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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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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

- **Day 0**: Screening (up to 90d before Enrollment)
- **Day 1**: Visit 1 Enrollment/Randomization
- **Day ~30***: Visit 2 Crossover
- **Day ~60***: Visit 3 Crossover
- **Day ~90***: Visit 4 Closing

*REMOTE VISITS FOR MALE PARTNERS

IVR #1

IVR #2

IVR #3

WOMEN ONLY
Daily text messages
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

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

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

<table>
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<tr>
<th>Characteristic</th>
<th>Bronx (n=12)</th>
<th>Atlanta (n=12)</th>
<th>Overall (n=24)</th>
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<td>Mean Age (SD)</td>
<td>27(4.65)</td>
<td>26.3(2.84)</td>
<td>26.7(3.78)</td>
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<td>Mean Age (Range)</td>
<td>25(23-40)</td>
<td>26(23-33)</td>
<td>25.5(23-40)</td>
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<td>BMI</td>
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<td>18.5-&lt;25</td>
<td>5 (42%)</td>
<td>6 (50%)</td>
<td>11 (46%)</td>
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<tr>
<td>25-&lt;30</td>
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<td>4 (33%)</td>
<td>9 (38%)</td>
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<td>≥ 30</td>
<td>2 (17%)</td>
<td>2 (17%)</td>
<td>4 (17%)</td>
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<tr>
<td>Race</td>
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<tr>
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<td>15 (63%)</td>
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<td>2 (17%)</td>
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<tr>
<td>Asian</td>
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<td>4 (33%)</td>
<td>6 (25%)</td>
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<td>0 (0%)</td>
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<td>5 (21%)</td>
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<tr>
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<td>11 (92%)</td>
<td>19 (79%)</td>
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<td>1 (8%)</td>
<td>5 (21%)</td>
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<tr>
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<td>11 (92%)</td>
<td>19 (79%)</td>
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<td>2 (8%)</td>
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<td>10 (83%)</td>
<td>22 (92%)</td>
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<td>Parity</td>
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<tr>
<td>Nulliparous</td>
<td>11 (92%)</td>
<td>11 (92%)</td>
<td>22 (92%)</td>
</tr>
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</table>
Results: Adherence and Preference

Adherence by Ring Type, Overall

- A (n=22): 73% Perfect, 82% Adequate
- B (n=19): 58% Perfect, 74% Adequate
- C (n=20): 40% Perfect, 55% Adequate
- Overall (n=18): 28% Perfect, 50% Adequate

Preference, Females End of Study (n=22)

- A: 18%
- B: 18%
- C: 18%
- No preference: 59%
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
Acknowledgements

Study Participants

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Thank you!

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