

Sex effect on Vasopressor use after non-cardiac Surgery

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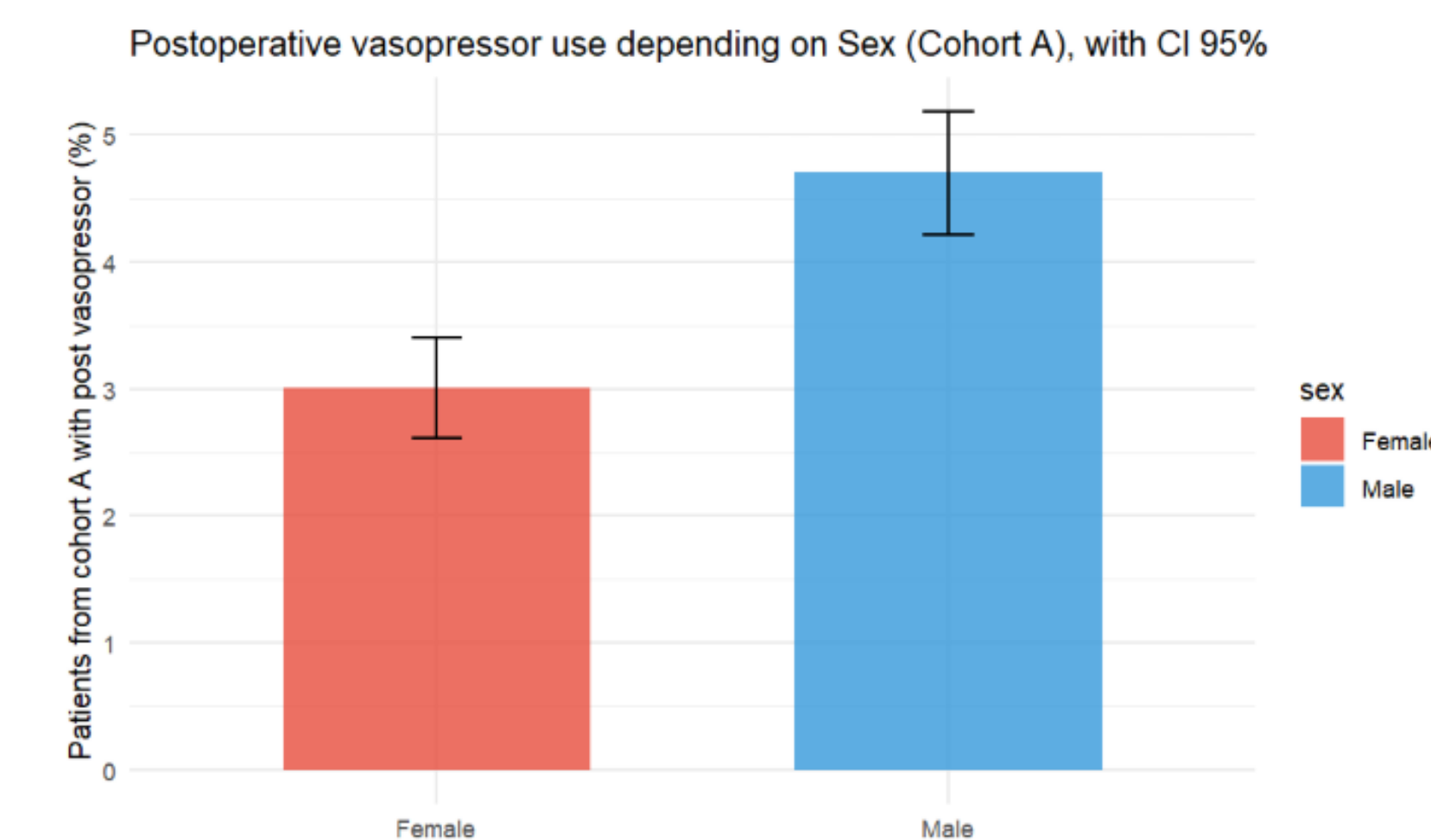
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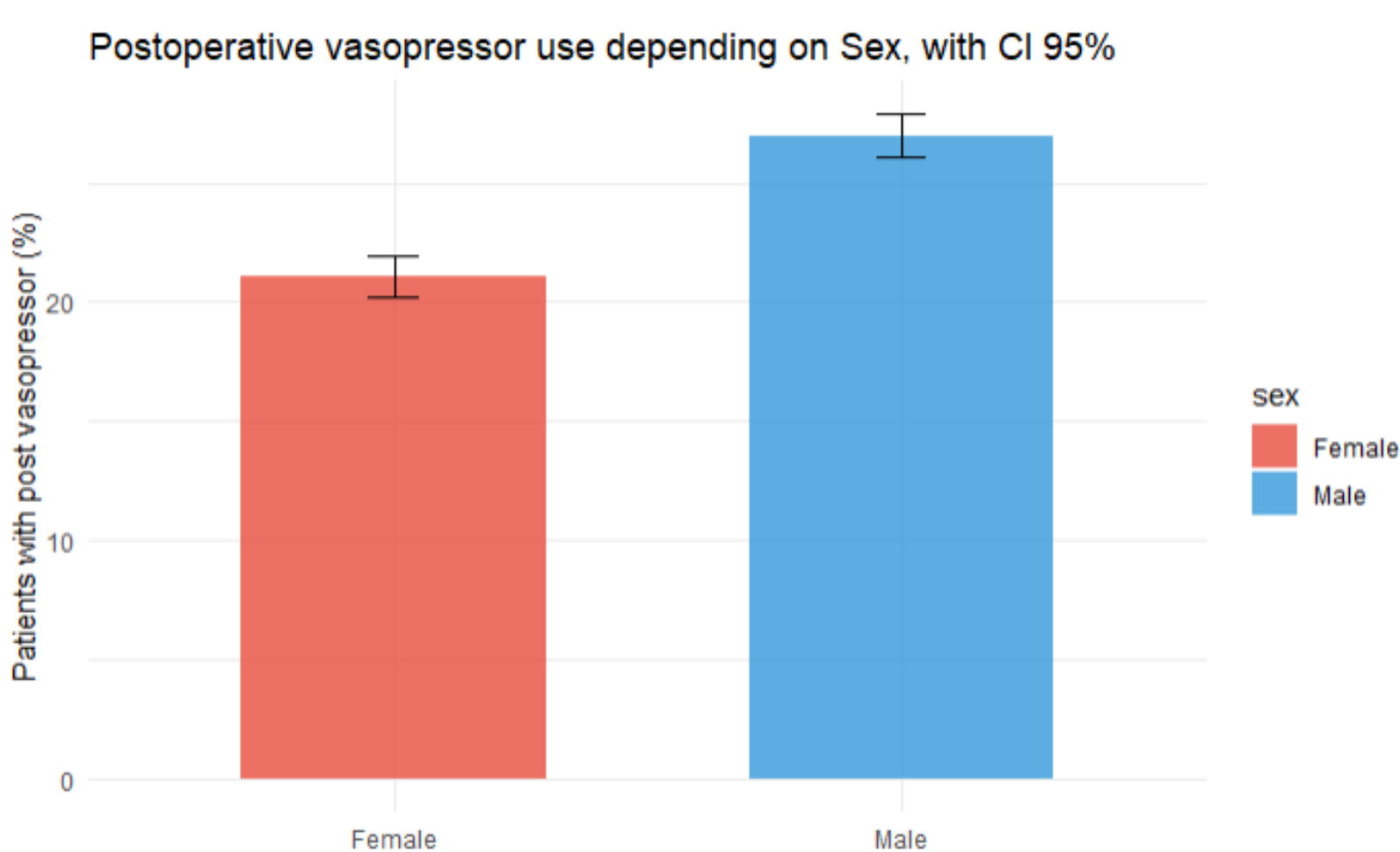
1. Introduction

