Hormonal Contraceptives and HIV Risk: HPTN 035

Z. Mike Chirenje MD FRCOG
UZ-UCSF Collaborative Research Program
Harare, Zimbabwe **chirenje@uz-ucsf.co.zw**

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MTN
microbicide trials network

Outline of Presentation

- Background
- What was HPTN 035?
- Statistical analysis for the sub-study
- Results of the sub-analysis
- Study Results
- Summary/Conclusions

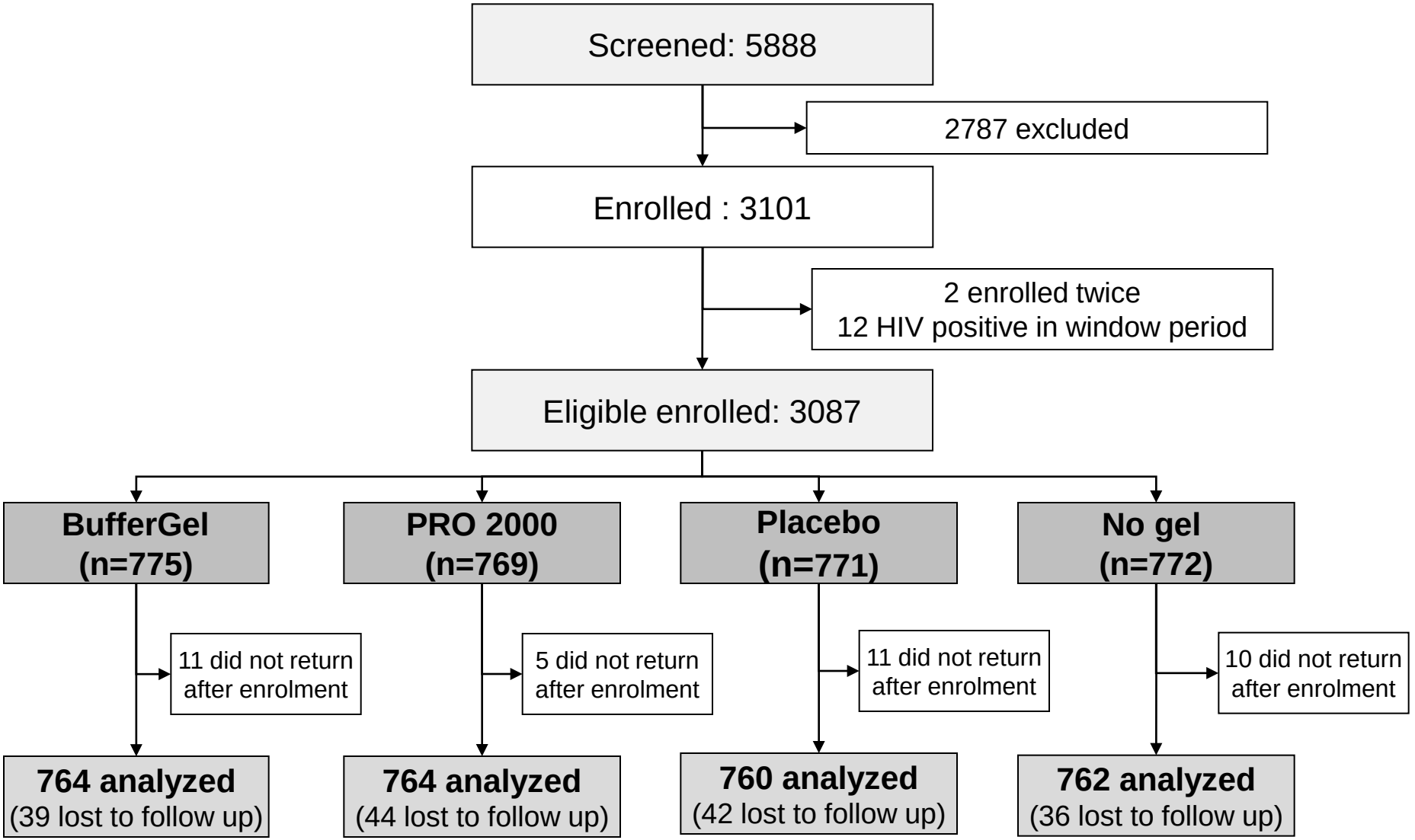
Background

- Inconsistent study results association HC and HIV risk acquisition (range of HR risk of 10(harmful) to 0.5(protective)
- HC use (COCs >100m; DMPA >50m) widely used by women of reproductive health age who are at risk of acquiring HIV
- HC widely used in SSA(has 80% of 16m women with HIV) to avoid poor pregnancy outcome, we therefore need robust data policy makers

What was HPTN 035

- HPTN 035 was a phase II/IIb, four arm, multi-site, randomized, controlled trial that tested the safety and effectiveness of two vaginal microbicides between Feb 2005- Aug 2008
  - BufferGel: has gelling and buffering agent, maintains low vaginal ph
  - 0.5% PRO 2000 Gel: a polyanionic polymer that acts by blocking attachment of HIV to host cell

Screening, Randomization & Follow-up



HPTN 035 Study Sites

AFRICA

USA

Study Participants

- To be eligible, women were required to be:
  - Able and willing to provide informed consent
  - HIV-uninfected and in general good health
  - Sexually active, >18yrs
  - Not intending to relocate from the study area
  - Not pregnant or planning to become pregnant in the 30 months of expected study time
  - Data on current contraceptive use were captured by face to face interview at enrollment and quarterly visits

Study Participants

- Sites were encouraged to offer contraceptive option within CRS
