

# The cost of infertility therapy for women with a history of hysteroscopic adhesiolysis, as compared to those with other or no previous intrauterine surgery

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## INTRODUCTION

- Intrauterine surgery can lead to basilar endometrial trauma and intrauterine adhesion (IUA) formation.
- The damage to the endometrium may persist despite adhesiolysis, impacting fertility and pregnancy outcomes. [1,2]
- Endometrial impairment can increase infertility treatment costs and elevate risks for pregnancy complications and neonatal adverse outcomes. A published model suggests that adhesiolysis alone is associated with **higher rates of adverse outcomes** and **increased healthcare costs**. [3]
- There is a need for a comprehensive approach to minimizing surgically-induced endometrial trauma and optimizing functional endometrial repair to improve fertility, pregnancy and neonatal outcomes.

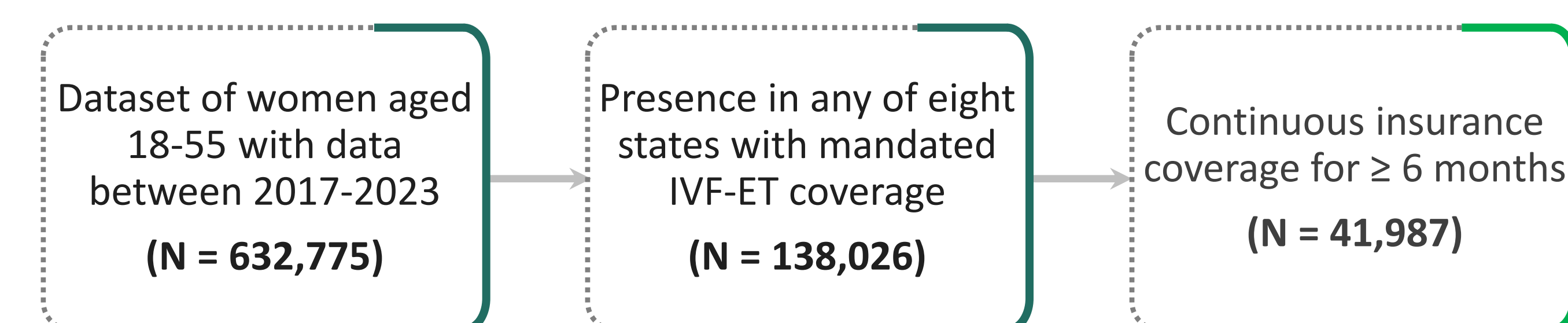
## OBJECTIVE

- This analysis aims to assess the financial impact of intrauterine surgery on infertility treatment costs by comparing the direct economic costs of infertility-related services among three cohorts of women in U.S. states with mandated infertility coverage.
- The three cohorts compared are comprised of women who have (1) **undergone hysteroscopic adhesiolysis**, (2) **undergone intrauterine surgery, excluding adhesiolysis**, and women with (3) **no history of intrauterine surgery (Procedure-Free)**.

## DATA AND METHODS

- Study Design & Data Source:** Retrospective study for women within the reproductive-age group (18–55 years) using the HealthVerity® Marketplace™ database with ICD-10, CPT and cost data from 150 U.S. payors, covering commercial, Medicaid, and Medicare plans.
- Study Population:** Infertility-related data analyzed from 2017 to mid-2023 with > 6 years of continuous follow-up, limited to 8 states with mandates for coverage of in vitro fertilization-embryo transfer (IVF-ET) before 2017: Arkansas, Connecticut, Hawaii, Illinois, Maryland, Massachusetts, New Jersey, & Rhode Island.
- Study Cohorts:** Three study cohorts (≥6 months of continuous data, Apr 2017–Dec 2019); Cohort 1: hysteroscopic adhesiolysis (Adhesiolysis), Cohort 2: intrauterine surgery excluding adhesiolysis (Procedure-Experienced), Cohort 3: No record of previous intrauterine surgery (Procedure-Free random sample, N=10,000).
- Statistical Analysis:** Propensity score matching applied based on comorbidities, age, race, payor type, and geographic location.

