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Does size matter? A randomized controlled trial to assess the impact of external diameter on adherence to 3 different intravaginal rings among 24 US couples

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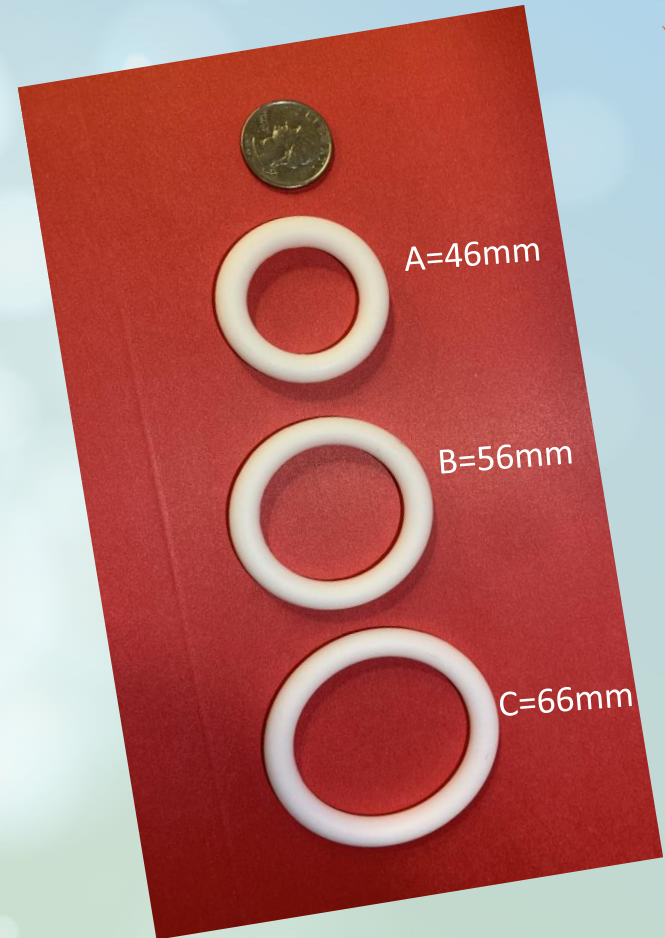
Rationale

- Women of reproductive age would benefit from a multipurpose prevention technology (MPT) that combines protection against pregnancy and HIV/STIs
- Intravaginal rings (IVRs) have been used for over 40 years and are a promising delivery system for MPTs
- No empirical data exists to support the current 54-58mm size as ideal
- Understanding the impact of IVR size on adherence is critical for developing a product that can be used correctly and consistently



Primary Objectives

- **Adherence**
 - To determine which of 3 non-medicated IVRs (A, B or C) each used continuously for ~30 days yields the highest adherence
- **Preference**
 - To assess which of 3 non-medicated IVRs (A, B or C), each used continuously for ~30 days, is preferred by women enrolled with their male partners