- All women in the 4 study groups received ongoing HIV risk reduction counseling, condoms, and testing and treatment for sexually transmitted infections
- HIV testing was done at quarterly visits

Study Participants

- Urine SDA for chlamydia and gonorrhea were tested annually or clinically indicated
- HSV-2 testing done on enrollment specimen and study exit batches
- Also tested for BV, TV, syphilis and swab for multiple PCR tests if GUD seen
- Assed for cervical ectopy, recorded vaginal ph

Statistical Analysis Plan

- Excludes 200 women from US site (low HIV incidence /differrent demographics /differrent contraceptive profile)
- Multivariate analysis based on 2887 HIV negative women from 7 African sites
- Limited to first 12 months of follow up per participant
- Primary outcome was detection HIV-1

Statistical Analysis Plan

Logistic regression and GEE used to identify baseline and follow up predictors associated with HIV-1 infection and HC use

Time dependent Cox proportion hazards regression, stratified by site, was used to assess the effect of DPMA and OCP on HIV-1 risk

Contraceptive Choices By Site

Contrac Type	All 6 African Sites	Blant.	Lilon	Durban	Hlabisa	Lusaka	Harare
DPMA	51%	63%	66%	48%	42%	66%	22%
OCP	21%	8%	10%	11%	5%	19%	72%
Male Condom	13%	7%	6%	27%	20%	11%	2%
No Contra	9%	13%	9%	8%	25%	2%	<1%
Surg. Steri	5%	6%	8%	6%	5%	1%	0
Norplant	1%	1%	2%	<1%	0	1%	4%

Follow up Characteristics (Site)

Baseline Demographics	All 6 African Sites	Blant.	Lilong.	Durban	Hlabisa	Lusaka	Harare
N Enrolled	2887	441	596	702	346	319	483
Mean Follow Up- Yrs	1.7	1.6	1.9	1.8	1.9	1.4	1.4
HIV incidence/ 100 PY	4.0	3.7	1.4	4.6	9.1	4.1	2.5
1st Preg Rate/100 PY	11.5	17.1	12.8	9.5	9.7	12.0	9.4
HSV-2 Incidence Rate/100 PY	7.7	7.4	5.0	8.6	10.3	12.3	6.3

