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Association between vaginal progesterone use and risk of preterm birth among high-risk pregnancies: a real-world evidence study

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BACKGROUND

- **Preterm birth** is the leading cause of neonatal mortality.
  - In 2022, the preterm birth rate in the US was 10.4%, higher than the rate in most developed countries.[1]
- **Injectable hydroxyprogesterone caproate** was approved by FDA to prevent preterm birth but has been withdrawn from the market since 2023.
  - As a result, there is currently no FDA-approved medication available for preterm birth prevention.
- The American College of Obstetricians and Gynecologists (ACOG) suggests that **vaginal progesterone** may be considered as an option for preterm prevention.[2]
  - Previous randomized control trials (RCTs) have found ***conflicting*** results on the efficacy of vaginal progesterone in preterm birth prevention.[3]

OBJECTIVE

- To evaluate the association between receipt of vaginal progesterone during pregnancy and the risk of preterm birth among pregnancies at high risk for preterm birth, using real-world data.

METHODS - DATA SOURCE

- This study used administrative commercial health claims data from a large national payor.
  - The payor covers individuals in the 50 US states, the District of Columbia, and US territories.
  - **The Sentinel Common Data Model (SCDM)** was used in this study to capture longitudinal information on enrollment dates, demographic characteristics, dispensed prescriptions, inpatient and outpatient diagnoses, treatments and procedures of commercially insured members.

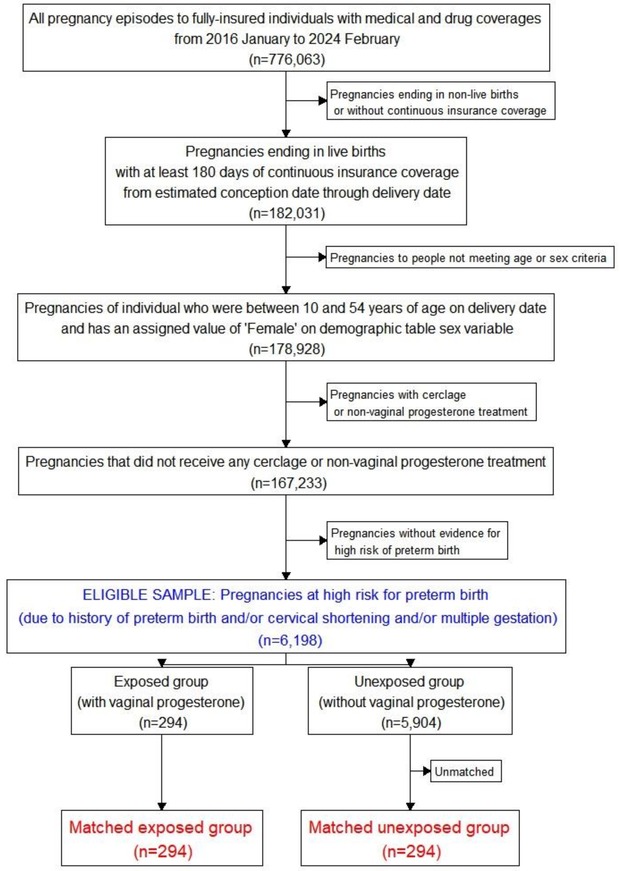
REFERENCES

1. *The Centers for Disease Control and Prevention. "Preterm Birth". November 2024. https://www.cdc.gov/maternal-infant-health/preterm-birth/index.html*
2. *The The American College of Obstetricians and Gynecologists. "Updated Clinical Guidance for the Use of Progestogen Supplementation for the Prevention of Recurrent Preterm Birth." April 2023. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2023/04/updated-guidance-use-of-progestogen-supplementation-for-prevention-of-recurrent-preterm-birth*
3. *Conde-Agudelo, Agustin, and Roberto Romero. "Does vaginal progesterone prevent recurrent preterm birth in women with a singleton gestation and a history of spontaneous preterm birth? Evidence from a systematic review and meta-analysis." American journal of obstetrics and gynecology 227, no. 3 (2022): 440-461.*

METHODS - STUDY SAMPLE

- **Study Sample:** Pregnancies among people who enrolled in non-administrative services only (non-ASO) health insurance plan, had a live birth outcome during 2016-2024, and met all inclusion and exclusion criteria (see **Figure 1**).

Figure 1. Sample derivation and matching process



- **Statistical Analyses:** A comparable unexposed group was identified through **propensity score matching (PSM).**
  - The propensity score model included demographic factors (e.g., age, race/ethnicity) and clinical factors (e.g., cervix shortening, history of preterm labor, multiple gestation, smoking, existing/gestational diabetes or hypertension, and placenta previa).

RESULTS

- **Figure 1: 6198** pregnancies were at high risk for preterm birth.
  - **294 (4.7%)** received vaginal progesterone during pregnancy.
- **Figure 2:** The PSM identified 294 unexposed pregnancies that had similar covariates distributions as the exposed pregnancies.
- **Table 1:** The rate of preterm birth was 33.7% in the unexposed group and 30.3% in the exposed group, resulting in a **risk difference of -3.4% (95% CI, -10.9% to 4.1%).**
  - The subgroup analyses restricted to *singleton* pregnancies with either short cervix or history of preterm birth. Vaginal progesterone use was not associated with reduced risk for preterm birth within these subgroups.

Figure 2. Covariates balance between exposed and unexposed groups before and after propensity score matching

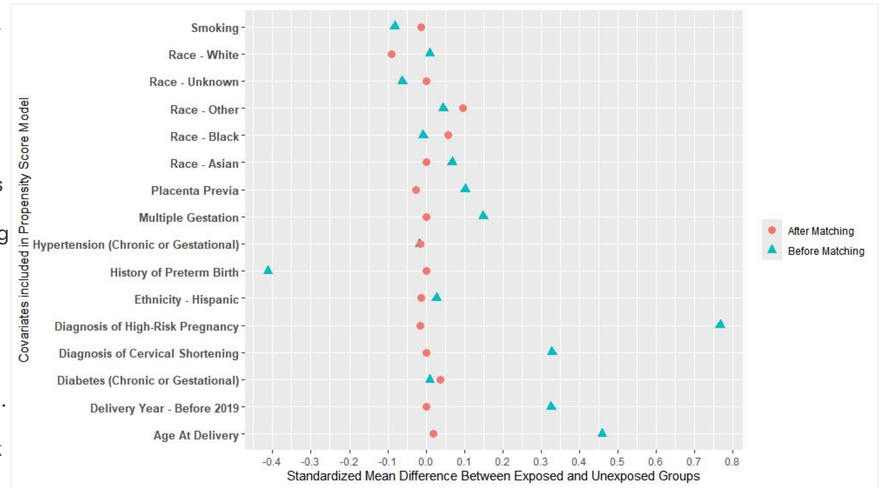


Table 1. Outcome rates and risk difference between exposed and comparison groups

	Number of matched pairs	Rate of preterm birth in the matched unexposed group	Rate of preterm birth in the matched exposed group	Risk Difference (Exposed – Unexposed) (95% CI)
Full Sample	294	33.7%	30.3%	-3.4% (-10.9%, 4.1%)
Subgroup Analyses:				
Singleton pregnancies with short cervix	95	15.8%	22.1%	6.3% (-4.8%, 17.4%)
Singleton pregnancies with history of preterm birth	46	17.4%	28.3%	10.9% (-6.1%, 27.9%)

CONCLUSION

- In a sample of commercially insured pregnancies that were at high risk for preterm birth, there was no evidence of an association between vaginal progesterone use and risk of preterm birth.

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