

SAFETY OF CARRAGUARD® AMONG HIV-POSITIVE WOMEN AND MEN IN SOUTH AFRICA

Abstract No. TuPeB4662

S Braunstein
Population Council

NS Morar
Medical Research
Council of
South Africa

H Jones
Population Council

M Moodley
Medical Research
Council of
South Africa

J Aboobaker
Medical Research
Council of
South Africa

G Ndlovu
Medical Research
Council of
South Africa

G Ramjee
Medical Research
Council of
South Africa

J van de Wijert
Population Council and
International Antiviral
Therapy Evaluation Center

BACKGROUND: CARRAGUARD® AS A VAGINAL MICROBICIDE

- Carraguard is the Population Council's lead candidate microbicide
- Carraguard gel formulation: Carrageenan mixture dissolved in purified water with 0.1% p-hydroxybenzoic methyl ester as a preservative
- Carrageenans are used in food and in the pharmaceutical/cosmetic industry as lubricants, emulsifiers, and dispersing agents
- Compounds are on the US Federal Drug Administration's "generally recognized as safe" (GRAS) list: Safe for human consumption and topical application



Medical Research Council, Durban, South Africa

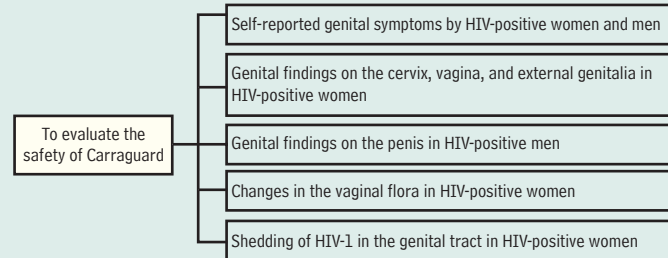


Medical Research Council waiting area

STUDY RATIONALE

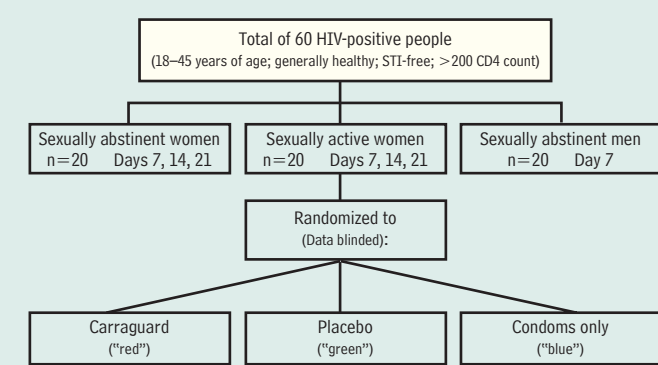
- Microbicides are likely to be used by women and men who are not aware of their HIV status
- HIV-positive persons may use a microbicide to avoid other sexually transmitted infections, or to protect their partners
- It is important to know whether HIV-positive women and men can safely use a potential microbicide

STUDY OBJECTIVES



Medical Research Council examination room

STUDY DESIGN



STUDY PROCEDURES

- Sexually abstinent women inserted gel into the vagina once a day for 14 days
- Sexually active women inserted gel into the vagina each time they had sex (gel was used together with condoms) for 14 days, and inserted gel in the evening of those days when sex did not take place
- Sexually abstinent men applied gel directly to the penis once a day for 7 days
- Pelvic exams and self-reported symptoms for women at enrollment, day 7, day 14, and day 21 study visits (day 21 visit was 7 days post-gel use completion)
- Penile exams and self-reported symptoms for men at enrollment and day 7 study visits



Gel applicator



Medical Research Council clinic

COHORT RETENTION/ADHERENCE

	Screening	Enrollment	Day 7	Day 14	Day 21	Reasons for noncompliance
Sexually abstinent women	98	20	20	19	19	One woman withdrew consent at day 7 visit; did not use gel for 14 days
Sexually active women	46	20	20	20	20	NA
Sexually abstinent men	45	20	19	NA	NA	One man was lost to follow-up after enrollment visit; did not use gel

BASELINE DEMOGRAPHICS

	Sexually abstinent women (n=20)	Sexually active women (n=20)	Sexually abstinent men (n=20)
Median age in years (range)	30 (19–42)	28 (22–41)	32 (21–50)
Mean education in years (range)	12 (6–15)	12 (5–14)	10 (4–16)
Married*/steady partner (proportion)	80% (16/20)	100% (20/20)	90% (18/20)
Mean live births (range)	1.80 (0–5)	1.85 (0–5)	NA

*Defined as legally married or some lobola (i.e., brideprice) paid.

