

# Evidence of Low Androgenicity and Little Impact on Sexual Function or Activity with Annovera™, a Novel Contraceptive Vaginal System Releasing Segesterone Acetate and Ethinyl Estradiol

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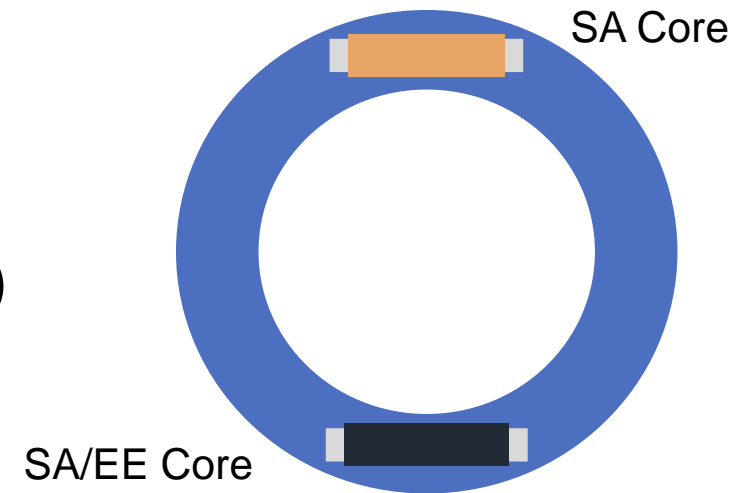
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# Disclosures

- **Advisory board member:** AMAG
- **Consultant:** Dare, JDS Therapeutics, Sprout, Strategic Scientific Technologies (SST), TherapeuticsMD, and Proctor & Gamble
- **Writing support:** AMAG and TherapeuticsMD

# Background

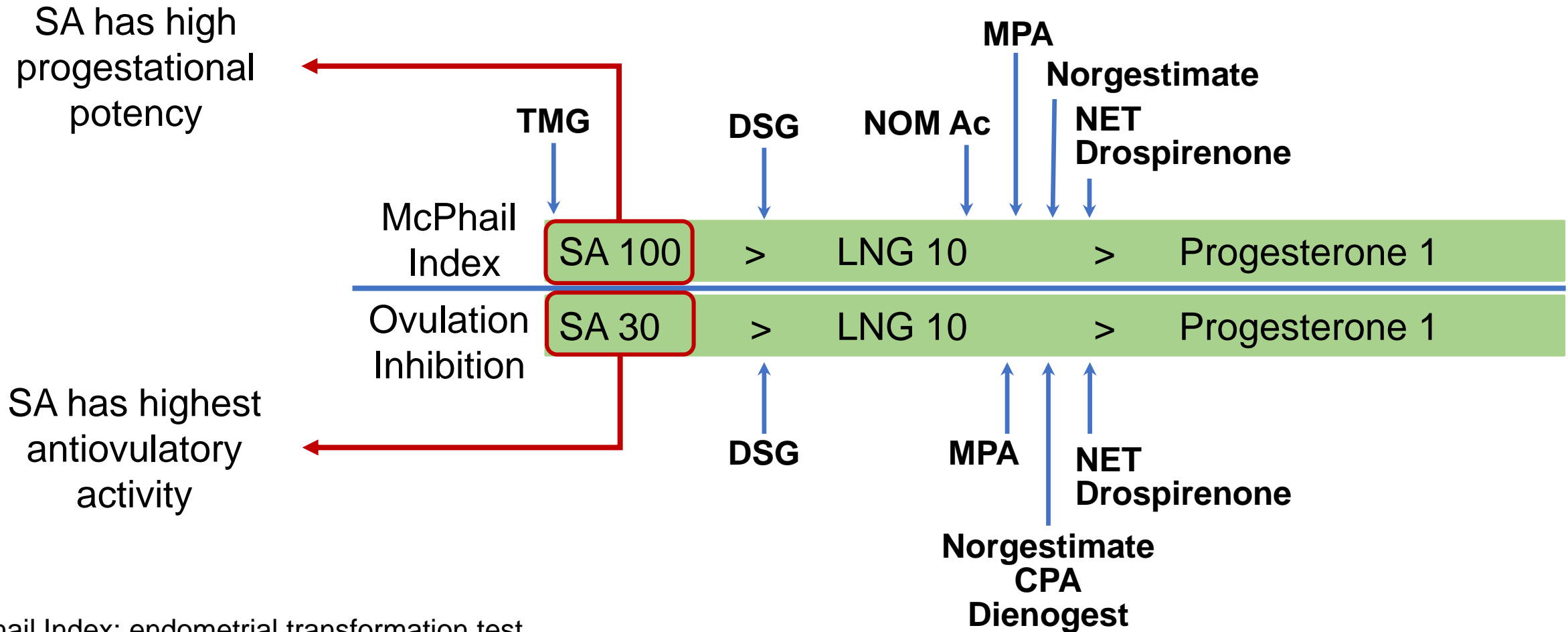
- Combined hormonal contraceptives (CHCs) may impact sexual function, in part due to interaction of the progestin component with the androgen receptor
- Some CHCs have been previously reported to decrease or increase libido
- Annovera™ is a new contraceptive vaginal system (CVS) recently approved by the FDA (August 2018)
  - Ring-shaped CVS
  - Releases 150 mcg segesterone acetate (SA) and 13 mcg ethinyl estradiol (EE) per day
  - 21-day in, 7-day out pattern for up to 1 year (13 cycles)
  - PEARL index: 2.98 (women ≤35 years of age)