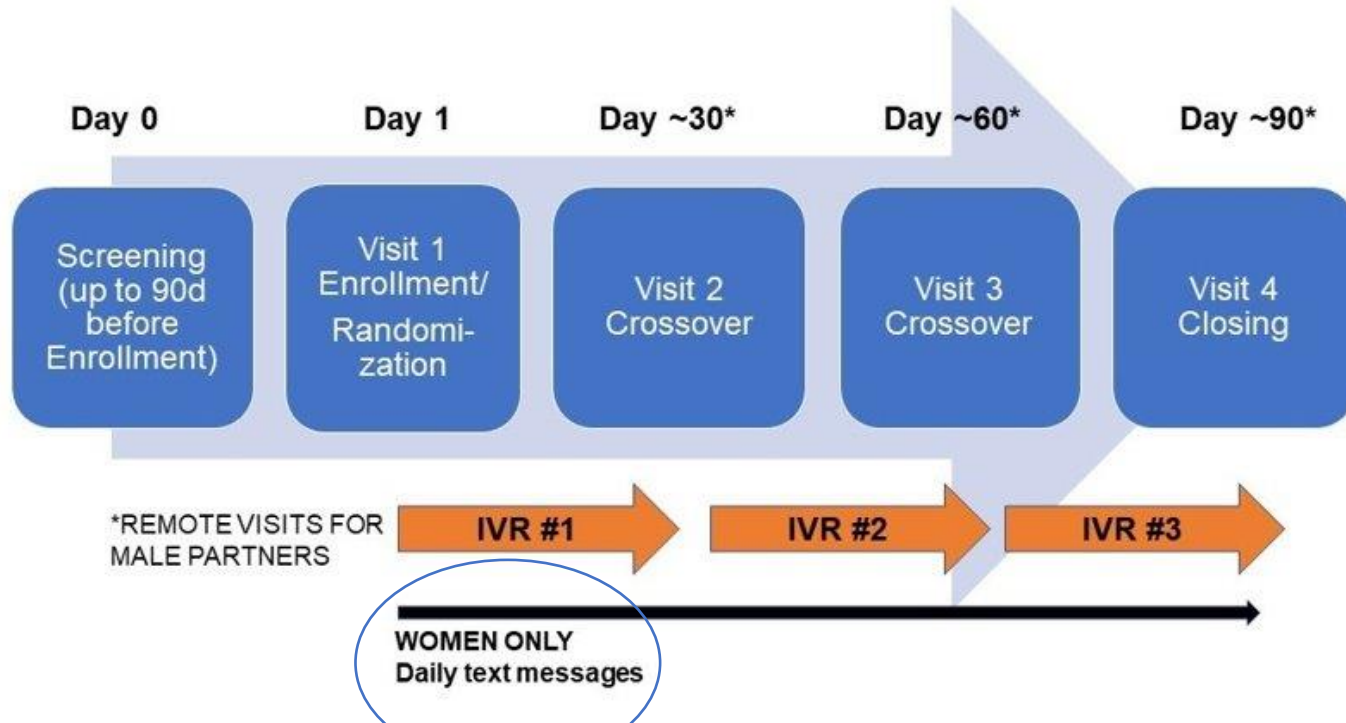


Study Design

- Randomized, open-label, parallel group, 3-way crossover
- Population: 24 healthy, HIV-seronegative couples (n=48)
 - Mutually monogamous, low-risk
 - Women 18-40 yrs
 - Males ≥ 18 yrs
 - Sexually active
- Sites
 - Albert Einstein College of Medicine, Bronx NY
 - Emory University, Atlanta GA
- Duration
 - 3 months per couple (one month per ring)
 - 16 months overall for data collection (Sept 2021-Dec 2022)

Study Schema

#ADHERENCE2023





Text message questions

Question 1:

In the past 24 hours, has the ring been out of your vagina? Enter the number corresponding to your answer:

1 = No, it was in place the entire time

2 = Yes, it was completely out of my vagina for the entire time

3 = Yes, it was out of my vagina for part of the time

Question 2:

In the past 24 hours, how did the ring come out?

1 = I removed it

2 = I felt like it was slipping/starting to come out, so I removed it

3 = It came out on its own (expulsion)

4 = I had already taken the ring out more than 24 hours ago and had not reinserted it

Question 3:

In the past 24 hours, about how long in total was the ring out of your vagina?