BASELINE HIV AND SEXUAL BEHAVIOR

	Sexually abstinent women (n=20)	Sexually active women (n=20)	Sexually abstinent men (n=20)
Any male condom use in last month* (proportion)	64% (7/11)	90% (18/20)	62% (8/13)
Mean lifetime sex partners (range)	3 (1–15)	3 (1–6)	15 (3–90)
Mean number vaginal sex acts in last month (range)	3 (1–4)	6 (1–18)	5 (1–30)
Percent ever tested for HIV (proportion)	85% (17/20)	100% (20/20)	80% (16/20)

*Among those who reported vaginal sex in last month.

RTIs AT SCREENING: ALL WOMEN BY ENROLLMENT

RTI % (proportion)	Enrolled women	Nonenrolled women
HIV-positive	100 (40/40)	97 (93/96)
Syphilis	0 (0/40)	10 (9/93)
Gonorrhoea	0 (0/40)	2 (2/91)
Chlamydia	0 (0/40)	10 (9/91)
CD4 count ≤200	0 (0/40)	19 (18/96)
CD4 count >200	100 (40/40)	81 (78/96)
Trichomoniasis	0 (0/40)	7 (6/88)
Yeast	10 (4/40)	9 (8/88)
Bacterial vaginosis (Nugent)	10 (4/39)	20 (17/87)

RTIs AT SCREENING: ALL MEN BY ENROLLMENT

RTI % (proportion)	Enrolled men	Nonenrolled men
HIV-positive	100 (20/20)	77 (17/22)
Syphilis	0 (0/20)	0 (0/22)
Gonorrhoea	0 (0/20)	0 (0/22)
Chlamydia	0 (0/20)	5 (1/22)
CD4 count ≤200	0 (0/20)	46 (10/22)
CD4 count >200	100 (20/20)	55 (12/22)
Trichomoniasis	0 (0/19)	0 (0/21)
Bacterial vaginosis (Nugent)	0 (0/20)	0 (0/22)

Note: The majority of women and men screened for the study tested positive for HIV due to targeted recruitment efforts; none of the enrolled women and men had an RTI per eligibility criteria for study participation.

SELF-REPORTED SYMPTOMS (EVER) BY STUDY ARM: SEXUALLY ABSTINENT WOMEN

Symptoms (proportion)	Red	Green	Blue (condoms only)
Genital rash	1/6	1/7	1/7
Genital itching	2/6	3/7	1/7
Genital burning	1/6	2/7	0/7
Genital pain	1/6	1/7	0/7
Pain when urinating	1/6	3/7	1/7
Increased urinary frequency	2/6	3/7	1/7
Genital sores or ulcers	1/6	2/7	0/7
Any of the above symptoms	4/6	5/7	2/7

SELF-REPORTED SYMPTOMS (EVER) BY STUDY ARM: SEXUALLY ACTIVE WOMEN

Symptoms (proportion)	Red	Green	Blue (condoms only)
Genital rash	0/7	0/7	1/6
Genital itching	0/7	1/7	0/6
Genital burning	1/7	1/7	0/6
Genital pain	1/7	0/7	0/6
Pain when urinating	1/7	0/7	1/6
Increased urinary frequency	1/7	1/7	0/6
Genital sores or ulcers	0/7	1/7	0/6
Any of the above symptoms	3/7	4/7	3/6

SELF-REPORTED SYMPTOMS (EVER) BY STUDY ARM: SEXUALLY ABSTINENT MEN

Symptoms (proportion)	Red	Green	Blue (condoms only)
Genital rash	0/6	0/7	0/6
Genital itching	0/6	0/7	0/6
Genital burning	0/6	0/7	0/6
Genital pain	0/6	0/7	0/6
Pain when urinating	0/6	0/7	0/6
Increased urinary frequency	0/6	1/7	1/6
Genital sores or ulcers	0/6	0/7	0/6
Any of the above symptoms	0/6	1/7	1/6

Note: Fisher's exact showed no statistical significance between the three study arms.