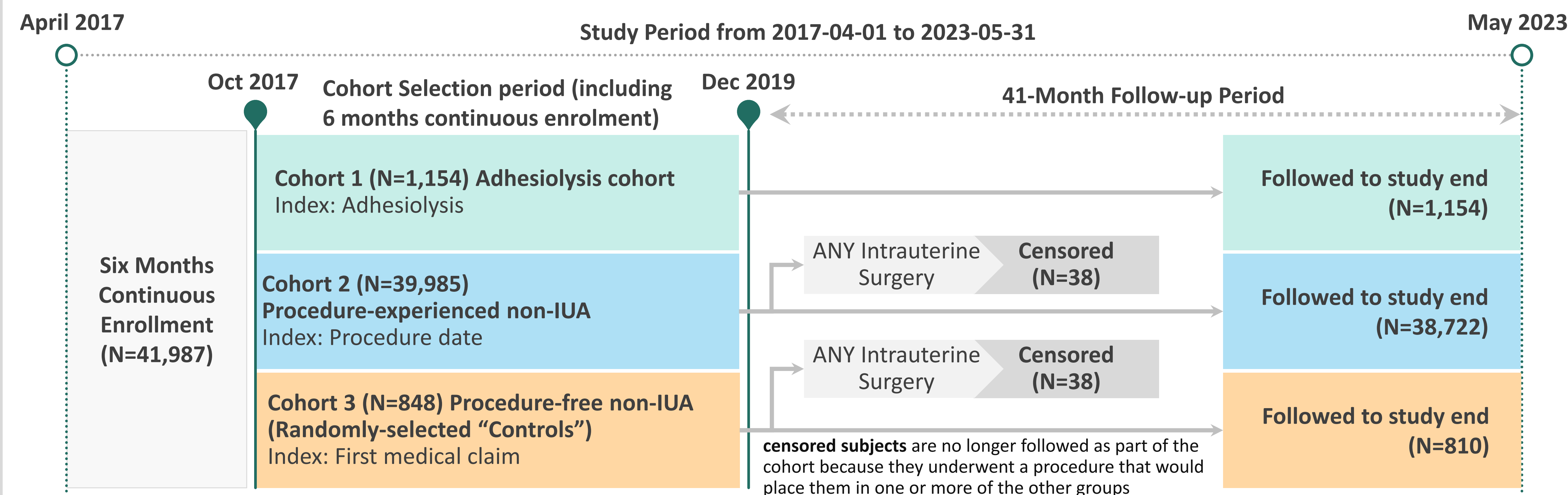
FIGURE 1. DATA FLOW CHART



## LIMITATIONS

- Adjuvant Use Could Not Be Captured:** There are no CPT codes for the off-label use of IUDs and Foley balloons that may have been used for IUA prevention so the use of these adjuvants will not have been captured in the payor database.
- Potential for Missing Procedures in Study Groups:** Subjects may have undergone procedures of interest outside the study time frame and network.
- Capturing Fertility Treatment Costs:** Self-paid fertility treatments are not recorded in the database, and mandated IVF-ET coverage varies by state and may have restrictions on:
  - Number of cycles covered
  - Total coverage in dollar value
- Exclusion of Costs Associated with Pregnancy Outcomes:** The scope of this study did not include evaluation and comparison of pregnancy outcomes like pre-term labor, peri-partum hemorrhage, and other adverse outcomes.
- Exclusion of Costs Associated with Neonatal Outcomes:** Newborn care costs and outcomes, including those for premature infants, are excluded from the study database, and likely represent significant sources of healthcare resource use and costs.

