

# Previaible “Provoked” Feto-Maternal Hemorrhage May Represent Insensible Cell Exchange

## Results of the EQUATE Study: Evaluating Quantities of Antenatal Transplacental Cell Exchange

Stefanie J. Hollenbach, MD, MS<sup>1</sup>, Matthew Cochran, MS<sup>2</sup>, Amy Harrington MD<sup>1</sup>

<sup>1</sup>Obstetrics and Gynecology, University of Rochester Medical Center, Rochester, NY; <sup>2</sup>Flow Cytometry Shared Resource Laboratory, University of Rochester Medical Center, Rochester NY

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Sample processing performed with FMH QuikQuant Flow Cytometry Version which is a commercially available assay from Trillium Diagnostics. Trillium Diagnostics contributed no monetary support to this study nor contributed to the design or analysis of the samples.

### Abstract

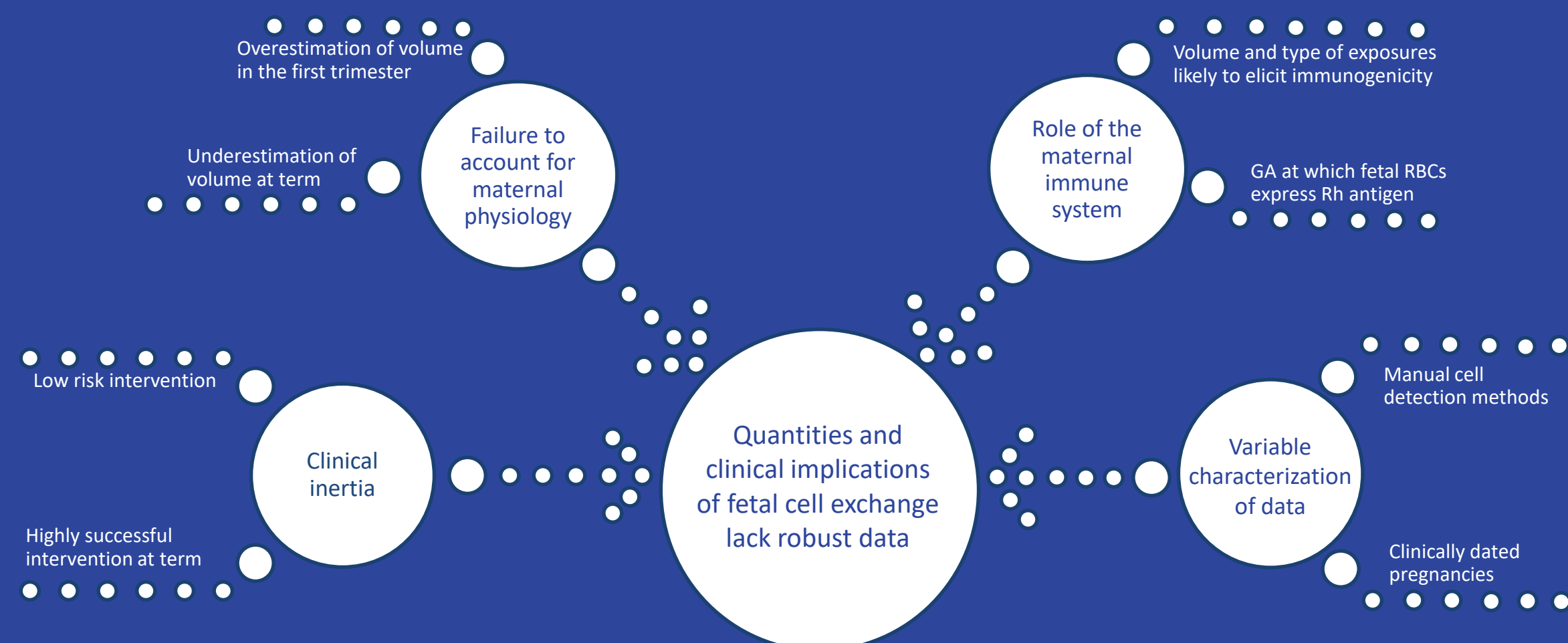
**OBJECTIVE:** To quantify spontaneous and provoked maternal fetal cell exchange in the first half of pregnancy. Transfer of fetal red blood cells (FRBCs) into the maternal circulation during the previaible period is poorly characterized but of clinical relevance for miscarriage management and invasive procedures.