1 = less than ½ hour

2 = more than ½ hour, but less than an hour

3 = 1-2 hours

4 = more than 2 hours



Analysis methods

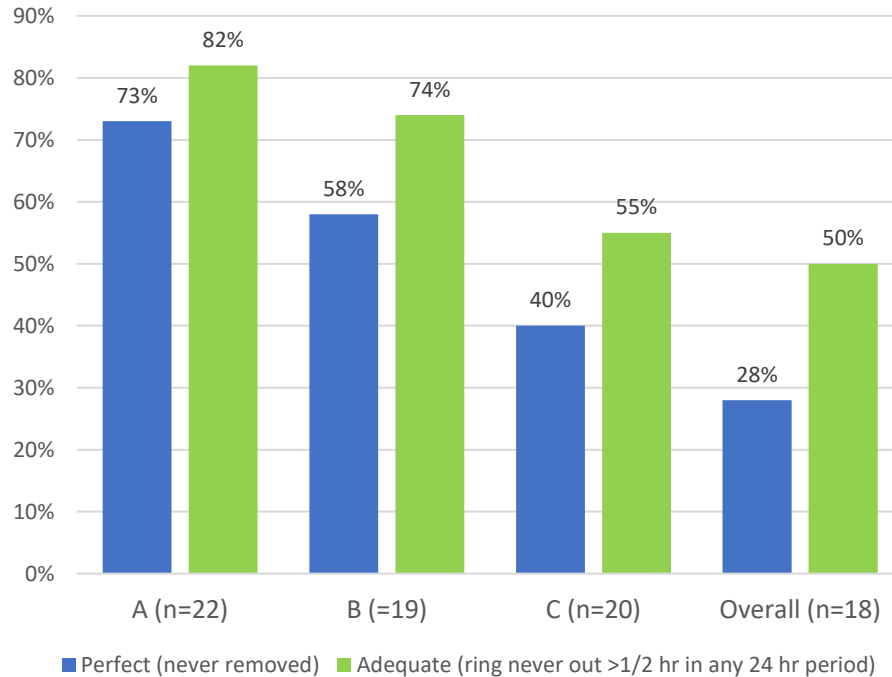
- We summarized the number of days the IVR was out at all, out all day, or expelled, and the proportion of women adherent to each IVR
- Mixed methods logistic regression models with random intercepts (per participant) compared the probability of each event happening per day of IVR use, per IVR

Results: Background Demographics, Females

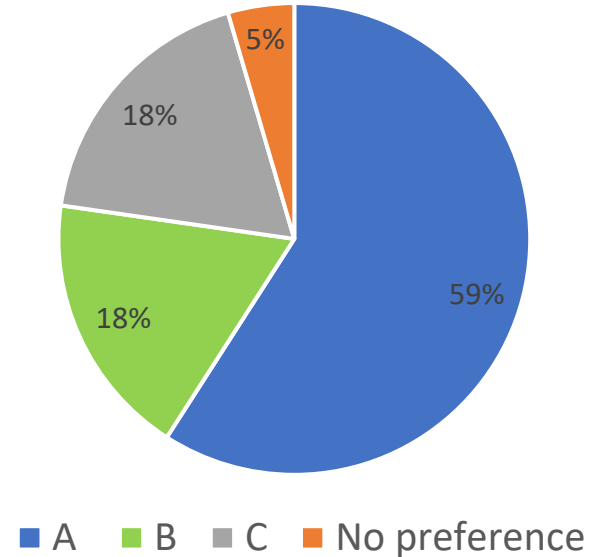
Characteristic	Bronx (n=12)	Atlanta (n=12)	Overall (n=24)
Mean Age (SD)	27(4.65)	26.3(2.84)	26.7(3.78)
Mean Age (Range)	25(23-40)	26(23-33)	25.5(23-40)
BMI			
18.5-<25	5 (42%)	6 (50%)	11 (46%)
25-<30	5 (42%)	4 (33%)	9 (38%)
≥ 30	2 (17%)	2 (17%)	4 (17%)
Race			
White	8 (67%)	7 (58%)	15 (63%)
Black/African	1 (8%)	2 (17%)	3 (13%)
Asian	2 (17%)	4 (33%)	6 (25%)
Other	1 (8%)	0 (0%)	1 (4%)
Ethnicity			
Hispanic	4 (33%)	1 (8%)	5 (21%)
Not Hispanic	8 (67%)	11 (92%)	19 (79%)
Born in the US	8 (67%)	10 (83%)	18 (75%)
Marital Status			
Married/Cohabiting	4 (33%)	1 (8%)	5 (21%)
Single	8 (67%)	11 (92%)	19 (79%)
Highest Level of Education			
Some College	0 (0%)	2 (17%)	2 (8%)
College Grad	12 (100%)	10 (83%)	22 (92%)
Parity			
Nulliparous	11 (92%)	11 (92%)	22 (92%)