# Objective

- To review evidence from preclinical studies investigating the androgenicity of the SA component of the CVS
- To report the impact of the CVS on sexual function or activity in women who used the CVS for 1 year during a multi-country phase 3 trial

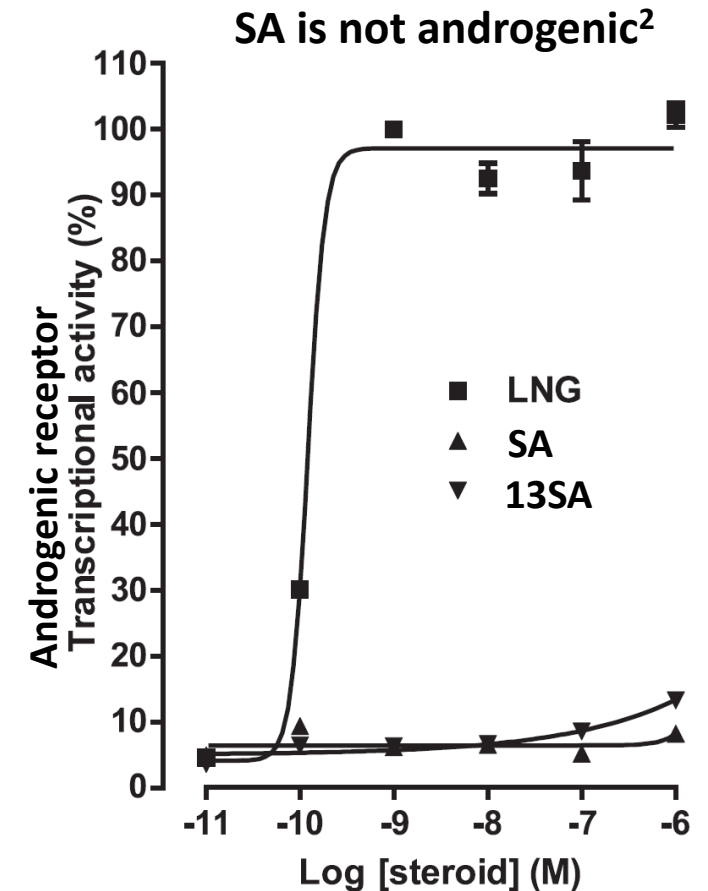
# Progestational Effects of Progestins



McPhail Index: endometrial transformation test.

