets index using principal components analysis (PCA). The first factor was categorized into quartiles. Additionally, participants' responses to the Household Hunger Scale were scored to identify those living in households experiencing moderate to severe hunger.[143]

Participants were also asked about HIV testing self-efficacy ("How confident are you that you can get tested for HIV if you need it?") and contraceptive self-efficacy ("How confident are you that you could get your partner(s) to use contraceptives/condoms if you desired it?"). For each, participants who were at least somewhat confident were classified as having high efficacy, while those who reported being not confident or unsure were classified as having low efficacy. To assess peer norms around family planning, participants indicated their level of agreement with the statement "Most of my friends think that family planning services are only for married men and women or women who already have children" on a 5-point Likert scale. Participants who agreed were classified as having prohibitive peer norms, while those who neither agreed nor disagreed were classified as middling, and those who disagreed were classified as having supportive peer norms. Participants who reported ever having had sex were administered the decision-making and freedom-from-coercion subscales of the Reproductive Autonomy Scale, and responses were averaged to produce subscale scores.[144]

Statistical analyses

We evaluated bivariate differences in knowledge, beliefs and behavior by sex or other characteristics using modified t-tests for continuous variables and chi-square tests for categorical variables adjusted for clustering by school.[145] We estimated unadjusted and adjusted prevalence ratios (aPRs) to assess whether HIV knowledge and condom beliefs were associated with HIV testing in the past year (full sample) and current condom use (sexually experienced subsample). Log-Poisson regression models were constructed using generalized estimating equations with an exchangeable covariance structure to account for clustering by school.[99] In secondary analyses, we re-ran models using the alternative definitions of the dependent variables (i.e., ever HIV tested, condom use at last sex).

Although the cross-sectional study design prevents temporal ordering of the independent and dependent variables, these analyses were motivated by causal questions (i.e., what are the effects of HIV knowledge and beliefs about condoms on HIV testing and condom use?). Therefore, covariates included in multivariable regression models were selected a priori using directed acyclic graphs.[146] All adjusted models included sex, age, school grade, district, partnership status, household assets index, and household hunger. Additional covariates included in HIV testing models were sexual experience (ever had sex vs. never had sex) and HIV testing self-efficacy, while

condom use models included contraceptive self-efficacy, peer norms around family planning, and reproductive autonomy scores. To examine whether associations varied by sex, we ran adjusted models with interaction terms between sex and the primary independent variables (HIV knowledge and condom beliefs scores). We did not find evidence of effect modification of the aPRs by sex (Wald p-values>.1) and, thus, present results without stratifying by sex.

Finally, motivated by the findings of the previous analyses, we used parametric g-computation to compare the prevalence of condom use among sexually experienced participants under observed condom beliefs to the predicted prevalence at different levels of condom beliefs. Following the approach described by Ahern et al.,[147] these analyses were intended to provide a more interpretable, policy-relevant estimate of the potential impact of changing condom beliefs through intervention. In brief, we first constructed multivariable regression models estimating condom use based on condom beliefs score and all covariates included in condom use models as described above. From this model, we predicted the probability of condom use for individual participants in counterfactual data sets in which participants' condom beliefs score were deterministically re-assigned to each possible value (range: 0-8). The resulting individual-level probabilities were averaged for each set condom beliefs score to obtain the predicted prevalence of condom use across the study population at a given condom belief score. We calculated marginal prevalence differences comparing the predicted prevalence of condom use at each score against the prevalence of use with observed (actual) condom beliefs. To estimate corresponding standard errors and confidence intervals, we sampled school clusters from the data with replacement 1,000 times to generate a sampling distribution for the prevalence estimates.

Analyses were conducted in R, version 4.1.0.[69]

Ethical approvals

This study was approved by the Rwanda National Ethics Committee in Rwanda and the University of California, Berkeley Committee for Protection of Human Subjects.

3.4 Results

Participant characteristics

We enrolled 6,079 participants (51% female), 82% of those invited to participate (Figure S3.1). Invited students who did not enroll were slightly older on average than participants (Table S3.3). Participants averaged 15.4 years old, 19% had a steady partner, and 26% lived in households experiencing moderate to severe hunger (Table 3.1). According to school officials, 55 of the 60 (92%) schools from which participants were recruited included SRH in the curriculum. Most participants (55%) reported that teachers were their most important source of information about puberty and reproductive systems, and 82% had attended classes on these topics at school.

Almost all participants had heard of at least one type of condom (98% male condoms, 68% female condoms), and 82% had seen a condom before. Most (80%) participants reported being at least somewhat confident they could get their partner(s) to use contraceptives if desired; male participants were more confident than females (87% vs. 74%, p<.001). Half of participants (47%) indicated that their peers believed family planning is only for married couples or women who have already had children.

Male participants were more likely than female participants to report ever having had sex (37% vs. 20%, p<.001). Most sexually experienced participants stated that they personally had the most say in whether they used contraception (46%) or that it was a joint decision with their partner (35%), although 15% reported that it was their partners' decision alone and 10% indicated that their partner had stopped them from using a method to prevent pregnancy when they wanted to use one; these findings were similar among male and female participants.

HIV knowledge and condom-related beliefs

Most (74%) participants answered at least 6 of 7 HIV knowledge questions correctly. More than a third (37%) correctly answered all questions (classified as 'high' knowledge), while only 8% missed more than two questions (classified as 'low' knowledge). The most common misconceptions were that a healthy-looking person could not have HIV/AIDS (19%) and that HIV/AIDS could be spread via mosquito bite (15%) (Table S3.1), both of which were included in the DHS definition for comprehensive HIV knowledge met by less than half of participants (47%). Male participants were more likely to know that circumcision reduces men's risk of contracting HIV (92% vs. 81%, p<.001) and had slightly higher HIV knowledge scores than female participants on average (mean: 6.1 vs. 6.0, p<.001).

Beliefs about condoms were mixed, with participants responding favorably to 4 of 8 condom-related statements on average. While most participants agreed that condoms are effective for preventing pregnancy (95%) and sexually transmitted diseases (97%), many believed condoms could disappear inside the body (64%), were not suitable for casual (50%) or steady (40%) relationships, or were too embarrassing to buy (37%) (Table S3.2). Male participants had more favorable condom beliefs than female participants on average (mean score: 4.6 vs. 4.1, p<.001). For example, male participants were less likely to report feeling too embarrassed to buy condoms (32% vs. 42%, p<.001) and more likely to agree that condoms are suitable for steady relationships (46% vs. 38%, p<.001).

HIV testing and condom use

Although 95% of all participants reported being at least somewhat confident that they could get tested for HIV if needed, only one third (38%) had ever HIV tested, of whom half (20% of the overall sample) had tested within the past year. Sexually experienced participants were more likely than participants who had never had sex to report ever HIV testing (44% vs. 36%, p<.001) or recent HIV testing (22% vs. 19%, p=.002).

