PrEPVacc: trial implementation and baseline data

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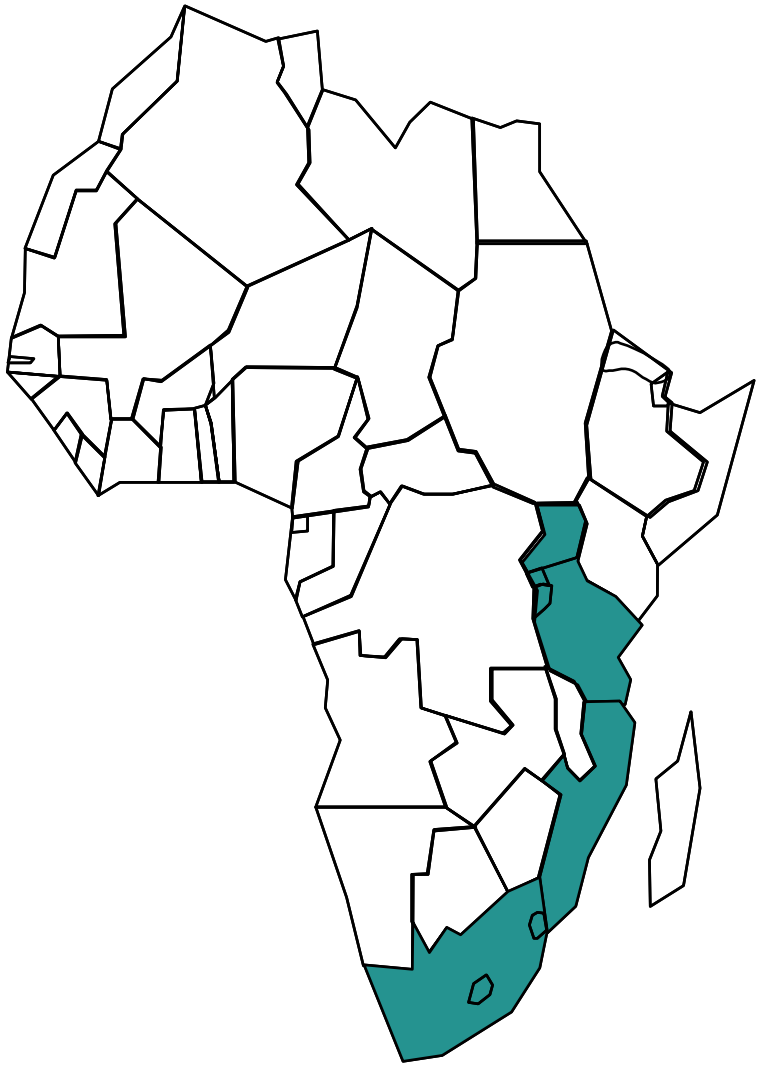

Study populations

- Fisherfolk, FSW, and other at-risk populations in **Masaka, Uganda**
- Bar workers and Female Sex Workers, **Dar Es Salaam, Tanzania**
- Female bar workers, **Mbeya, Tanzania**
- General and key populations, **Maputo, Mozambique**
- General population, **Durban, South Africa**