# SA Preclinical Data Summary

- No androgenic or estrogenic effect,<sup>1,2</sup> does have antiestrogenic activity<sup>1</sup>
  - Androgenic progestins such as LNG have agonist activity at the androgen receptor and stimulate androgenic target tissues<sup>1,2</sup>
- Not orally active, not bound to SHBG<sup>1</sup>
- No glucocorticoid effect at contraceptive doses<sup>1</sup>



13SA: 13 ethyl SA; AR: androgen receptor; LNG: levonorgestrel; SA: segesterone acetate; SHBG: steroid hormone binding globulin.

Adapted from Kumar N, et al.  
*Endocrinology*. 2017; 158:170-182.

# Does the SA/EE CVS Impact Sexual Function?

- Phase 3 clinical trial at 12 sites in US, Latin America, Europe, and Australia (2006-2009)
- CVS was used for 13 cycles: 21 days in and 7 days out during each cycle
- Participants completed a questionnaire, that included sexual domain questions
  - At baseline and study end
  - 80% (905/1135) of women completed the questionnaire
  - Mean age 27 years; most were white (80%) and had at least some college education (63%)

## Inclusion Criteria

- Healthy, sexually active women
- 18 to 40 years old
- Body mass index <29 kg/m<sup>2</sup>
- No medical contraindications to CHC use
- Not sterilized
- No use of monthly injectable contraceptives ≤2 months of study initiation or DMPA use ≤6 months

# Sexual Health Questions

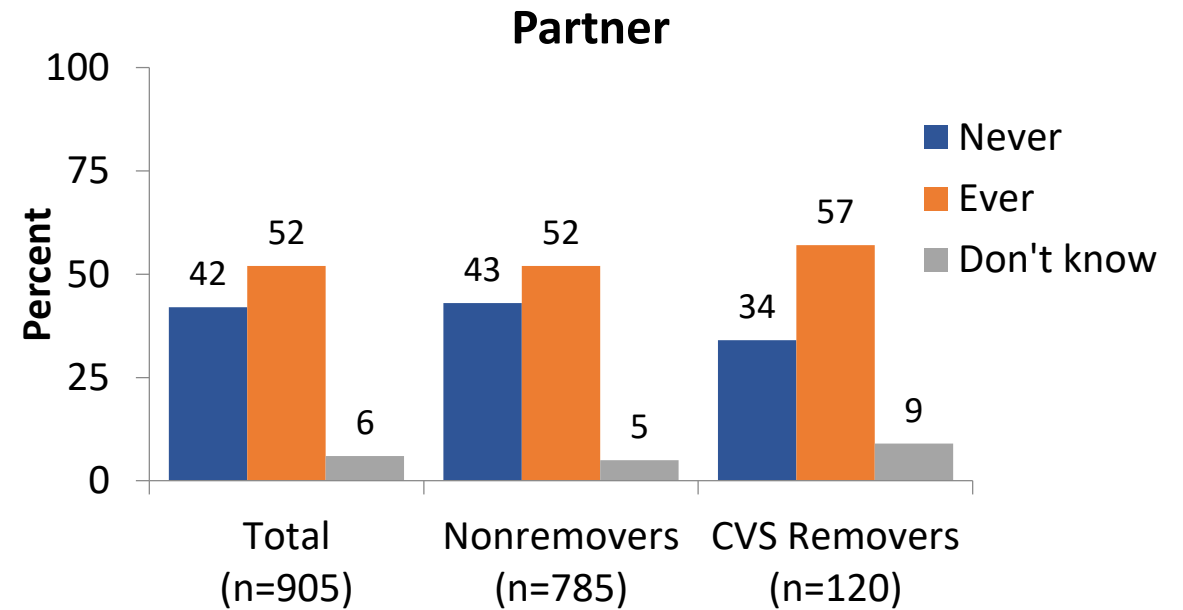
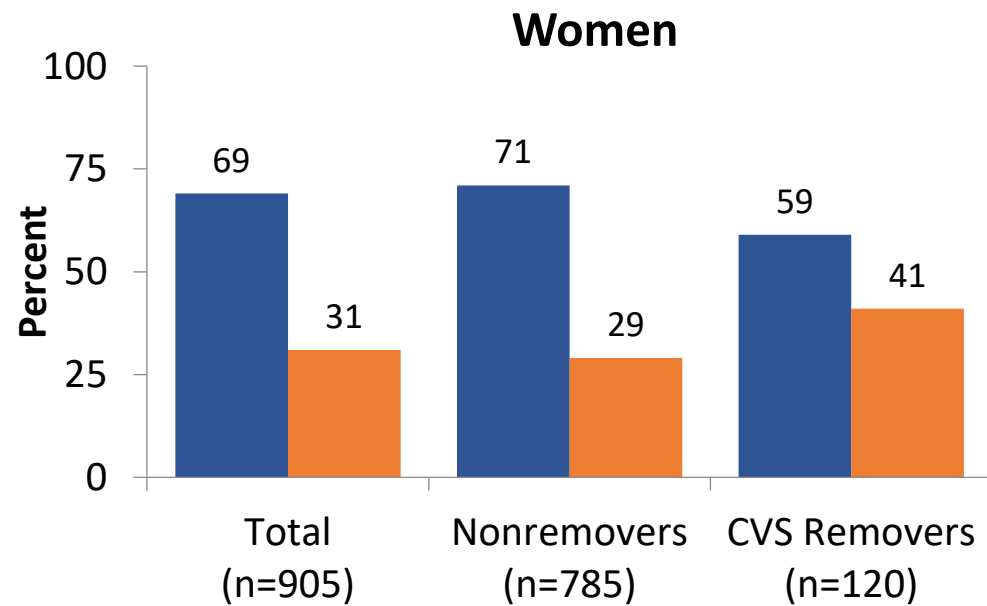
| Questions                                | Choices                           |
|--|-----------------------------------|
| 1. Feel ring during sex?                 | Never or ever                     |
| 2. Partner feels ring during sex?        | Never, ever, or don't know        |
| 3. Change in frequency of sex?           | No change or increased, decreased |
| 4. Change in sexual pleasure?            | No change or increased, decreased |
| 5. Ring affects partner sexual pleasure? | Never, ever, or don't know        |