HC and HIV Acquisition Risk

Factor	HR (95% C.I.)	p-value
BASELINE		
Age at enrollment	0.984 (0.938, 1.033)	0.5262
Married or living with husband/partner (baseline)	0.519 (0.275, 0.983)	0.0441
FOLLOW-UP CONTRACEPTION		
Injectables	1.423 (0.785, 2.578)	0.2445
Oral pills	0.860 (0.405, 1.826)	0.6952
FOLLOW-UP		
Chlamydia	2.506 (1.384, 4.537)	0.0024
Gonorrhea	5.934 (2.556, 13.777)	<.0001
pH > 4.5	1.620 (1.042, 2.520)	0.0322
Trichomonas vaginalis	1.900 (0.920, 3.923)	0.0829
HSV-2 positive	1.930 (1.252, 2.975)	0.0029
Cervical ectopy	1.749 (1.216, 2.515)	0.0026

HC and HIV Acquisition Risk

Factor	HR (95% C.I.)	p-value
FOLLOW-UP CONTRACEPTION:		
❑ **Sensitivity to Missed Visits**		
Injectables	1.209 (0.656, 2.227)	0.5425
Oral pills	0.774 (0.362, 1.656)	0.5096
❑ **Sensitivity to pregnancy**		
Injectables	1.301 (0.719, 2.354)	0.3845
Oral pills	0.840 (0.392, 1.801)	0.6548
❑ **Baseline HSV-2 Positive ppts only**		
Injectables	0.963 (0.470, 1.973)	0.9178
Oral pills	0.727 (0.288, 1.833)	0.4992
❑ **Baseline HSV-2 Negative ppts only**		
Injectables	2.801 (0.930, 8.433)	0.0671
Oral pills	1.339 (0.345, 5.188)	0.6730

HC and HIV Acquisition Risk

Factor	HR (95% C.I.)	p-value
FOLLOW-UP CONTRACEPTION:		
▫ **Baseline HSV-2 Positive ppts only (Sensitivity to missed visits)**		
Injectables	0.816 (0.393, 1.696)	0.5860
Oral pills	0.642 (0.252, 1.639)	0.3541
▫ **Baseline HSV-2 Negative ppts only (Sensitivity to missed visits)**		
Injectables	2.483 (0.752, 8.200)	0.1356
Oral pills	1.282 (0.310, 5.298)	0.7313

Summary

- Multivariate analysis demonstrates DPMA use was not significantly associated with HIV infection (HR 1.4; 95% C.I. 0.78, 2.57; p-value =0.24), we do not see direction towards harm seen in 3 published studies
- OCP use was not significantly associated with HIV (HR 0.86; 95% C.I. 0.40,1.82; p-value=0.69) in this analysis

Summary

- HC users who were married or living with partner at baseline were associated with a significantly decreased risk of HIV (HR 0.5; p-value=0.0441)
- At follow up, HC users with gonorrhea, chlamydia, TV, HSV-2, cervical ectopy, ph > 4.5 had variable rates of increased risk of HIV (HR ranging from 5.93 to 1.62)

Summary

- Trend toward significant increased risk of HIV among HSV-2 negative DMPA users observed (HR 2.8; 95% CI 0.93, 8.43; p-value=0.0671)
- Limitations: observational data, self selection of method, low IUCD & Implants use in this data set, no account on contraceptive switching, provision of contraception outside CRS at some sites
- More data from sub-analysis is continuing

Thank You

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HPTN HIV Prevention Trials Network

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Protocol Chair: Salim S Abdool Karim

Blantyre, Mal **khoma, E Kachale**

Durban and H **mi, N Dladla-Qwabe**

Harare, Zimb **agure, M Mlingo, N Mg**

Lilongwe, Ma **Mvalo**

Lusaka, Zam **i**

Philadelphia,

Coordinating **ter: W Cates, A Coletti, K Gomez, R White**

Statistical Center: M Cianciola, T Fleming, C Kelly, C Miller, B Mâsse, B Richardson

Network Laboratory: S Hillier, E Piwowar-Manning, L Rabe

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