Project Brief: South African Male User Research on Acceptability of Implants and Injections

Full Title of Study/Programme	**South African Male User Research on Acceptability of Implants and Injections** **Short Title:** SAMURAI
Technical Focus Area/Key Words	HIV risk among men, Long-acting PrEP (implants and injectables) acceptability in men, measuring acceptability in a cross-over clinical study with placebo products and, assessing product preferences and trade-offs using a discrete choice experiment.
Rationale	Our previous formative research has shown that young people – both women and men – in Cape Town, South Africa, are willing to use injectable and implantable products for HIV prevention. In the iPrevent Discrete Choice Experiment (DCE) that our team conducted, men demonstrated a high level of interest in Long-acting (LA) delivery methods. iPrevent findings highlight that men are theoretically more amenable than women to the concept of using an implant for HIV prevention: 67% of heterosexual men and MSM expressed a preference for a 6-month implant over a bimonthly injection, whereas only 52% of women had the same preference. Placebo crossover studies offer another approach to measure end-user "revealed" preferences through observable product choice and use. This study design yields findings that extend to real-world settings more readily than those from highly controlled clinical trials that typically evaluate a single product against a placebo and likewise permit examination of product acceptability and implementation considerations for products still in early-stage clinical development or with proven efficacy but not yet licensed for use. By using placebo products in this study, men have the opportunity to actually experience using the dosing platforms as opposed to measuring hypothetical attitudes. As seen in our previous Trio and Quatro studies, opinions regarding a novel HIV prevention method changed after actual product use. The design will permit us to focus on attributes of the delivery forms free from drug-related side effects or varying (or unknown) efficacy that might influence acceptability. Additionally, the design of our study, such that implant use has a longer visit interval and the less invasive injection has more frequent visits, offers an innovative counterbalance in user experience, replicating future real-world scenarios. The use of placebo versions of novel drug delivery platforms for HIV prevention enables us to learn valuable information about acceptability and safety, contributing important data to optimize the success and investment in product development, testing and roll-out. The objective of the DCE is to enhance our understanding of men's acceptability of LA products through a rigorous assessment of product preferences and trade-offs which will complement the experiential acceptability assessed during

	the clinical portion of the study. Ultimately the aim is to develop an HIV prevention method (both delivery form and API) that is not only efficacious but that will be liked and consistently used by men – both heterosexual and MSM – and thereby will have a global public health impact. The risks to human subjects are minimal to moderate in this study – there are no pharmaceutical drugs being investigated, implant insertions are a moderate clinical procedure, and injections are a minor clinical procedure. This research will result in important knowledge about men's willingness and ability to use an implant in the context of HIV prevention. The knowledge gained in this study will address the overall acceptability of HIV prevention product delivery forms to men, with particular focus on implant acceptability compared to injections.
Primary Objectives	**Acceptability:** • To assess acceptability of placebo implants and injections as LA-PrEP delivery formulations • To measure willingness to use active LA-PrEP in the future **Adherence:** • To measure initiation and persistence of placebo LA-PrEP use
Secondary Objectives	**Expanded Acceptability:** • To measure preferences for LA-PrEP attributes through product ranking and a discrete choice experiment **Burden:** • To assess pain and tolerability of signs and symptoms associated with placebo LA-PrEP use **Safety Outcomes:** • To assess adverse events (AEs) and social harms (SH) associated with placebo LA-PrEP use
Tertiary Objectives	N/A
Primary Endpoints/Outcomes	**Acceptability:** • Self-reported satisfaction rating **Adherence:** • Proportion of participants initiating products and duration of use, in months
Secondary Endpoints/Outcomes	**Expanded Acceptability:** • Self-reports of acceptability of and dissatisfaction with product-specific attributes (e.g., use regimen, visibility of implant, implant insertion/removal or injection site) • Results of DCE **Burden: product-specific pain and symptoms:** • Visual analogue pain scale • Reported tolerability of signs and symptoms at injection/insertion site **Safety endpoints:** • Number, relatedness, and severity of reported AEs and serious adverse events • Number and severity of SH reported
Tertiary Endpoints/Outcomes	N/A

Study Design	Clinical crossover study in which participants are randomized 1:1 to receive one placebo implant for 6 months and a bimonthly placebo injection for 6 months and switch to use the second product for the next 6 months. Participants will complete a DCE at baseline and at 12 months, and a subset (~10%) will be purposively selected to complete IDIs to augment and enrich our acceptability assessment.
Study arms	N/A
Study population	Healthy, HIV-uninfected heterosexual men (100) and men-who-have-sex-with-men (MSM; 100) aged 18–35 years in South Africa
Study sample size	200 participants (100 heterosexual men and 100 men-who-have-sex-with-men)
Follow up/duration	Approximately 12 months.
Study/Programme sites	Wits Reproductive Health and HIV Institute (Wits RHI) Desmond Tutu Health Research Foundation (DTHF)
Study/Programme duration	Approximately 18 months.
Intervention	Participants will be randomized in a 1:1 ratio to one of two study products: • **Six months of placebo subdermal implant use** • **Six months of bimonthly placebo intramuscular injection** Thereafter, participants will receive the other study product for the following six months for a total of twelve months. All participants will complete a DCE at baseline and at 12 months, and a subset (~10%) will complete an IDI at 12 months to augment and enrich our acceptability assessment.
Operations	Data and Specimen Collection
Investigators	**Wits Reproductive Health and HIV Institute (Wits RHI)** Prof Thesla Palanee-Phillips (Co-Principal Investigator) Dr Nkosiphile Ndlovu (Co-Principal Investigator)
Other Partners & Collaborators	**Desmond Tutu Health Research Foundation (DTHF)** Dr Katherine Margaret Kill (Principal Investigator) **Women's Global Health Imperative (WGHI) at RTI International** Elizabeth Montgomery (Principal Investigator) Alexandra Minnis (Co-Principal Investigator)
Linked Sub Studies and post grad projects	Formative Research Related to South African Male User Research on Acceptability of Implants and Injections
Publications/key presentations to date	*AIDS 2024, the 25th International AIDS Conference* **Abstract**: Baseline preferences and acceptability ratings for long-acting pre-exposure prophylaxis (LA-PrEP) implants and injections: Evidence for choice in HIV prevention among South African men
Progress Update	The site achieved the accrual target in June 2023. The first participant was exited after completing all study visits in August 2023. Follow-up and Exit Visits continue with 27 of the 100 enrolled participants pending Exit Visits. The last visit is planned for the end of May 2024.
Frequency of donor narrative report	n/a

Overall Study/Project Contact	Prof Thesla Palanee-Phillips
Briefing owner and date	Sihle Zulu, 03 April 2024