## FIGURE 2. COHORTS SELECTED & ANALYSIS OVER 41 MONTHS



## TABLE 1: BASELINE CHARACTERISTICS OF STUDY POPULATION

Baseline Characteristics	Unmatched Cohort			SMD	Matched Cohort (Using Propensity Score Matching)			SMD
	Adhesiolysis (%)	Procedure-Experienced Non-IUA (%)	Procedure-Free Non-IUA (%)		Adhesiolysis (%)	Procedure-Experienced Non-IUA (%)	Procedure-Free Non-IUA (%)	
	N = 1,154	N = 38,722	N = 810		N = 1,154	N = 38,722	N = 810	
Age Group								
18-25	2.4%	15.7%	16.5%		2.4%	15.7%	16.5%	
26-45	80.2%	64.5%	59.1%		80.2%	64.5%	59.1%	
46+	17.2%	18.8%	18.5%	0.48	17.2%	18.8%	18.5%	0.48
Unknown	0.1%	1.0%	5.8%		0.1%	1.0%	5.8%	
Insurance Plan Types								
Commercial	85.0%	59.7%	63.5%		85.0%	59.7%	63.5%	
Medicaid	14.0%	37.3%	33.0%	0.40	14.0%	37.3%	33.0%	0.40
Medicare Advantage	0.3%	1.4%	1.9%		0.3%	1.4%	1.9%	
Unknown	0.8%	1.6%	1.7%		0.8%	1.6%	1.7%	
US Geographic Region								
Northeast	55.6%	58.0%	51.4%		55.6%	58.0%	51.4%	
Midwest	0.4%	0.9%	0.6%	0.13	0.4%	0.9%	0.6%	0.13
South	43.4%	39.8%	46.4%		43.4%	39.8%	46.4%	
West	0.5%	1.3%	1.6%		0.5%	1.3%	1.6%	
Charlson Comorbidity Index Score								
Very Mild: 0	85.5%	82.6%	86.8%		85.5%	82.6%	86.8%	
Mild: 1	11.9%	13.3%	11.6%	0.11	11.9%	13.3%	11.6%	0.11
Moderate or severe: 2+	2.6%	4.1%	1.6%		2.6%	4.1%	1.6%	

By using propensity score matching (PSM) on these cohorts, the analysis ensured:

- Comparability among the three study cohorts
- Balance between key factors influencing infertility-related costs through the matching of key confounding variables
- Reduced bias due to the balance of patient demographics, comorbidities, and insurance coverage
- Fair comparisons and enhanced accuracy of cost analysis by isolating surgical history effects
- Accurate, unbiased assessment of how different intrauterine surgical histories impact infertility-related healthcare costs

## TABLE 2. TOTAL COHORT COSTS OF INFERTILITY DIAGNOSIS AND MANAGEMENT

Cost Category	Adhesiolysis		Procedure-Experienced Non-IUA			Procedure-Free Non-IUA		
	N = 594		N = 594			N = 594		
	Per subject	Cohort	Per subject	Cohort	P	Per subject	Cohort	P
Evaluation *	\$740	\$439,599	\$148	\$87,774	<0.001	\$44	\$25,981	<0.001
Management **	\$1,807	\$1,073,351	\$289	\$171,586	<0.001	\$35	\$20,796	<0.001
Total	\$2,547	\$1,512,950	\$437	\$259,360	<0.001	\$79	\$46,777	<0.001

P-value <0.05 is considered significant (from Chi-Square tests)

\* Evaluation included services for diagnosis of infertility, such as office visits, imaging, and laboratory tests

\*\* Management included services to improve fertility, such as interventional imaging, repeat adhesiolysis, in vitro fertilization, drug administration, and the cost of drugs themselves

- Higher per Cohort Cost with a History of Endometrial Trauma:** The mean per subject cost in the adhesiolysis cohort was approximately:
  - 5.8x higher than the procedure-experienced cohort
  - 32x higher than the procedure-free cohort
  - P < 0.001 when comparing to either cohort

- Increased Evaluation and Management Costs:** Both diagnostic and procedural costs contribute to the overall impact that surgically induced endometrial trauma can have on the health system.