Among the 28% of participants who reported having had sex, 50% (n=860) indicated that they were currently using condoms as a method of contraception (Table 3.1). Male participants were more likely than females to report current condom use (54% vs. 44%, p=.002). However, only 40% of sexually experienced participants reported *ever* having used a condom, while 38% reported using a condom at last sex. Male condoms accounted for 99% of condom use. Only 12 participants indicated current use of female condoms, while 2 used female condoms at last sex.

Notably, the use of other modern contraceptive methods was also rare in this sample. Less than 5% of sexually experienced participants reported that they or their partner were currently using a non-condom modern method, most commonly oral contraception (1.7%, n=29) followed by injectable contraception, the implant, and the Standard Days Method (0.7%, n=12 each).

Multivariable analyses

In multivariable models, continuous HIV knowledge score was not associated with HIV testing in the past year, nor was having comprehensive HIV knowledge (Table 3.2, Figure S3.3). However, participants with medium or high HIV knowledge were more likely than those with low knowledge to have tested in the past year (e.g., aPR high vs. low: 1.3; 95% confidence interval [CI]: 1.1, 1.5).

Among sexually experienced participants, HIV knowledge was not associated with condom use, but condom beliefs were associated with current condom use (aPR per one-unit change in condom beliefs score: 1.1; 95% CI: 1.1, 1.2) (Table 3.3, Figure S3.3, Figure S3.4). Participants with supportive or middling condom beliefs were more likely to report condom use than participants with prohibitive beliefs (aPR supportive vs. prohibitive: 1.5; 95% CI: 1.3, 1.8; aPR middling vs. prohibitive: 1.3; 95% CI: 1.1, 1.6).

We compared the predicted marginal prevalence of condom use at each condom beliefs score with the marginal prevalence of use under observed beliefs (Table 3.4). The predicted prevalence of current condom use if sexually experienced participants had entirely supportive condom beliefs (condom beliefs score: 8) was 73%, a 22% absolute increase from the prevalence expected under observed beliefs (95% CI: 13%, 30%).

Results were similar when using the secondary outcomes of ever HIV testing (Table S3.4) and condom use at last sex (Table S3.5, Table S3.6).

3.5 Discussion

We evaluated HIV and condom-related knowledge/beliefs and their associations with HIV testing and condom use in a school-based sample of Rwandan adolescents to identify enduring gaps in HIV and family planning education. Most participants were knowledgeable about HIV but held mixed beliefs about condoms.

We found weak associations between HIV knowledge and HIV testing; participants with the lowest HIV knowledge scores were less likely than other participants to have recently tested. However, unlike previous studies of household-based sample of youth in Rwanda and elsewhere in sub-Saharan Africa,[129,148,149] we did not observe an association between comprehensive HIV knowledge and HIV testing. It is possible that this school-based sample of students with similar levels of education also had more homogenous HIV knowledge, reducing knowledge-related variability between those classified as having or not having comprehensive HIV knowledge. Supporting this possibility, 70% of participants who did not meet the DHS definition for comprehensive knowledge incorrectly answered only one of the five assessment questions.

While we found no associations between HIV knowledge and condom use, prohibitive condom beliefs were associated with lower condom use among sexually experienced participants. Although condoms were by far the most frequently reported contraceptive method in this sample, most participants believed that condoms could disappear inside a woman's body or were not suitable for casual partnerships. Consistent with past research, female youth held less favorable condom beliefs than male youth.[131] Forty years into the HIV epidemic, these findings warrant renewed attention to educational gaps about condoms' value in prevention and motivate school-based interventions to address misconceptions and create supportive social norms around condoms. Knowledge and attitudes toward condoms may be especially important among sexually active youth, because of their dual role in pregnancy and HIV/STI prevention, their widespread availability in shops and kiosks, and youth's concerns about the potential side-effects and age-appropriateness of other methods.[150]

As evidenced by these data, social norms can be at odds with initiatives to provide family planning services to youth.[111] For example, widely-held beliefs that contraceptives are only appropriate for adult married women create stigma around young unmarried women seen requesting contraceptives.[115,151] Cultural inhibitions around open discussions of sex also discourage parental communication about adolescent SRH, with discussions that do take place primarily focusing on consequences of sex (e.g., HIV) and abstinence as prevention.[115,152] Although such inhibitions may result from concern that talking openly about sex could encourage adolescents to be sexually active, lack of parental communication on SRH is associated with adolescent pregnancy elsewhere in sub-Saharan Africa.[153] School-based educational interventions have increasingly been implemented to address these challenges.[138]

While school-based interventions often demonstrate impacts on SRH-related knowledge and self-efficacy, many do not show corresponding impacts on behavior (e.g., condom use) and downstream SRH outcomes (e.g., HIV/STI, pregnancy).[24,154–164] Potential for impact varies based on intervention and implementation characteristics. For example, while peer education programs have shown limited success, including one in Rwanda that did not increase HIV knowledge *or* condom use,[165] school-based, adult-led comprehensive sex education interventions in sub-Saharan Africa have shifted condom norms and increased condom use.[155,157–159] However, our analyses also suggest that intervening upon condom beliefs alone would not fully address gaps in use; even if

condom beliefs were perfectly supportive, we estimated in our simulations that more than one in four youth would still not use condoms. Instead, there is need for multifaceted interventions that target other barriers to access. For example, Rwandan youth have suggested condom provision in schools,[114] a step that could enhance the effects of comprehensive sex education by reducing structural, economic, and social barriers to condom procurement.

A key strength of this study is the sizable school-based sample of youth, randomly sampled from 60 schools across eight districts. These data provide a useful snapshot of SRH knowledge and beliefs among secondary school students ages 12-19 years during a critical window of adolescent development. This sample is especially relevant when considering persistent gaps in school-based sex education, as participants were surveyed five years after Rwanda adopted comprehensive sex education and most reporting attending school SRH classes. While there are other large household surveys of SRH knowledge and behavior among Rwandan youth,[109,113] they are not specific to secondary students who are the primary targeted recipients of sex education. Our findings are also strengthened by robust assessment and control for other factors, such as self-efficacy and reproductive autonomy, and our application of analytic methods to provide more practical estimates of potential impacts of intervening upon condom beliefs.

There remain several limitations. All analyses were cross-sectional, making it impossible to establish the temporal ordering of knowledge/beliefs and behaviors or preclude reverse causality as an explanation for observed associations. Therefore, the present analysis is hypothesis-generating and should be replicated in longitudinal samples. The sensitive nature of questions about sexual behavior increases the potential for information bias, such as underreporting of sex or overreporting of condom use. We aimed to minimize potential for bias during data collection by using trained interviewers and encouraging participants to privately answer sensitive questions on tablets. Still, if participants with supportive condom beliefs were also more likely to overreport condom use (i.e., more strongly affected by social desirability bias), our estimates would be biased away from the null.

In conclusion, despite high HIV knowledge among Rwandan youth, HIV and pregnancy prevention may be stymied by prohibitive beliefs about condoms which we found to be common and inversely associated with condom use. Further research is necessary to measure the impact of school-based interventions to reduce misconceptions and create supportive social norms around condom use among secondary students in Rwanda.