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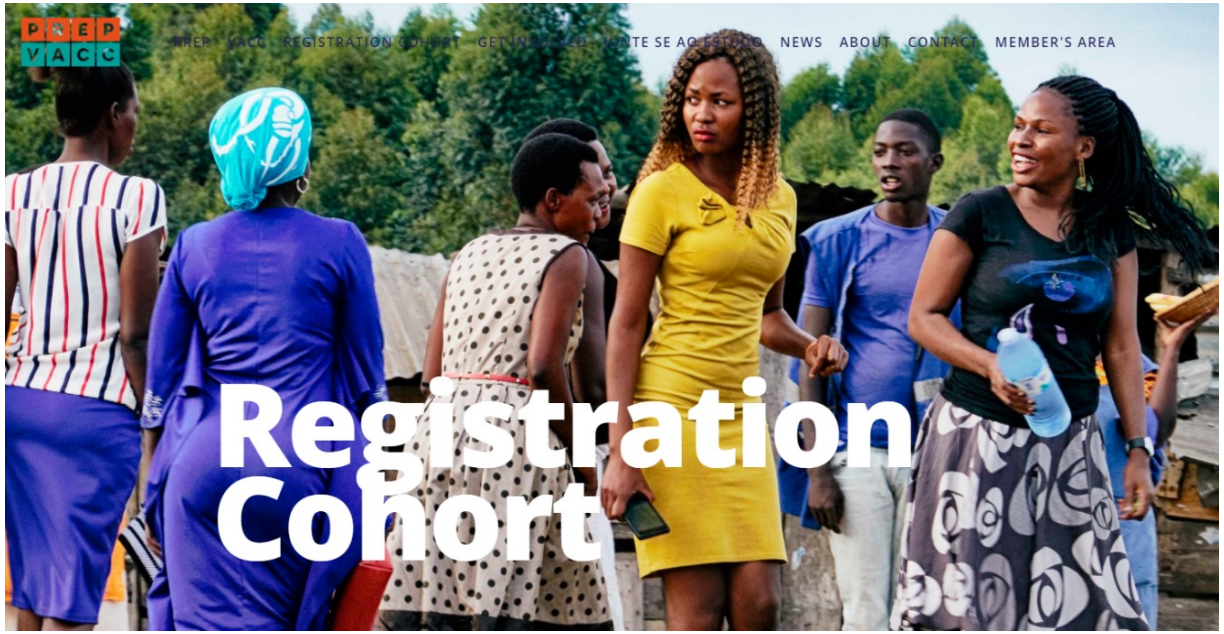
Registration Cohort: A Prospective, Longitudinal Observational Study

- **Objective:** to prepare a population of HIV negative individuals at risk of acquiring HIV for possible participation in the PrEPVacc trial

- Target HIV incidence threshold of 2/100 PY to proceed to trial



Registration cohort overview (N=4,067)

Site	Date first Participant enrolled	Date last Participant enrolled	Number enrolled	Proceeded to trial
Masaka	Jul 2018	Aug 2022	1,317	Yes
Phoenix, Durban	Aug 2018	Apr 2019	199	Closed in 2019 Transitioned to Verulam as infrastructure already there to support trial
Mbeya	Sep 2018	Jun 2022	920	Yes
Dar es Salaam	Oct 2018	Jun 2022	1,003	Yes
Maputo	Jan 2019	Jun 2021	272	Closed in 2021 Low HIV incidence, COVID-19 disruptions
Verulam, Durban	Sep 2020	Jan 2022	356	Yes

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First trial enrolments

Trial successfully opened at four sites despite COVID-19 disruptions (https://www.prepvacc.org/news)

Masaka

December 2020

16 DECEMBER 2020

First enrolments to PrEPVacc clinical trial at Masaka

Mbeya

July 2021

29 JULY 2021

Mbeya begins enrolment to PrEPVacc clinical trial

Dar es Salaam

September 2021

16 SEPTEMBER 2021

MUHAS enrols its first participants to the PrEPVacc clinical trial

Verulam, Durban

September 2021

30 SEPTEMBER 2021

First enrolments to PrEPVacc clinical trial at SAMRC in Durban

Challenges in implementation

- **Loss of Maputo site:** HIV incidence at the site was lower than 2/100 PY – good news for the community but one less clinical research centre in the trial
- **Delayed start:** COVID-19 slowed everything down, so enrolment did not start until December 2020, and it was slow despite >3000 participants in the cohort
- **Vaccination pauses:** In May 2021 and April 2022, we had to pause all 3rd and 4th vaccines to allow for regulatory reviews of IP stability data
  - Consequently, we adapted the trial to fully enrol to meet the target of 556 per arm for at least one of the combination regimens
- **Disruption of supply chains:** COVID-19 impacted supply of laboratory reagents and test kits, and this remains a challenge