- A study concerning non-cardiac surgery revealed that **3.9 %** of patients receive post-vasopressor treatment. This group experiences a heightened mortality rate.



- In Cohort A (representative sample), males show higher vasopressor use than females (4.6% vs 3%).
- This study investigates the clinical and biological drivers of this disparity.

2. Definition & Population



- Post vasopressors are medications used to elevate arterial pressure by constricting blood vessels, administered after a surgery.
- In our combined dataset (Cohorts A + B), approximately **22% of women** and **27% of men** use postoperative vasopressors. *Note that this rate is higher than the population estimate ($\approx 3-4.6\%$) due to the enriched design of Cohort B, which oversamples vasopressor patients.*
- We analyzed **18,387 patients** from SQUEEZE dataset, tracking 21 variables, providing by two Cohorts from 228 hospitals across 42 countries (Cohort A that represents all consecutive patients for 1 week, and Cohort B an additional sample of up to 30 consecutive patients administered postoperative vasopressor infusions within 1 year).

3. Methods

- Mixed-Effects Logistic Regression** with random effect for countries and hospitals:

$$\ln \left(\frac{P(Y=1)}{1-P(Y=1)} \right) = \beta_0 + \beta_1 \cdot \text{sex} + \sum \beta_i \cdot X_i$$

Where Y : postoperative vasopressor use (1 = Yes, 0 = No), sex : indicator for sex, and X_i : fixed clinical covariates (including surgical procedure type, age, ASA score, preoperative MAP,...).

- To rank the predictors, we used a **Random Forest algorithm**.
- We utilized a **mediation analysis** to examine the direct and indirect relationships between two variables, 1:1 Propensity-Score Matching (PSM), and computed an E-value to assess unmeasured confounding.

4. Results

The primary mixed-effect logistic regression including all raw variables has been conducted: sex emerges as a non-significant variable. A Random Forest algorithm confirmed that fluid volume, complication degree, and arterial pressure are the top predictors.