3.6 Tables and Figures

Table 3.1 Baseline characteristics of participants in the CyberRwanda cohort by sex.

Full sample	All	Female students	Male students
N (row %)	6,079 (100)	3,128 (51.5)	2,951 (48.5)
Age, mean ± SD	15.4 ± 1.5	15.1 ± 1.5	15.6 ± 1.6
Grade, n (column %)			
Secondary 1	3,456 (56.9)	1,787 (57.1)	1,669 (56.6)
Secondary 2	2,623 (43.1)	1,341 (42.9)	1,282 (43.4)
District, n (column %)			
Bugesera	517 (8.5)	263 (8.4)	254 (8.6)
Gasabo	1,320 (21.7)	667 (21.3)	653 (22.1)
Gatsibo	409 (6.7)	209 (6.7)	200 (6.8)
Huye	720 (11.8)	377 (12.1)	343 (11.6)
Kayonza	202 (3.3)	105 (3.4)	97 (3.3)
Nyagatare	913 (15.0)	462 (14.8)	451 (15.3)
Nyarugenge	507 (8.3)	274 (8.8)	233 (7.9)
Rwamagana	1,491 (24.5)	771 (24.6)	720 (24.4)
Partnered, n (column %)	1,183 (19.5)	666 (21.3)	517 (17.5)
Moderate to severe hunger, n (column %)	1,577 (25.9)	898 (28.7)	679 (23.0)
Ever had sex, n (column %)	1,723 (28.3)	633 (20.2)	1,090 (36.9)
High HIV testing self-efficacy, n (column %)	5,763 (94.8)	2,918 (93.3)	2,845 (96.4)
High contraceptive self-efficacy, n (column %)	4,882 (80.3)	2,303 (73.6)	2,579 (87.4)
Family planning peer norms, n (column %)			
Prohibitive	2,854 (46.9)	1,476 (47.2)	1,378 (46.7)
Middling	854 (14.0)	404 (12.9)	450 (15.2)
Supportive	2,346 (38.6)	1,233 (39.4)	1,113 (37.7)
Ever HIV tested, n (column %)	2,324 (38.2)	1,118 (35.7)	1,206 (40.9)
HIV tested in past year, n (column %)	1,209 (19.9)	733 (23.4)	476 (16.1)
Sexually experienced subsample	All	Female students	Male students
N (row %)	1,723 (100)	633 (36.7)	1,090 (63.3)
Reproductive autonomy scores*, mean ± SD			
Decision-making (range: 1-3)	2.2 ± 0.5	2.2 ± 0.5	2.3 ± 0.5
Freedom from coercion (range: 1-4)	3.2 ± 0.5	3.2 ± 0.5	3.2 ± 0.5
Current condom use, n (column %)	860 (49.9)	276 (43.6)	584 (53.6)
Ever condom use, n (column %)	685 (39.8)	231 (36.5)	454 (41.7)
Condom use at last sex, n (column %)	656 (38.1)	221 (34.9)	435 (39.9)

SD: standard deviation.
Missing responses: n=5 partnered, n=9 moderate to severe hunger, n=22 ever had sex, n=6 HIV testing self-efficacy, n=20 contraceptive self-efficacy, n=25 family planning peer norms, n=2 ever HIV tested, n=214 HIV tested in past year, n=36 decision-making, n=49 freedom from coercion, n=14 current condom use, n=16 ever condom use, n=51 condom use at last sex.
*Averaged response scores for two subscales from the reproductive autonomy scale; higher scores indicate greater autonomy.[144]

Table 3.2 Multivariable regression results for models of recent HIV testing in the CyberRwanda cohort.

	HIV tested in past year	No HIV test in past year	Unadjusted PR (95% CI)	Adjusted PR (95% CI)*
N (row %)	1,209 (20.6)	4,656 (79.4)	-	-
HIV knowledge score (range: 0-7), mean ± SD	6.1 ± 0.9	6.0 ± 1.0	1.06 (1.00, 1.12)	1.04 (0.99, 1.09)
HIV knowledge category, n (row %)				
Low (score: 0-4)	76 (15.5)	415 (84.5)	Reference	Reference
Medium (score: 5-6)	669 (21.2)	2,482 (78.8)	1.41 (1.14, 1.76)	1.38 (1.13, 1.67)
High (score: 7)	459 (20.9)	1,735 (79.1)	1.41 (1.10, 1.80)	1.33 (1.08, 1.64)
Comprehensive HIV knowledge, n (row %)				
No	630 (20.4)	2,455 (79.6)	Reference	Reference
Yes	576 (20.8)	2,194 (79.2)	1.04 (0.93, 1.16)	1.00 (0.90, 1.11)

PR: prevalence ratio, CI: confidence interval, SD: standard deviation.
Missing responses: n=214 HIV tested in past year, n=31 HIV knowledge score/category, n=11 comprehensive HIV knowledge; bivariate n=5,836 (HIV knowledge) and n=5,855 (comprehensive HIV knowledge).
*Adjusted for age, sex, school grade, district, partnership status, household assets index, household hunger, sexual experience, HIV testing self-efficacy; n=5,800 (HIV knowledge) and n=5,819 (comprehensive HIV knowledge) after exclusions due to missing covariates.

Table 3.3 Multivariable regression results for models of current condom use among participants who have had sex in the CyberRwanda cohort.

	Current condom user	Not currently using condoms	Unadjusted PR (95% CI)	Adjusted PR (95% CI)*
N (row %)	860 (50.3)	849 (49.7)	-	-
HIV knowledge score (range: 0-7), mean ± SD	6.1 ± 1.0	6.0 ± 1.0	1.03 (0.98, 1.07)	0.99 (0.96, 1.04)
HIV knowledge category, n (row %)				
Low (score: 0-4)	60 (48.4)	64 (51.6)	Reference	Reference
Medium (score: 5-6)	446 (50.1)	444 (49.9)	1.04 (0.87, 1.24)	0.94 (0.80, 1.12)
High (score: 7)	351 (51.2)	334 (48.8)	1.06 (0.90, 1.26)	0.94 (0.80, 1.11)
Condom beliefs score (range: 0-8), mean ± SD	4.8 ± 1.3	4.3 ± 1.3	1.13 (1.10, 1.17)	1.11 (1.07, 1.15)
Condom beliefs category, n (row %)				
Prohibitive (score: 0-3)	129 (36.8)	222 (63.2)	Reference	Reference
Middling (score: 4-5)	485 (51.2)	462 (48.8)	1.40 (1.18, 1.67)	1.34 (1.12, 1.59)
Supportive (score: 6-8)	246 (60.7)	159 (39.3)	1.67 (1.42, 1.96)	1.53 (1.28, 1.82)

PR: prevalence ratio, CI: confidence interval, SD: standard deviation.
Missing responses: n=14 current condom use, n=11 HIV knowledge score/category, n=6 condom beliefs score/category; bivariate n=1,699 (HIV knowledge) and n=1,703 (condom beliefs).
*Adjusted for age, sex, school grade, district, partnership status, household assets index, household hunger, contraceptive self-efficacy, family planning peer norms, reproductive autonomy scores; n=1,617 (HIV knowledge) and n=1,622 (condom beliefs) after exclusions due to missing covariates.