- Results were stratified as “CVS removers” (n=120, removed CVS for >2 hours per cycle outside of scheduled removal periods) versus “nonremovers” (n=785)
- Women who removed the CVS >2 unscheduled hours in a cycle were 4 times more likely to get pregnant than nonremovers
  - OR 4.07 (95% CI 1.58-10.50)



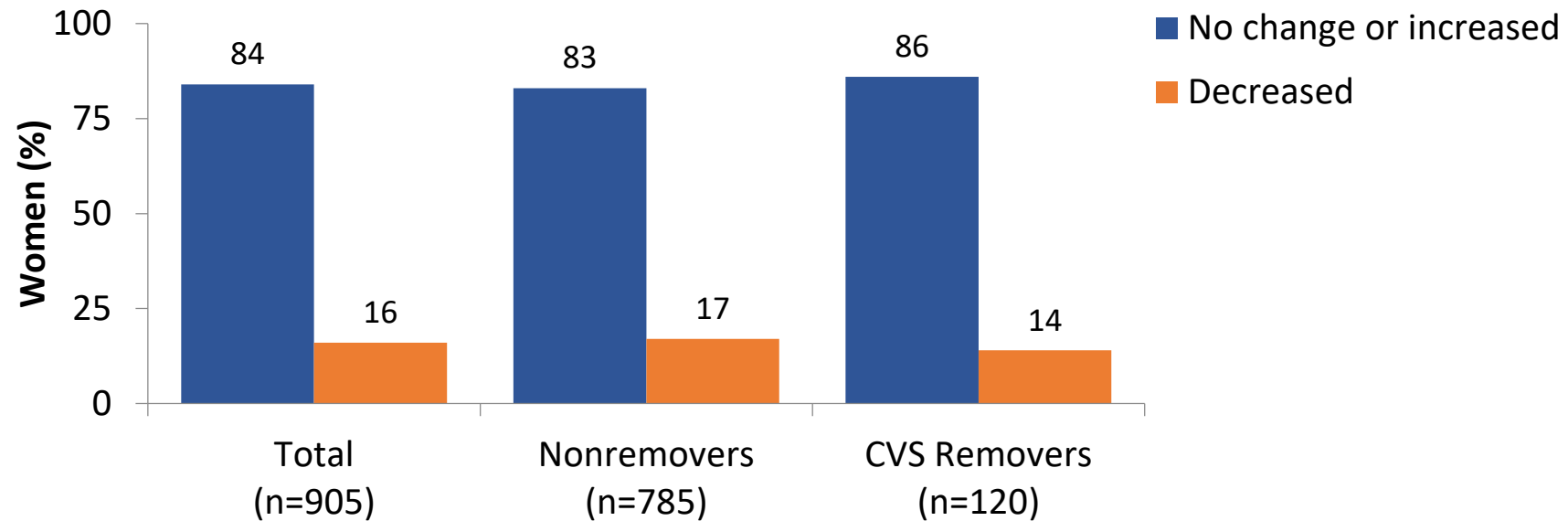
# Feel the Ring (CVS) During Sex?

- 31% of women could feel the ring during sex
  - Feeling the ring was associated with CVS removal >2 h ( $P=0.012$ )
- About half of partners could feel the CVS during sex