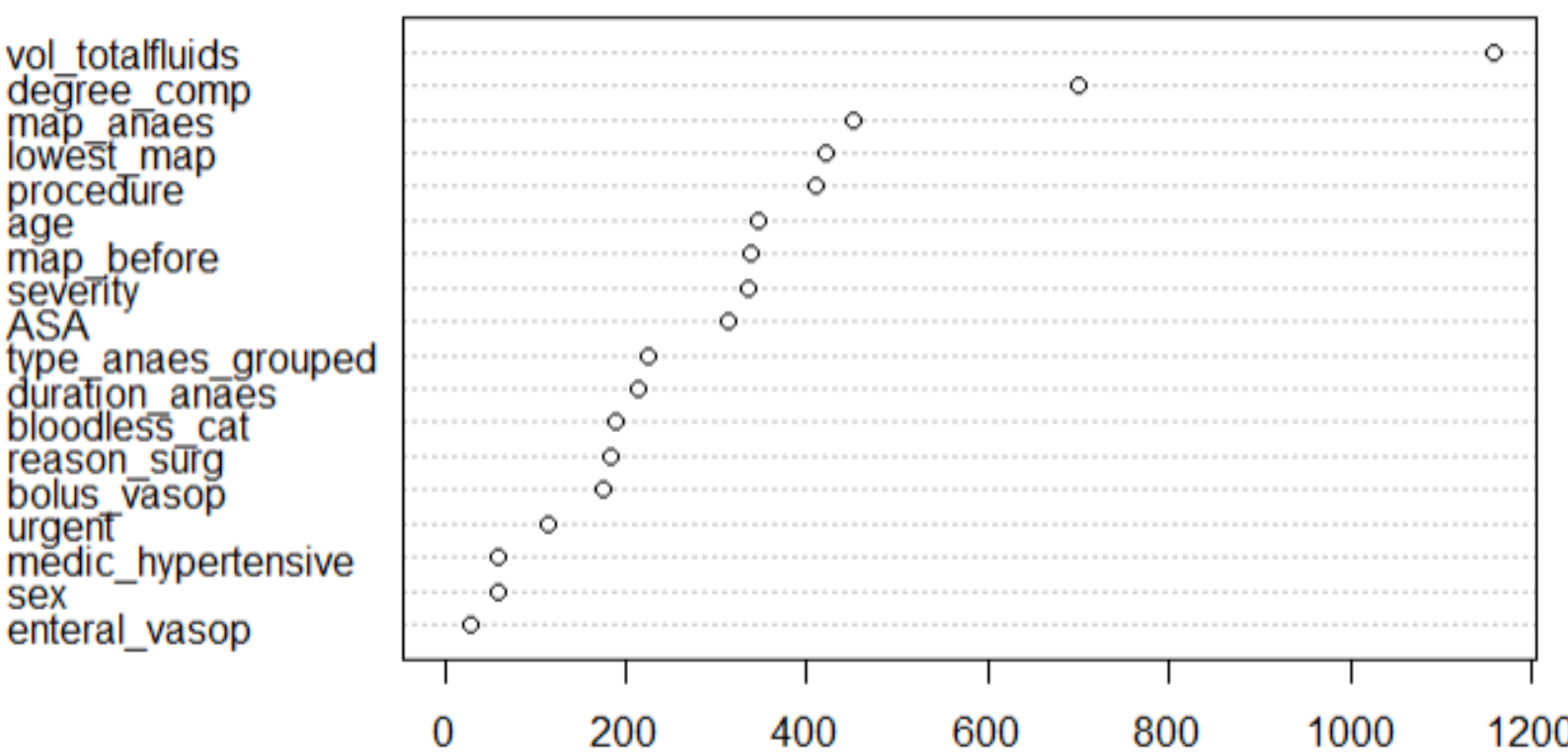
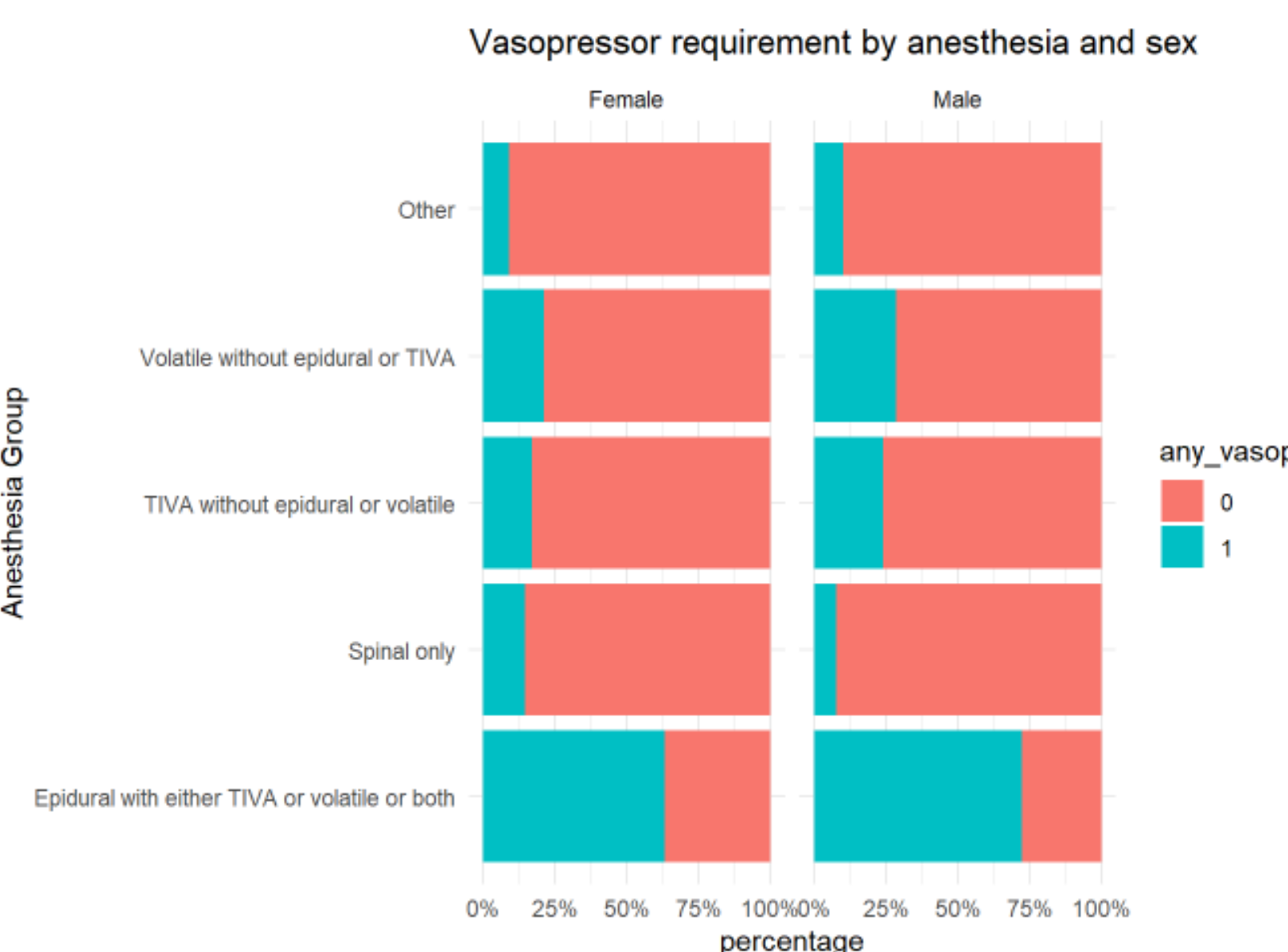