Table 3.4 Predicted marginal prevalence of current condom use by condom beliefs score among participants who have had sex.

Condom beliefs score	Marginal prevalence of current condom use, % ± SE	Marginal prevalence difference (95% CI)
Observed scores (mean: 4.55)	50.97 ± 1.53	Reference
Deterministically set scores		
0 (all prohibitive beliefs)	31.14 ± 3.04	-19.83 (-25.06, -14.59)
1	34.58 ± 2.77	-16.39 (-20.97, -11.80)
2	38.41 ± 2.44	-12.55 (-16.29, -8.82)
3	42.69 ± 2.05	-8.28 (-10.93, -5.63)
4	47.45 ± 1.69	-3.52 (-4.81, -2.22)
5	52.76 ± 1.59	1.80 (1.11, 2.48)
6	58.69 ± 2.05	7.73 (5.03, 10.42)
7	65.31 ± 3.07	14.34 (9.05, 19.64)
8 (all supportive beliefs)	72.70 ± 4.54	21.73 (13.26, 30.21)

SE: standard error, CI: confidence interval.

3.7 Supplementary Materials

Figure S3.1 Flow diagram of CyberRwanda participant sampling, recruitment, and analytic exclusions.

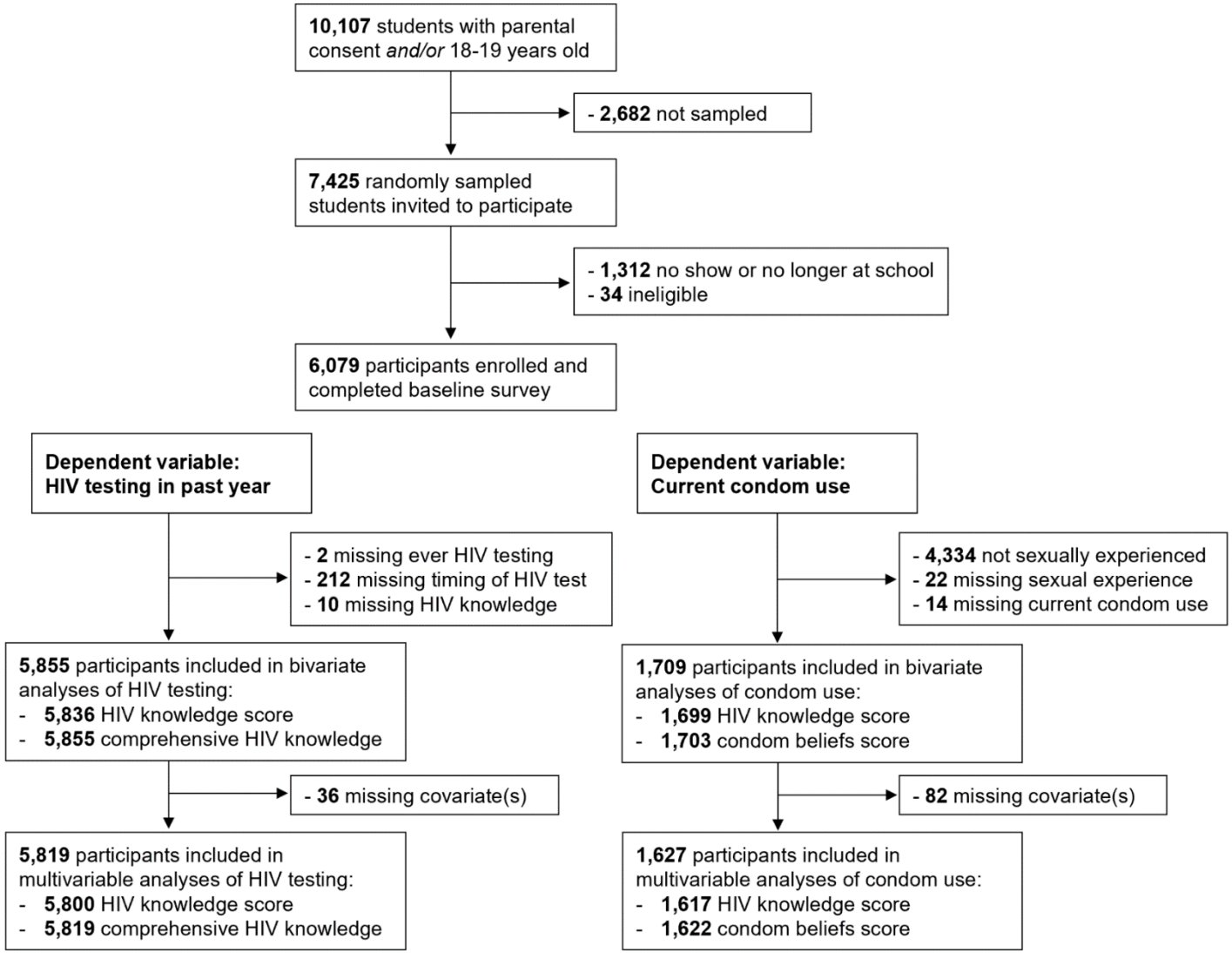


Table S3.1 Descriptive statistics of HIV knowledge by sex.