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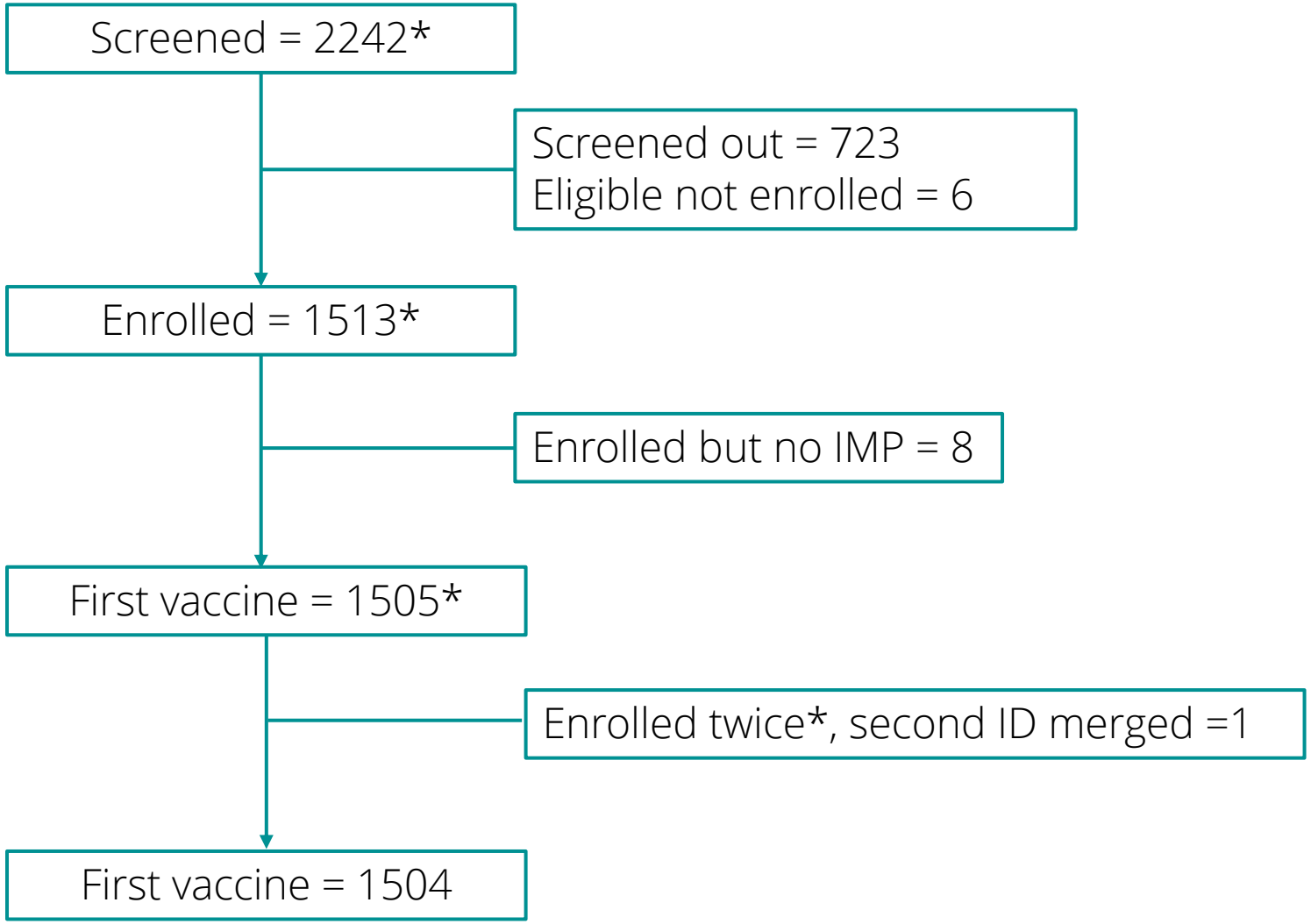
Consort for the trial



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Baseline characteristics by centre

	Masaka N=512	Mbeya N=455	Dar es Salaam N=185	Verulam N=360	All centres N=1,512
From Cohort, N (%)	376 (73)	199 (44)	140 (76)	212 (59)	927 (61)
Median age (IQR)	25 (22-29)	24 (21-27)	26 (24-30)	25 (22-29)	25 (22-29)
Female, N (%)	413 (81)	455 (100)	185 (100)	269 (75)	1322 (87)
Any STI, N (%)	160 (31)	146 (32)	17 (9)	68 (19)	391 (26)
≥3 condomless sex partners last 3m, N (%)	434 (85)	401 (88)	131 (71)	92 (26)	1058 (70)
Ever taken PrEP	30 (6)	12 (3)	12 (6)	2 (1)	56 (4)

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Vaccines by centre – 02 Oct 2023

	Masaka N=512	Mbeya N=455	Dar es Salaam N=185	Verulam N=360	All centres N=1,512
First Vaccine	508	452	185	359	1504
Second Vaccine	485	430	177	354	1446
Third Vaccine	435	373	174	332	1314
Fourth Vaccine	347	242	166	261	1016

Data extract of 2nd October 2023, data entry ongoing

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Study PrEP by centre – 02 Oct 2023