**STUDY DESIGN:** Prospective, descriptive cohort study of women presenting for surgical termination of pregnancy with sonographically confirmed gestational age (GA). Pre-procedural (1-2 days prior to procedure) and post-procedural (5 minutes after placental extraction) blood samples were collected to characterize both spontaneous and provoked cell exchange. Samples were analyzed via flow cytometry to quantify FRBCs present in the maternal sample with a sensitivity to 4.3 FRBCs per 10,000 maternal red blood cells.

**RESULTS:** A total of 100 patients at 6-22 weeks GA contributed 200 matched pre- and post-procedural samples. FRBCs were identified in 69 patients (69%) including 4 (4%) who exhibited FRBCs pre-procedure only and 9 (9%) post-procedure only, for a total of 65 patients (65%) having post-procedural FRBCs. Of all the patients with FRBCs following their procedure, the majority (n = 56, 86%) also exhibited evidence of cells before the procedure with only 9 patients (14%) exhibiting FRBCs only after. Of the 56 concordantly positive patients, 36 (64%) demonstrated an increase in the cell count, 18 (32%) demonstrated a decrease in the cell count, and 2 (4%) demonstrated an equivalent value. No dose-response relationship was appreciable between GA and FRBC count.

**CONCLUSION:** Following all patients undergoing disruption of the placenta with instrumentation, roughly two thirds of patients had detectable FRBCs in the maternal circulation following their procedure but—among those that did—the majority were also present prior to the procedure. This leads to further questions regarding the relationship between risk events and alloimmunization potential in the first half of pregnancy as the rate of spontaneous transplacental cell exchange may be underappreciated and the magnitude of provoked transfer may be overestimated.

### Background: Challenges in Understanding Early Pregnancy Alloimmunization Risks



### Methods

- Descriptive cohort study: Women presenting for termination of pregnancy
- Primary outcome: Quantity of fetal cells present before and after termination
- Blood sampling: Pre- and post-procedural
- Flow cytometric analysis of fetal cells: Discrimination of maternal from fetal HgF with a sensitivity to 0.04% fetal RBCs