HIV knowledge (response score)	All (N=6,079)	Female students (N=3,128)	Male students (N=2,951)	P†
Can a person reduce the risk of getting HIV/AIDS by having sex with only one uninfected partner who has no other partners?*				
Yes (1)	5,067 (83.4)	2,575 (82.3)	2,492 (84.4)	.06
No (0)	840 (13.8)	449 (14.3)	391 (13.2)	
Don't know (0)	166 (2.7)	100 (3.2)	66 (2.2)	
Can a person reduce the risk of getting the HIV/AIDS virus by using a condom every time they have sex?*				
Yes (1)	5,768 (94.9)	2,943 (94.1)	2,825 (95.7)	.001
No (0)	249 (4.1)	135 (4.3)	114 (3.9)	
Don't know (0)	55 (0.9)	45 (1.4)	10 (0.3)	
Can a healthy-looking person have the HIV/AIDS virus?*				
Yes (1)	4,722 (77.7)	2,409 (77.0)	2,313 (78.4)	.008
No (0)	1,185 (19.5)	612 (19.6)	573 (19.4)	
Don't know (0)	167 (2.7)	106 (3.4)	61 (2.1)	
Can people get the HIV/AIDS virus because of witchcraft or other supernatural means?				
Yes (0)	441 (7.3)	207 (6.6)	234 (7.9)	.001
No (1)	5,250 (86.4)	2,690 (86.0)	2,560 (86.8)	
Don't know (0)	378 (6.2)	227 (7.3)	151 (5.1)	
Can a person get the HIV/AIDS virus by sharing food with someone who is infected?*				
Yes (0)	520 (8.6)	237 (7.6)	283 (9.6)	.02
No (1)	5,472 (90.0)	2,846 (91.0)	2,626 (89.0)	
Don't know (0)	85 (1.4)	43 (1.4)	42 (1.4)	
Can people get the HIV/AIDS virus from mosquito bites?*				
Yes (0)	902 (14.8)	412 (13.2)	490 (16.6)	.003
No (1)	4,979 (81.9)	2,605 (83.3)	2,374 (80.4)	
Don't know (0)	193 (3.2)	107 (3.5)	86 (2.9)	
Can men reduce their risk of getting the HIV/AIDS virus by getting circumcised?				
Yes (1)	5,268 (86.7)	2,548 (81.5)	2,720 (92.2)	<.001
No (0)	595 (9.8)	385 (12.3)	210 (7.1)	
Don't know (0)	214 (3.5)	193 (6.2)	21 (0.7)	
Comprehensive HIV knowledge‡	2,873 (47.3)	1,493 (47.7)	1,380 (46.8)	.4
HIV knowledge score, mean ± SD	6.0 ± 1.0	6.0 ± 1.0	6.1 ± 1.0	<.001
HIV knowledge category				
Low (score: 0-4)	506 (8.3)	291 (9.3)	215 (7.3)	.002
Medium (score: 5-6)	3,267 (53.7)	1,715 (54.8)	1,552 (52.6)	
High (score: 7)	2,275 (37.4)	1,106 (35.4)	1,169 (39.6)	

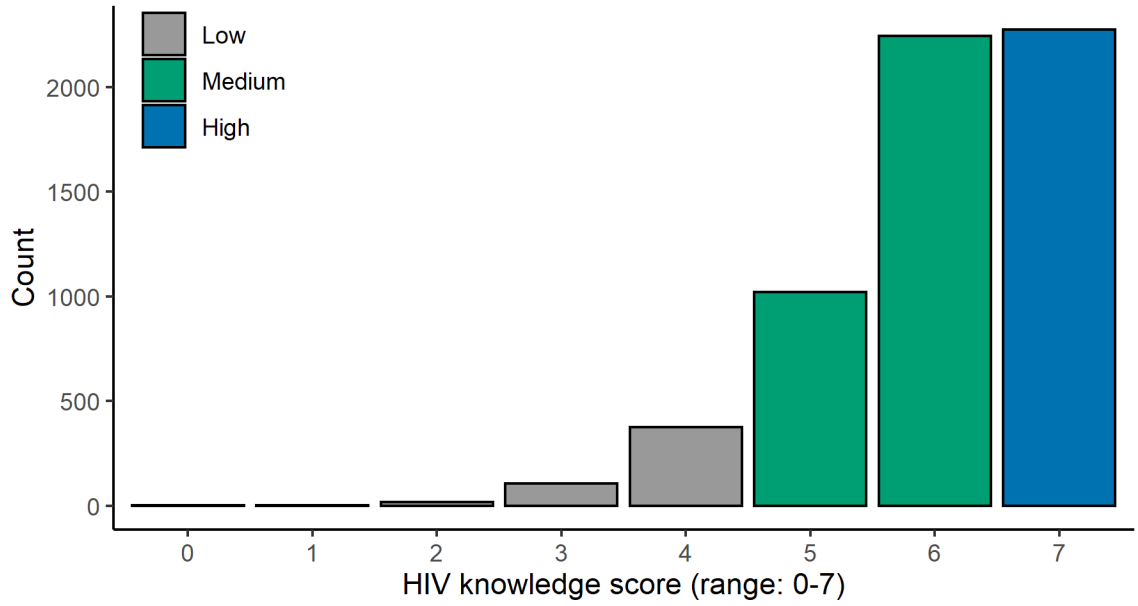
N (column %) unless otherwise noted. SD: standard deviation.
Missing responses: n=6 uninfected partner, n=7 condom, n=5 healthy-looking, n=10 supernatural, n=2 sharing food, n=5 mosquito bites, n=2 circumcised, n=11 comprehensive HIV knowledge, n=31 HIV knowledge score/category.
†P-values from chi-square tests for categorical variables and t-tests for continuous variables adjusted for school-level clustering.
‡Correctly responded to all five statements with asterisks (*).

Table S3.2 Descriptive statistics of condom beliefs by sex.

Condom beliefs (response score)	All (N=6,079)	Female students (N=3,128)	Male students (N=2,951)	P†
Condoms are an effective method of preventing pregnancy.				
Agree (1)	5,768 (94.9)	2,903 (92.8)	2,865 (97.1)	<.001
Disagree (0)	204 (3.4)	129 (4.1)	75 (2.5)	
Don't know/Not sure (0)	52 (0.9)	43 (1.4)	9 (0.3)	
Condoms are an effective way of protecting against sexually transmitted disease.				
Agree (1)	5,882 (96.8)	2,984 (95.4)	2,898 (98.2)	.01
Disagree (0)	112 (1.8)	69 (2.2)	43 (1.5)	
Don't know/Not sure (0)	29 (0.5)	22 (0.7)	7 (0.2)	
It would be too embarrassing for someone like me to buy or obtain condoms.				
Agree (0)	2,262 (37.2)	1,327 (42.4)	935 (31.7)	<.001
Disagree (1)	3,682 (60.6)	1,686 (53.9)	1,996 (67.6)	
Don't know/Not sure (0)	80 (1.3)	62 (2.0)	18 (0.6)	
If a girl suggested using condoms to her partner, it would mean that she didn't trust him.				
Agree (0)	2,106 (34.6)	1,117 (35.7)	989 (33.5)	.001
Disagree (1)	3,727 (61.3)	1,834 (58.6)	1,893 (64.1)	
Don't know/Not sure (0)	191 (3.1)	124 (4.0)	67 (2.3)	
Condoms reduce sexual pleasure.				
Agree (0)	1,916 (31.5)	813 (26.0)	1,103 (37.4)	<.001
Disagree (1)	1,820 (29.9)	829 (26.5)	991 (33.6)	
Don't know/Not sure (0)	2,288 (37.6)	1,433 (45.8)	855 (29.0)	
Condoms can slip off the man and disappear inside the woman's body.				
Agree (0)	3,888 (64.0)	1,883 (60.2)	2,005 (67.9)	<.001
Disagree (1)	622 (10.2)	291 (9.3)	331 (11.2)	
Don't know/Not sure (0)	1,514 (24.9)	901 (28.8)	613 (20.8)	
Condoms are suitable for casual relationships.				
Agree (1)	2,055 (33.8)	960 (30.7)	1,095 (37.1)	<.001
Disagree (0)	3,046 (50.1)	1,544 (49.4)	1,502 (50.9)	
Don't know/Not sure (0)	923 (15.2)	571 (18.3)	352 (11.9)	
Condoms are suitable for steady, loving relationships.				
Agree (1)	2,546 (41.9)	1,177 (37.6)	1,369 (46.4)	<.001
Disagree (0)	2,449 (40.3)	1,282 (41.0)	1,167 (39.5)	
Don't know/Not sure (0)	1,029 (16.9)	616 (19.7)	413 (14.0)	
Condom beliefs score, mean ± SD	4.3 ± 1.4	4.1 ± 1.4	4.6 ± 1.3	<.001
Condom beliefs category				
Low (score: 0-3)	1,621 (26.7)	1,017 (32.5)	604 (20.5)	<.001
Medium (score: 4-5)	3,174 (52.2)	1,553 (49.6)	1,621 (54.9)	
High (score: 6-8)	1,228 (20.2)	505 (16.1)	723 (24.5)	