Results: Adherence and Preference

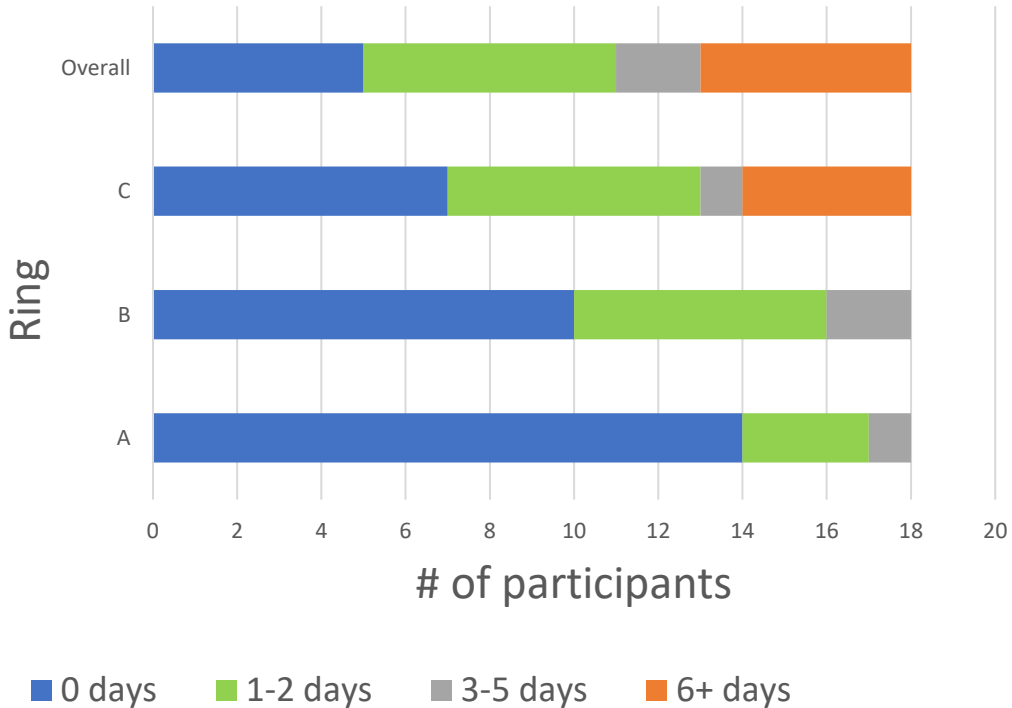
Adherence by Ring Type, Overall



Preference, Females End of Study (n=22)

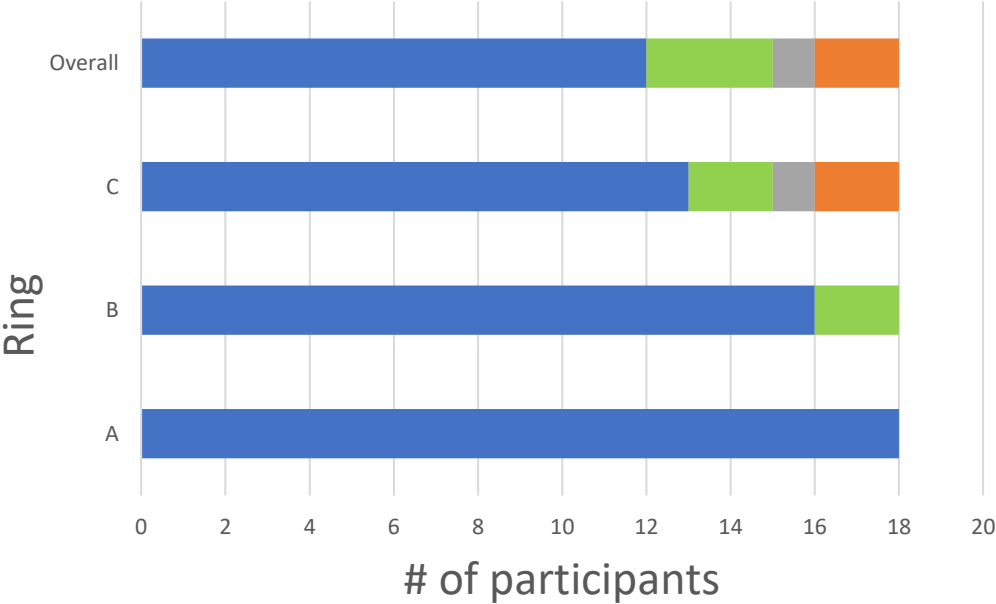


Number of participants with ring ever out by ring and overall (n=18)