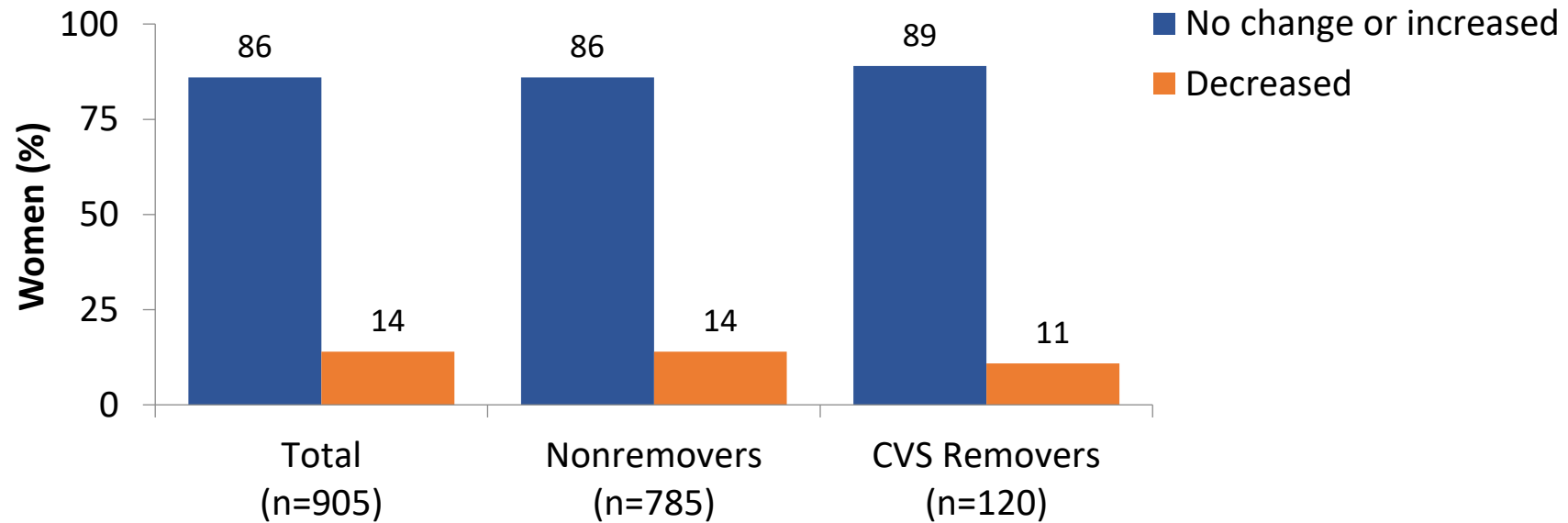
# Change in Frequency of Sex

- Frequency of sex increased or did not change in the majority of CVS users



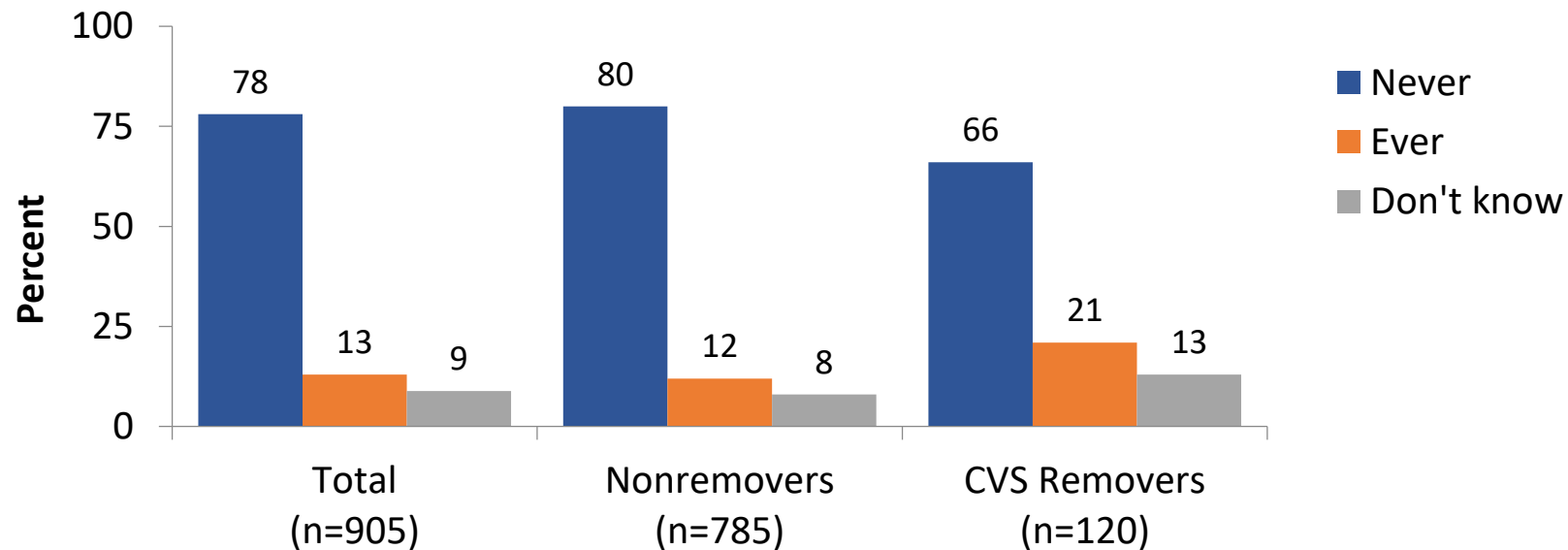
# Change in Sexual Pleasure

- In most CVS users, sexual pleasure increased or did not change



# Ring (CVS) Effects on Partner's Sexual Pleasure

- In most users, the CVS did not affect their partner's sexual pleasure
  - Effects of the ring on a partner's sexual pleasure was associated with ring removal >2 h ( $P=0.002$ )



# Conclusions

- Binding affinity and animal studies show that the SA component of Annovera was not associated with androgenic effects that are potentially detrimental to sexual function<sup>1-3</sup>
  - SA is a strong progesterone receptor agonist with no androgenic properties
- In a phase 3 trial, the CVS did not have a negative impact on sexual function and activity<sup>4</sup>
  - Majority of women (>80%) reported increased or unchanged
    - Frequency of sex
    - Sexual pleasure