N (column %) unless otherwise noted. SD: standard deviation.
Missing responses: n=55 pregnancy, n=56 sexually transmitted disease, n=55 embarrassing, n=55 trust, n=55 sexual pleasure, n=55 disappear, n=55 casual relationship, n=55 steady relationship, n=56 condom beliefs score/category.
†P-values from chi-square tests for categorical variables and t-tests for continuous variables adjusted for school-level clustering.

Figure S3.2 Histograms of summed scores for HIV knowledge and condom beliefs and corresponding categories.



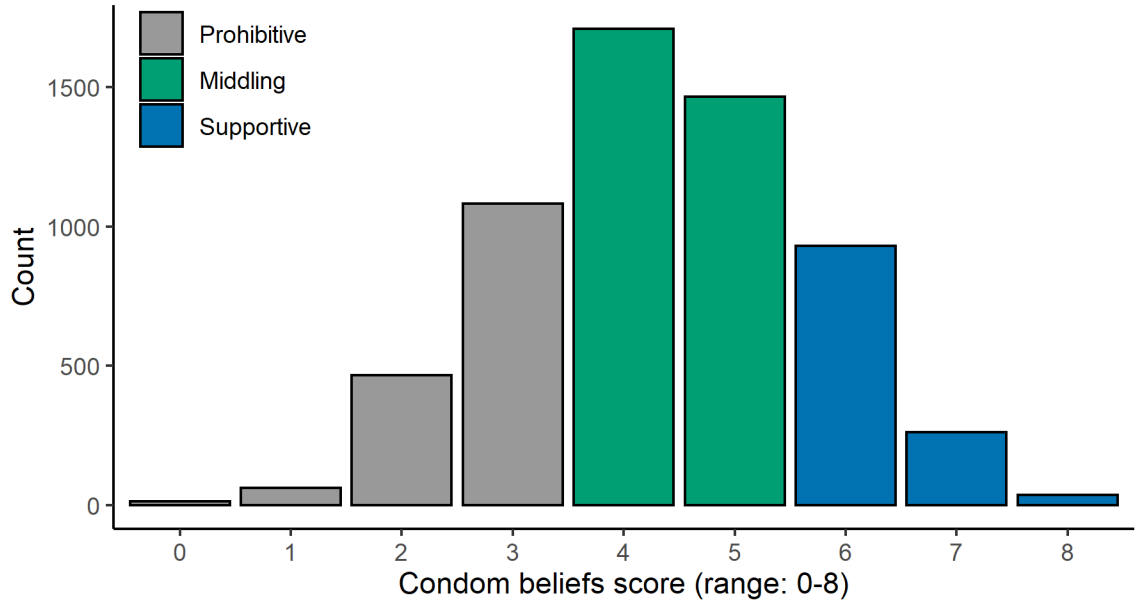


Table S3.3 Characteristics of students invited to participate by enrollment status.

	Enrolled participants	Invited non-participants	P†
N (row %)	6,079 (81.9)	1,346 (18.1)	
Age, mean ± SD	15.4 ± 1.5	15.7 ± 1.8	<.001
Sex, n (column %)			.54
Female	3,128 (51.5)	668 (49.6)	
Male	2,951 (48.5)	678 (50.4)	
Grade, n (column %)			.06
Secondary 1	3,456 (56.9)	788 (58.5)	
Secondary 2	2,623 (43.1)	558 (41.5)	
District, n (column %)			<.001
Bugesera	517 (8.5)	105 (7.8)	
Gasabo	1,320 (21.7)	222 (16.5)	
Gatsibo	409 (6.7)	136 (10.1)	
Huye	720 (11.8)	136 (10.1)	
Kayonza	202 (3.3)	32 (2.4)	
Nyagatare	913 (15.0)	414 (30.8)	
Nyarugenge	507 (8.3)	49 (3.6)	
Rwamagana	1,491 (24.5)	252 (18.7)	

SD: standard deviation.
Data sources: survey responses (enrolled participants), school records (invited non-participants).
†P-values from chi-square tests for categorical variables and t-tests for continuous variables adjusted for school-level clustering.

Figure S3.3 Probability of HIV testing and condom use by HIV knowledge and condom beliefs scores, respectively.