A vs B; OR 0.56; 95% CI 0.21-1.44
C vs B; OR 6.92; 95% CI 3.65-13.1

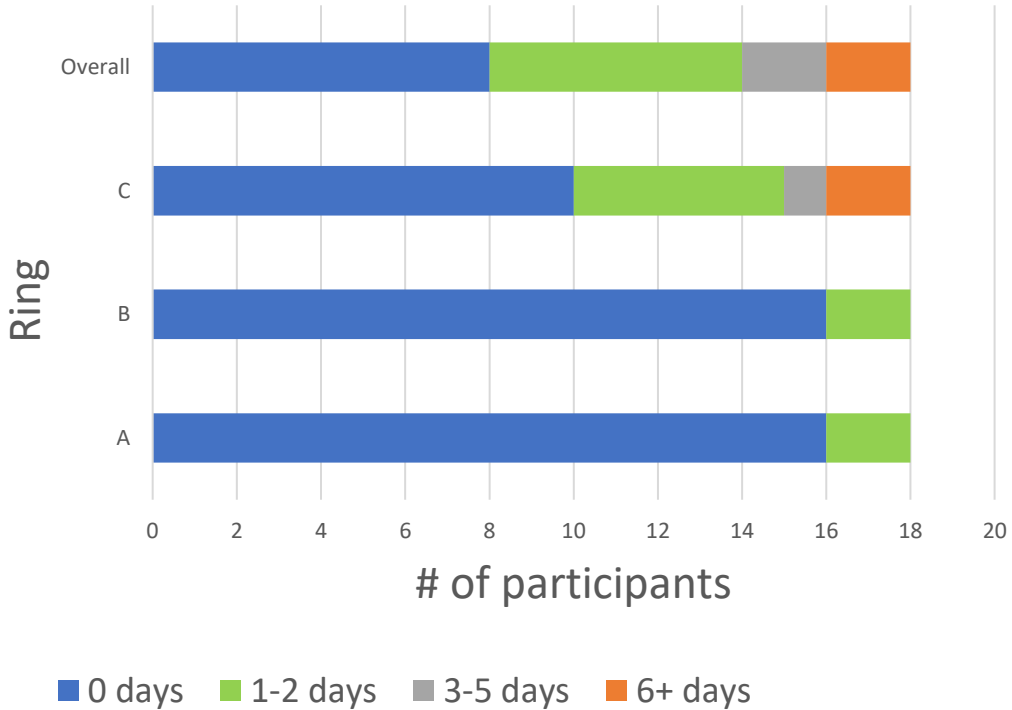
Number of participants with ring out all day by ring and overall (n=18)



C vs B; OR 16.4; 95% CI 3.79-71.3

(cannot calculate A vs B since no one had ring A out all day)

Number of participants with expulsions (partial or full) by ring and overall (n=18)



A vs B; OR 1.08 95% CI 0.15-7.8
C vs B; OR 27.8 95% CI 6.48-119



Summary

- Overall adherence (ring never out) was highest with the smallest ring (A, 46mm) and lowest with the largest ring (C, 66mm) but differences between the rings were not statistically significant
- The probability of expulsions was the highest with the largest ring (C, 66mm); there was no difference between ring A and ring B
- External diameter had an impact on adherence with 46mm and 56 mm performing better than the 66mm ring



Conclusions

- We only measured external diameter; other ring characteristics such as compressibility should be assessed and taken into consideration with ring development
- Adherence should not only be considered as a dichotomous endpoint; patterns of adherence over time and factors contributing to adherence should also be considered when developing IVRs
- A few women preferred ring C; developers should consider making rings in multiple sizes



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Study Participants

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Thank you!

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