Figure 3: Random Forest: variables sorted by importance

Surgical & Anesthesia Nuances:



While Epidural combined with TIVA or volatile or both increases risk for both sexes, a major exception exists:

- Females are more likely to require vasopressors under **spinal anesthesia**. This subgroup correlates with a higher median age for females (72 vs 64 years).
- Concerning **procedures**, the male excess is driven by higher case complexity (ASA 4-5) in hepatobiliary/vascular surgeries, but persists biologically in upper gastro-intestinal and neurological procedures.

The Fluid Standardization

The lack of significance for sex in early models was due to collinearity: males weigh more and receive larger fluid volumes. When fluid is standardized (mL/kg):

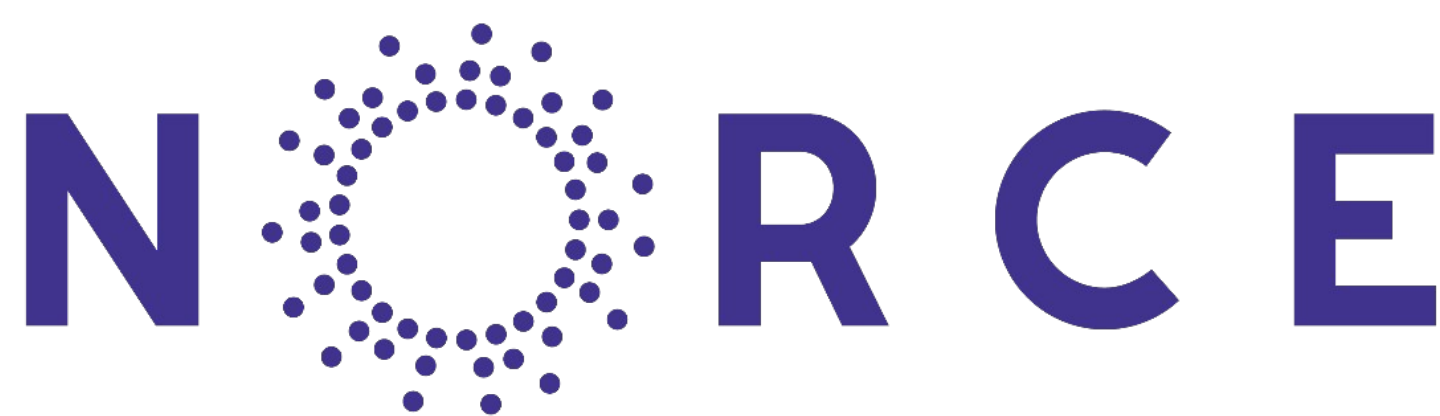
- Both sexes receive identical standardized volumes (approx. 15 mL/kg for males vs 14 mL/kg for females).
- A mediation analysis revealed a direct effect of **4.7 percentage points** persisting for males.
- In the final adjusted model (when we replace the volume of fluids and weight by the standardized volume of fluids), **male sex becomes a significant independent predictor** (OR = 1.26).

Progressive model specification reveals that the sex effect only emerges once fluid volume collinearity is addressed:

Statistical Model	Odds Ratio	95% CI	p-value
Primary Model (Raw Fluids)	1.09	[0.97 - 1.24]	0.150
Preoperative Variables Only	1.20	[1.10 - 1.30]	< 0.001
Final Model (mL/kg Fluids)	1.26	[1.11 - 1.42]	< 0.001
Propensity-Score Matched	1.53	[1.42 - 1.64]	< 0.001

5. Conclusions

- PSM (OR=1.53) and the mixed model (OR=1.26) converge to confirm a **statistically consistent sex effect**, with PSM providing a purer estimate by eliminating residual covariate imbalance.
- This disparity cannot be fully attributed to surgical complexity, procedural differences, or weight-based fluid management protocols.
- Current weight-based fluid standardizations (mL/kg) fail to close the gender gap, leaving male patients relatively more vulnerable.
- The **E-value of 1.46** suggests that residual confounding by an unmeasured factor cannot be excluded and represents a priority for future research.



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