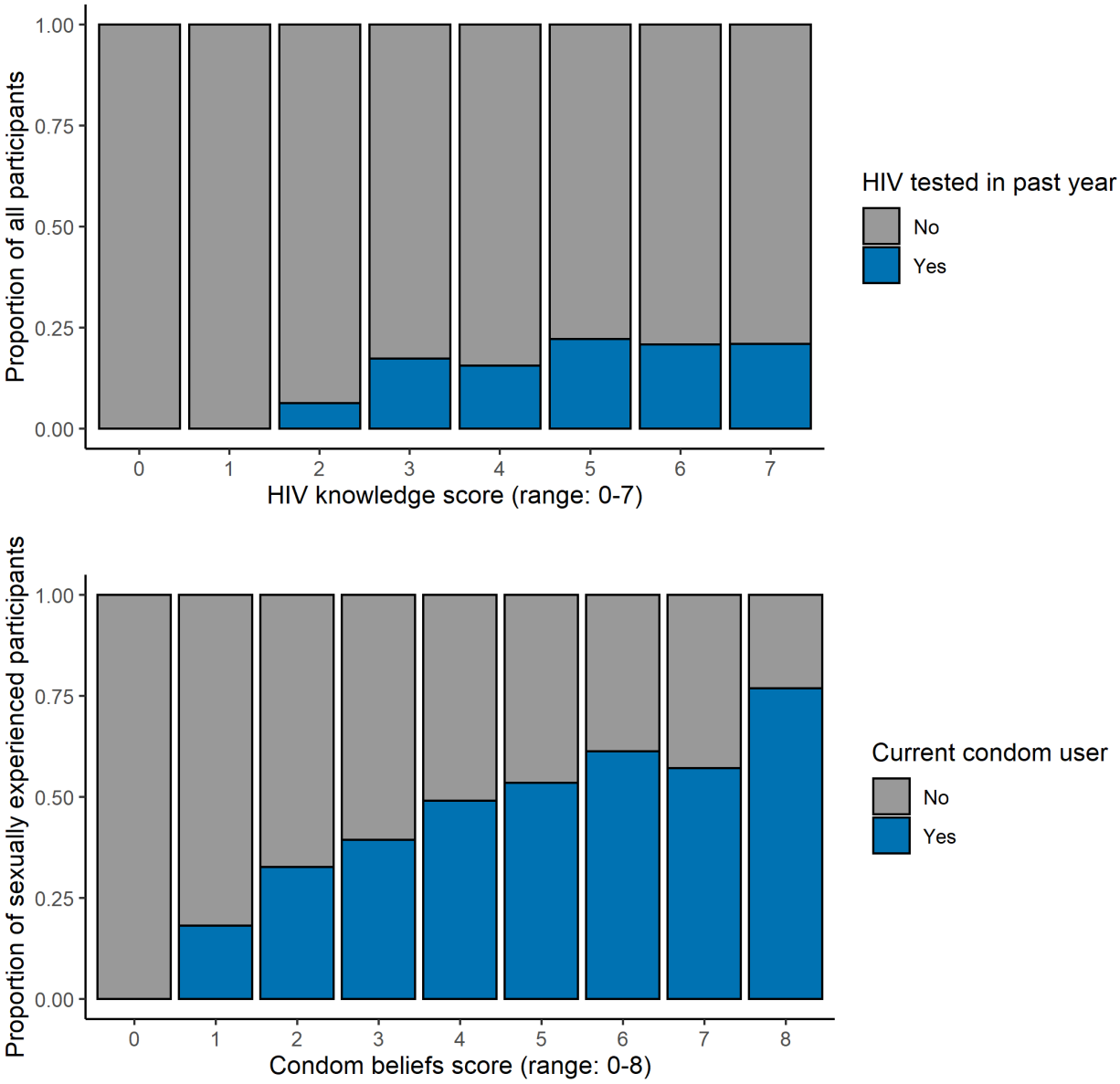
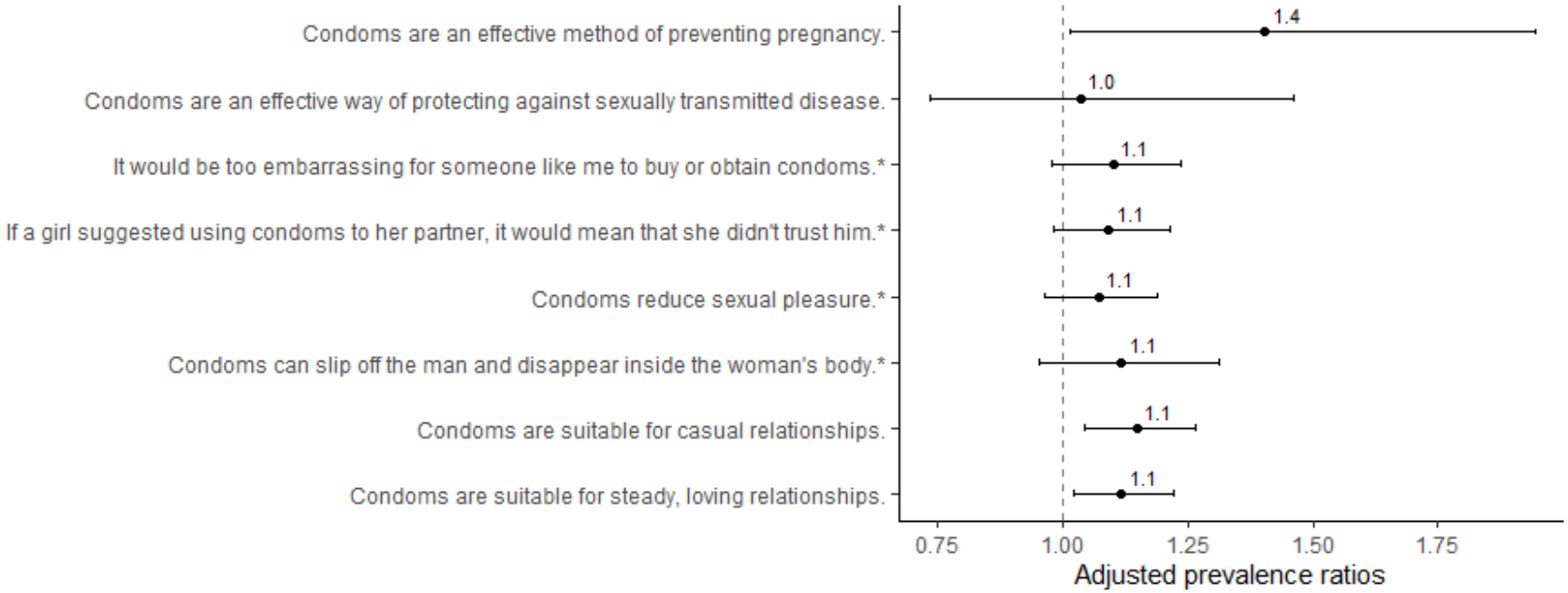


Figure S3.4 Multivariable regression results for model of current condom use by individual condom beliefs among participants who have had sex.



*Reverse coded.
Prevalence ratios adjusted for age, sex, school grade, district, partnership status, household assets index, household hunger, contraceptive self-efficacy, family planning peer norms, reproductive autonomy scores; n=1,622 after exclusions due to missing covariates.

Table S3.4 Multivariable regression results for models of ever HIV testing.

	Ever HIV tested	Never HIV tested	Unadjusted PR (95% CI)	Adjusted PR (95% CI)*
N (row %)	2,324 (38.2)	3,753 (61.8)	-	-
HIV knowledge score (range: 0-7), mean ± SD	6.1 ± 1.0	6.0 ± 1.0	1.06 (1.03, 1.10)	1.04 (1.01, 1.07)
HIV knowledge category, n (row %)				
Low (score: 0-4)	150 (29.6)	356 (70.4)	Reference	Reference
Medium (score: 5-6)	1,257 (38.5)	2,009 (61.5)	1.31 (1.14, 1.51)	1.25 (1.11, 1.41)
High (score: 7)	905 (39.8)	1,370 (60.2)	1.35 (1.17, 1.55)	1.23 (1.09, 1.39)
Comprehensive HIV knowledge, n (row %)				
No	1,214 (38.0)	1,980 (62.0)	Reference	Reference
Yes	1,106 (38.5)	1,767 (61.5)	1.01 (0.95, 1.08)	0.98 (0.92, 1.05)

PR: prevalence ratio, CI: confidence interval, SD: standard deviation.
Missing responses: n=2 ever HIV tested, n=31 HIV knowledge score/category, n=11 comprehensive HIV knowledge; bivariate n=6,047 (HIV knowledge) and n=6,067 (comprehensive HIV knowledge).
*Adjusted for age, sex, school grade, district, partnership status, household assets index, household hunger, sexual experience, HIV testing self-efficacy; n=6,009 (HIV knowledge) and n=6,029 (comprehensive HIV knowledge) after exclusions due to missing covariates.

Table S3.5 Multivariable regression results for models of condom use at last sex among participants who have had sex.