Study PrEP NOT taken	Masaka N=496	Mbeya N=436	Dar es Salaam N=180	Verulam N=357	All centres N=1,469
Since last visit, N (%)	151 (30)	5 (1)	5 (3)	11 (3)	172 (12)
Before last condomless sex, N (%)	229 (46)	42 (10)	20 (11)	65 (18)	356 (24)

Study PrEP dispensed at visits 2, 4 and 7 and other visits if required through to visit 9

Data in table taken from the last of visits 4, 6, 7 attended (~4, 8 and 16 weeks from enrolment)

- Target was 80% adherence and focused on PrEP taken around condomless sex acts

Data extract of 2nd October 2023, data entry ongoing

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Non-study PrEP by centre – 02 Oct 2023

At visit 12 Non-study PrEP taken	Masaka N=372	Mbeya N=256	Dar es Salaam N=166	Verulam N=263	All centres N=1,057
Since last visit, N (%)	12 (3)	9 (4)	45 (27)	17 (7)	83 (8)

- Note smaller numbers that have reached this timepoint in each centre
- Prior to visit 12, participants have study PrEP left over
- Dar es Salaam and Verulam provide non-study PrEP in the clinic; Masaka and Mbeya in liaison with local providers

Data extract of 2nd October 2023, data entry ongoing

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Summary of Safety

- Trial Safety Group reviews adverse event lists twice a month by centre
- Notable Events other than pregnancy and social harms
  - Severe (grade 3) reactions lasting >72 hours = 0
  - Grade 3 laboratory events that were confirmed on repeat testing = 5 (none related)
  - Adverse Event leading to a clinical decision to discontinue vaccines = 3 (syncope, eye inflammation and thrombocytopaenia)
  - Adverse Event leading to a clinical decision to discontinue PrEP = 0
- 24 Serious Adverse Events
  - 1 related (syncope within an hour of injections)
  - 3 fatalities (post-abortion haemorrhage, alcoholic liver disease, renal cancer)
  - 20 others (most commonly injury/poisoning and those related to pregnancy and childbirth)
- 23 participant pregnancies were within 18 weeks of a vaccine or whilst taking Descovy

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IDMC listing with 2nd October 2023 extract, data entry ongoing

Summary of Social Harms

- 27 moderately severe harms, all from East African sites
  - Mostly partners finding PrEP and assuming it was for treating HIV

- 3 significant social harms reported as Notable Events
  - Participant was unable to travel to another country for work due to vaccine induced seropositivity (VISP) in the recruitment agency test
  - Participant who was getting married went for HIV testing with her partner and was found to be reactive (uninfected in HIV testing algorithm) and her partner postponed the wedding until her test is no longer reactive
  - Participant beaten by her partner and shunned by her community after false allegation of transmitting HIV to her partner

IDMC listing with 2nd October 2023 extract, data entry ongoing

IDMC Recommendation

- The IDMC met on 9th November 2023 and recommended that injections stop, but the PrEP trial continue
- The primary reason was futility i.e., little or no chance of demonstrating effectiveness
- Injections were paused from 10th November 2023
- The Trial Steering Committee met with the trial team and the Sponsor on 22nd November 2023 and accepted the IDMC recommendation and injections were discontinued

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Impact on trial

- Participants, Community Advisory Boards, Community Working Groups and national authorities (regulatory and ethics) have informed of this change
- Enrolment was already complete, and there were only 10 participants who had yet to enter the primary vaccine analysis (the third vaccine timepoint)
- Follow-up for safety and HIV testing will continue for six months (24 weeks) after the last injections which will be the end of April
- The study team and participants will remain blind to allocation and results until the study database is locked
- Participants will be recalled and informed about their VISP status and provision of an ongoing HIV testing service
- Although the PrEP trial will finish in January 2024 at the latest, results will follow the vaccine trial results

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Conclusion and Lessons Learned

- The Registration Cohort informed which centres joined the trial, and their targets
- COVID was very disruptive – having an adaptive design helped us to achieve the target sample size for one of the vaccine trials
- Significant social harm, although infrequent, was seen with VISP and it will be critical to provide testing and support beyond the trial
- Although including a PrEP trial with the two vaccine trials was confusing for communities initially, centres overcame this - and it was very efficient, using a minimum number of participants
- PrEP awareness was raised in all communities, but we observed familiar challenges for oral PrEP – stigma and economic vulnerability often posing a greater risk than the perceived benefits

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