GENITAL FINDINGS DURING FOLLOW-UP

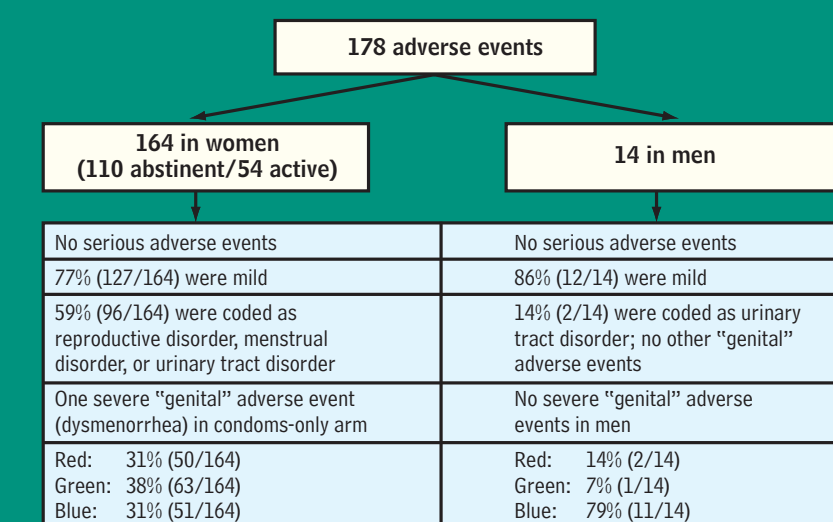
- Five findings in sexually abstinent women (similar in gel arms):
 - One ulcer on external genitalia with superficial disruption of epithelium (red arm: day 7 through day 21)
 - One erythematous excoriation on external genitalia with superficial disruption of epithelium (red arm: day 21)
 - One ulcer on external genitalia with superficial disruption of epithelium (green arm: day 7)
 - One erythema on cervix with intact epithelium (green arm: day 14)
 - One erythema on cervix with intact epithelium (green arm: day 7)
- No findings in sexually active women
- No findings in sexually abstinent men

EVER HAD A NEW RTI AFTER ENROLLMENT VISIT

RTI % (proportion)	Sexually abstinent women	Sexually active women	Sexually abstinent men
Syphilis	0 (0/20)	0 (0/20)	0 (0/20)
Gonorrhoea	0 (0/20)	0 (0/20)	0 (0/20)
Chlamydia	0 (0/20)	0 (0/20)	0 (0/20)
Trichomoniasis	0 (0/20)	0 (0/20)	0 (0/20)
Yeasts*	5 (1/20)	5 (1/20)	NA
Bacterial vaginosis (Nugent)*	35 (7/20)	45 (9/20)	NA

*For yeasts one in red, one in green; For BV three in red, seven in green, six in blue.

ADVERSE EVENTS (PRELIMINARY)



Note: Common adverse events included genital itching, genital burning, vaginal discharge, increased urinary frequency, and lower abdominal pain.

CONCLUSION

Preliminary blinded results show that the product and the placebo appear to be safe in HIV-positive sexually abstinent men and women and sexually active women.

ACKNOWLEDGMENTS

This study was made possible through support provided by the Population & Reproductive Health Office, Bureau for Global Health, US Agency for International Development under the terms of Award No. HRN-A-00-99-00010. The opinions expressed herein are those of the authors and do not necessarily reflect the views of USAID.

The authors acknowledge:

- Study participants (screened & enrolled)
- Medical Research Council and Population Council teams
- King Edward Hospital, Sinikethemba-McCords Hospital, and recruitment centres in Durban

The authors also acknowledge The Parthenon Trust for funding for this project.