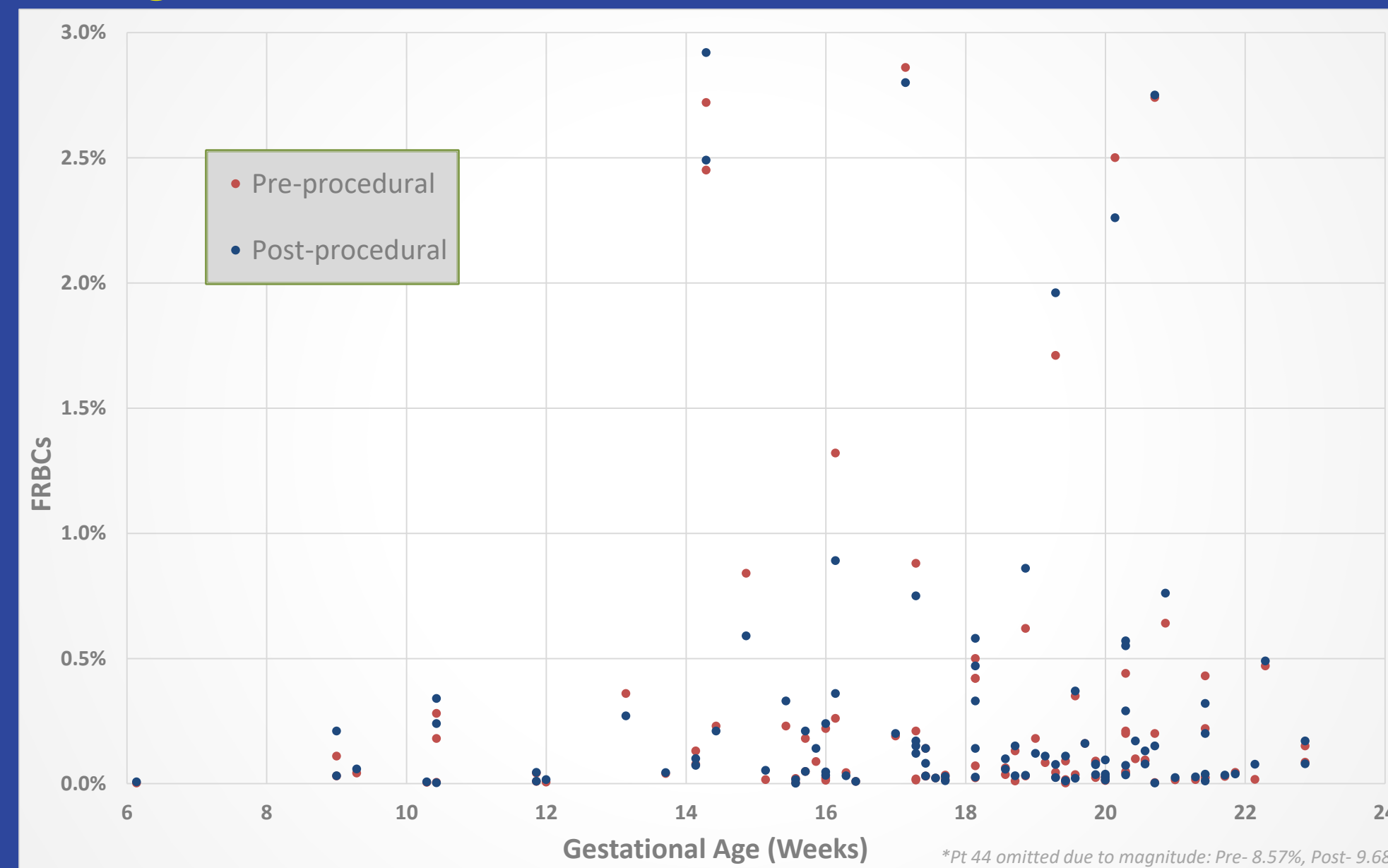
### Results

**Table 1: Patient Demographics and Procedural Characteristics**

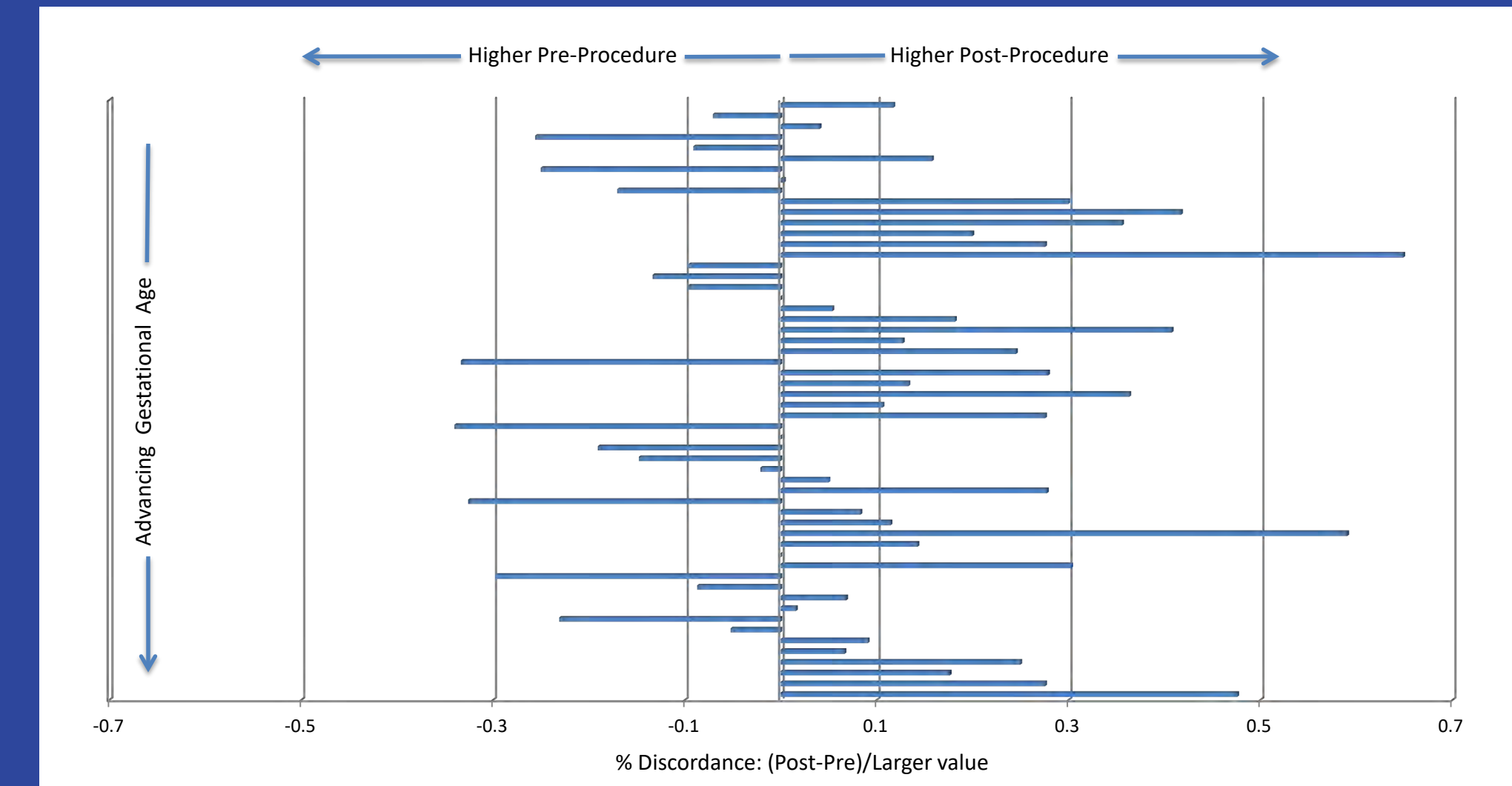
Patient Demographics and Characteristics of Cell Detection Groups*					
	Total Cohort n = 100	No FRBCs detected n = 31	FRBCs before only n = 4	FRBCs before/after n = 56	FRBCs after only n = 9
GA	17w4d ± 3.4	17w1d ± 4w	19w1d ± 2w	17w4d ± 3w	18w0d ± 2.1w
Pt age (yr)	26 ± 5.5	27.1 ± 5.0	30.5 ± 4.8	25.0 ± 5.3	30.1 ± 6.2
Pt wt (lb)	162 ± 40.7	168.9 ± 45.3	167.5 ± 21.8	158.7 ± 39.5	162.6 ± 42.8
Preop VB	26 (26%)	6 (19%)	2 (50%)	17 (30%)	1 (11%)
Laminaria	71 (71%)	22 (71%)	4 (100%)	37 (66%)	8 (89%)

\*No statistically significant difference between any groups for any variables by T test for continuous data or Fisher's exact test for categorical data.