	Condom used at last sex	No condom use last sex	Unadjusted PR (95% CI)	Adjusted PR (95% CI)*
N (row %)	656 (39.2)	1,016 (60.8)	-	-
HIV knowledge score (range: 0-7), mean ± SD	6.1 ± 1.0	6.0 ± 1.0	1.08 (1.02, 1.14)	1.04 (0.97, 1.10)
HIV knowledge category, n (row %)				
Low (score: 0-4)	44 (36.7)	76 (63.3)	Reference	Reference
Medium (score: 5-6)	318 (36.6)	551 (63.4)	0.99 (0.78, 1.25)	0.88 (0.70, 1.12)
High (score: 7)	291 (43.3)	381 (56.7)	1.18 (0.94, 1.48)	1.01 (0.80, 1.28)
Condom beliefs score (range: 0-8), mean ± SD	4.8 ± 1.3	4.4 ± 1.3	1.15 (1.09, 1.21)	1.13 (1.07, 1.20)
Condom beliefs category, n (row %)				
Prohibitive (score: 0-3)	93 (27.3)	248 (72.7)	Reference	Reference
Middling (score: 4-5)	372 (40.3)	552 (59.7)	1.50 (1.21, 1.85)	1.38 (1.11, 1.71)
Supportive (score: 6-8)	191 (47.6)	210 (52.4)	1.75 (1.38, 2.23)	1.60 (1.25, 2.06)

PR: prevalence ratio, CI: confidence interval, SD: standard deviation.
Missing responses: n=51 condom use at last sex, n=11 HIV knowledge score/category, n=6 condom beliefs score/category; bivariate n=1,661 (HIV knowledge) and n=1,666 (condom beliefs).
*Adjusted for age, sex, school grade, district, partnership status, household assets index, household hunger, contraceptive self-efficacy, family planning peer norms, reproductive autonomy scores; n=1,581 (HIV knowledge) and n=1,587 (condom beliefs) after exclusions due to missing covariates.

Table S3.6 Predicted marginal prevalence of condom use at last sex by condom beliefs score among participants who have had sex.

Condom beliefs score	Marginal prevalence of condom use at last sex, % ± SE	Marginal prevalence difference (95% CI)
Observed scores (mean: 4.55)	39.80 ± 1.49	Reference
Deterministically set scores		
0 (all prohibitive beliefs)	22.54 ± 3.60	-17.25 (-23.18, -11.32)
1	25.40 ± 3.32	-14.40 (-19.68, -9.12)
2	28.64 ± 2.93	-11.16 (-15.54, -6.77)
3	32.33 ± 2.44	-7.47 (-10.65, -4.30)
4	36.52 ± 1.87	-3.28 (-4.89, -1.67)
5	41.29 ± 1.51	1.49 (0.74, 2.24)
6	46.72 ± 1.98	6.92 (3.66, 10.19)
7	52.92 ± 3.36	13.12 (6.50, 19.74)
8 (all supportive beliefs)	59.99 ± 5.38	20.19 (9.32, 31.06)

SE: standard error, CI: confidence interval.

Conclusion

Adolescence and young adulthood are important developmental stages that lay the foundation for subsequent health behaviors and outcomes, yet youth experience unique challenges in accessing health products and services. In this dissertation, I apply epidemiologic methods to evaluate and inform several innovative approaches to increase access to health services among adolescents and young adults. Each chapter summarizes the findings of one of three studies focused on youth-centered approaches to address public health challenges such as unintended pregnancy, HIV/STI, and COVID-19.

Chapters 1 and 2 describe the successful implementation of multipronged approaches to reduce structural and social barriers to health services among primarily adolescent and young adult populations. Notably, both were voluntary, incentivized, and incorporated aspects of self-care interventions (i.e., HIV self-testing provided in neighborhood drug shops, engagement with a digital system to prompt self-scheduling of COVID-19 testing appointments) to encourage youth's uptake of potentially stigmatizing services.

This was achieved in Chapter 1 by using empathic design methodologies and behavioral science to develop a loyalty program intervention for young women at privately-owned drug shops in Tanzania. Alongside deep collaboration with community stakeholders, this approach resulted in an intervention which was closely attuned to young women's needs and preferences and smoothly integrated with the daily routines of both young women and drug shopkeepers. A pilot randomized trial found strong preliminary evidence that the intervention increased uptake of HIV self-testing, contraception, and health facility referrals among young women at drug shops. These findings suggest that enhancing private sector drug shops with specialized programs designed to cater to young women may be an effective strategy to reach them with SRH services.

The integrated testing and monitoring system presented in Chapter 2 was created in response to a pressing need to identify effective SARS-CoV-2 outbreak mitigation strategies for university students and employees during the first year of the COVID-19 pandemic. Designed and implemented through rapid collaboration across university departments, the system encouraged students to actively contribute to public health efforts via incentivized participation and easy-to-access self-scheduled testing. As practical constraints did not allow for a randomized assessment of this system, a cohort study design was used to collect and triangulate multiple sources of longitudinal data. Analyses provided evidence that the system identified a high proportion of incident SARS-CoV-2 infections and may have prevented community transmission after a superspreader event among students in congregate housing. These findings demonstrate that integrated monitoring systems can successfully identify and link at-risk students to COVID-19 testing and support continued investment in non-punitive approaches to infection control.

In contrast to the pilot studies in Chapters 1 and 2, which implemented and evaluated youth-friendly strategies to facilitate health service uptake, Chapter 3 relied upon purely observational data to inform the design of future interventions. I analyzed survey responses from more than 6,000 Rwandan secondary school students to explore knowledge- and norms-related barriers to HIV testing and condom use among adolescents. These analyses found relatively high HIV knowledge, but widespread misconceptions and prohibitive beliefs about condoms that were associated with a lower probability of condom use. While the cross-sectional study design precludes the assessment of temporality, the association between condom beliefs and condom use suggests that misinformation and negative social norms about condoms may hinder efforts to reduce the incidence of HIV and unintended pregnancy among Rwandan youth. These findings motivate renewed attention to educational gaps about condoms' value in prevention and school-based interventions to create supportive social norms around condom use among youth.

In summary, this dissertation provides evidence supporting the implementation of tailored, multipronged approaches to reduce barriers to health services experienced by adolescents and young adults. The three studies presented reinforce several key characteristics of effective interventions to promote health service uptake by youth. Youth-friendly interventions should offer ready access to reliable information and create low-barrier entry points to health services in tandem with theory-informed strategies to reduce stigma and engender supportive social norms around service uptake. Interventions should be designed for and with their intended recipients and aligned closely with the settings in which they will be implemented. To reach youth who face the greatest barriers to healthcare, interventions should move beyond formal health systems to other community settings, such as drug shops and schools. Taken together, this research also underscores the importance of epidemiologic data collection and analysis as a tool to identify gaps, evaluate impact, and enable evidence-based decision-making to reduce inequities experienced by youth and support health and well-being across the life span.

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