Project Brief: PrEP SMART

Title	**PrEP SMART: Evaluation of stepped PrEP adherence support for young South African women using a SMART design**
Purpose	To test a stepped model of scalable adherence support strategies in South African young women who initiate PrEP, using a SMART design.
Primary Objectives	To evaluate the proportion of young South African women who adhere well to PrEP with regular clinic visits and mHealth interventions alone, the proportion of women who adhere well to PrEP with intensified interventions (i.e. monthly visits and special issue counselling or quarterly visits with drug-level feedback about recent adherence), and the optimal sequence of intensifying adherence support among young women who have low adherenceafter the first two months of use.
Secondary Objectives	• To assess the proportion who achieve high adherence early (month 2). • To assess the correlates of PrEP adherence, after adjusting for study arm, including adherence at prior study visits, sociodemographic factors, individual-level and partner-level characteristics, use of adherence support, and risk practices. • To assess the proportion of young women who discontinue PrEP, timing of discontinuation, and factors associated with PrEP discontinuation. • To characterize SMS response rates and the content and frequency of use of WhatsApp groups. • To qualitatively explore factors that influence women's decisions to use PrEP and adhere to PrEP and their satisfaction/preferences for with their assigned intervention(s).
Study Design	Sequential, Multiple Assignment, Randomized, Trial (SMART) design, whereby participants are initially randomized to either two-way SMS or WhatsApp groups and then those who need more intensive PrEP adherence support are re-randomized to monthly counseling or drug-level feedback based on PrEP drug levels. Qualitative data collection conducted with a purposive sample of approximately 50 responders and non-responders after their 2-, 6-, and exit study visits.
Study population	HIV-uninfected women ages 18-25 in Johannesburg, South Africa.
Intervention	Eligible women who accept open-label daily oral PrEP will be enrolled and randomized to SOC adherence support (brief counseling) and either WhatsApp groups or weekly two-way SMS messages. These mHealth interventions are aimed at increasing PrEP adherence during follow-up by providing peer support for PrEP adherence (WhatsApp groups), clinical support to manage side effects and address adherence issues (SMS messages), and reminders about daily PrEP pill-taking (both WhatsApp groups and SMS messages). Follow-up visits will occur monthly for 3 months and, in both groups, tenofovir drug levels at month 2 will be used as an objective measure of adherence to determine whether they have achieved high adherence based on their initial randomization. Women with high adherence (i.e., TFV-DP ≥500 fmol/punch from DBS, 'responders') will continue with the adherence support to which they were initially randomized and will attend quarterly visits for a total of 9 months of follow-up. 'Non-responders' will be identified based on TFV-DP <500 fmol/punch or missed drug refills at their Month 1 or 2 study visits and will continue initial randomization (WhatsApp or two-way SMS) plus be randomized to either more intensive adherence support – continued monthly visits with adherence and problem-focused counseling at months 3-8 or quarterly

	visits between months 3-9 with feedback about adherence based on drug levels at months 2 and 6.
Follow-up/Duration	Approximately 48 months, including submissions to Institutional Review Boards (IRBs) and the South African Health Products Regulatory Authority (SAHPRA, formerly the Medicines Control Council), recruitment, and 9 months of follow-up per participant.
Study/Programme sites	Ward 21 CRS, Wits RHI, University of the Witwatersrand, in Johannesburg, South Africa.
Study sample size	Up to 500 women who accept PrEP will be consented and randomized (1:1) to SOC adherence support and either WhatsApp groups or weekly two-way SMS.
Primary Endpoint	The primary outcome for the combined intervention is the proportion with high adherence measured by TFV-DP levels at 9 months.
Secondary Endpoint	Secondary outcomes include measuring TFV-DP at 2 months to assess short-term intervention effects on PrEP use.
Investigators	Principle Investigator: Sinead Delany-Moretlwe Sub-Investigators: Nicole Poovan; Dr Jeanne Omony; Kim Comline; Dr Danielle Travill; Dr Carrie Mathew
Protocol Team	Connie Celum: Protocol Chair; Sinead Delany-Moretlwe: Co-chair
Other Partners & Collaborators	University of Washington (UW)
Sponsors/Donors	US National Institute of Mental Health (HIMH) and US National Institute of Health (NIH)
Key Words	HIV, PrEP, Adolescents
Progress Update as at 09 September	Screened: 696 Enrolled: 360 Product holds: 6 Terminations: 67 Total - Withdrawals: 11 - Death/s: 1 - Seroconversions: 4 - M12/Study Exits: 147
Linked Sub Studies and post grad projects	N/A
Publications/key presentations to date	N/A
Frequency of donor narrative report	Annually
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