**Figure 1: FRBCs in Maternal Circulation as Function of GA**



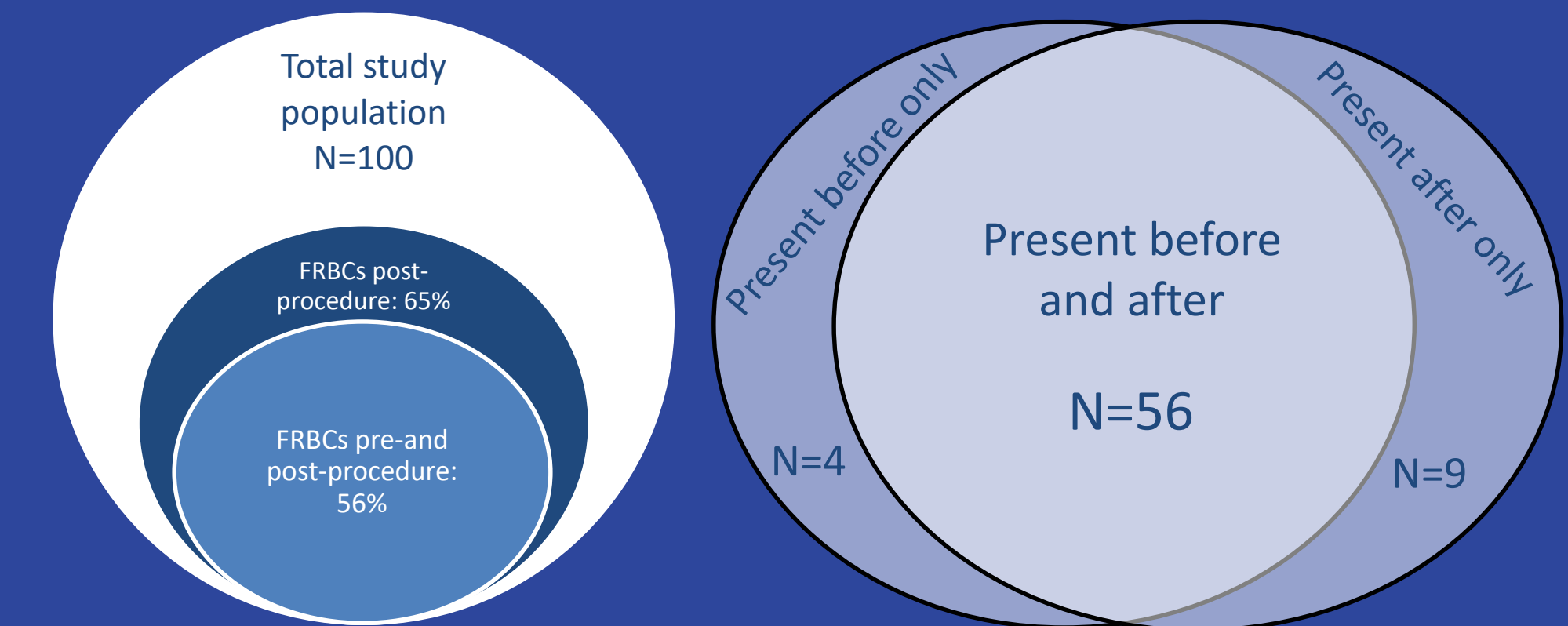
**Figure 2: FRBC Weighted Discordance**



**Figure 3: Fetal Cell Detection in Patients 6w-22w Gestational Age**

**Total Study Population**

**Patients with FRBCs Detected n = 69**



### Discussion/Conclusions

- First study of cell exchange in ultrasound dated pregnancies- expands the understanding of 1<sup>st</sup> and 2<sup>nd</sup> trimester maternal-fetal cell exchange.
- Lack of attention to background fetal cell transfer likely overstates magnitude of cell exchange from risk events.
- The clinical relevance of these findings includes appropriate allocation of resources and better understanding of residual seroconversion risk.
- Future studies planned to explore the expression of Rh antigen by fetal cells.