## TABLE 3. PROPORTION OF WOMEN CARRYING FINANCIAL BURDEN

Cost Category	Adhesiolysis		Procedure-Experienced Non-IUA		Procedure-Free Non-IUA		
	N = 594		N = 594		N = 594		
	%	Mean	(%)	Mean	(%)	Mean	P
Costs of evaluation for infertility (Including Diagnostic)							
Evaluation & management	40.7%	\$339	11.4%	\$342	<0.001	2.7%	\$327 <0.001
Imaging	41.9%	\$861	10.1%	\$587	<0.001	2.4%	\$768 <0.001
Laboratory tests	41.4%	\$582	10.6%	\$465	<0.001	2.2%	\$769 <0.001
Costs of management of infertility, including IVF							
Evaluation & management	36.2%	\$1,133	6.1%	\$934	<0.001	1.9%	\$415 <0.001
Imaging	36.7%	\$956	5.7%	\$895	<0.001	1.9%	\$529 <0.001
Laboratory tests	38.6%	\$715	6.9%	\$632	<0.001	1.9%	\$482 <0.001
Subsequent adhesiolysis	1.7%	\$3,106	N/A (N = 0)	N/A	N/A (N = 0)	N/A	N/A
Gamete or embryo management	16.7%	\$1,029	2.5%	\$1,038	<0.001	0.2%	\$303 <0.001
Pharmaceuticals	11.3%	\$4,846	1.3%	\$8,256	<0.001	0.2%	\$4,807 <0.001
Average per patient	\$2,547		\$437		\$79		
Total per cohort	\$1,512,950		\$259,360		\$46,777		

P-value <0.05 is considered significant (from Chi-Square tests)

\* Evaluation included services for diagnosis of infertility, such as office visits, imaging, and laboratory tests

\*\* Management included services to improve fertility, such as interventional imaging, repeat adhesiolysis, in vitro fertilization, drug administration, and the cost of drugs themselves

- The adhesiolysis cohort experienced the highest infertility-related financial burden of all three cohorts, with significantly higher diagnostic, procedural, IVF (including embryo management), and pharmaceutical costs
- Approximately 40% of subjects that underwent adhesiolysis had evaluation and management charges and required imaging and laboratory tests compared to approximately 10% (procedure-experienced) and approximately 3% (procedure-free)
- IVF and fertility treatment costs were substantially higher and more common among the adhesiolysis subjects.
- These findings demonstrate a substantial financial burden associated with those subjects exposed to surgically induced endometrial trauma, especially those subjects requiring hysteroscopic adhesiolysis.

## CONCLUSIONS

- Higher Infertility-Related Costs in Adhesiolysis Patients:** Women requiring transcervical intrauterine surgery, especially adhesiolysis, have significantly higher utilization of infertility-related healthcare services and costs compared to women that have not undergone transcervical intrauterine surgery.
- Surgically Induced Endometrial Trauma Drives Increased Resource Use:** Elevated costs and treatment needs are likely due to endometrial trauma from surgery, leading to a higher dependency on IVF, diagnostic evaluations, and pharmaceutical interventions.
- Financial Burden Is Substantial and Disproportionate:** Adhesiolysis patients experience ~5.8x higher costs than the those in the procedure-experienced group and ~32x higher than the procedure-free group, with significant expenditures on repeat interventions and fertility management.
- Minimizing Surgically-Induced Endometrial Trauma, and Optimizing Functional Endometrial Repair May Reduce Costs and Improve Outcomes:** Facilitation of IUA-free endometrial repair, could lower healthcare costs, reduce infertility burdens, and improve reproductive outcomes for affected women.

## REFERENCES

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## DISCLOSURES

- CM, MPB, JM, RW, and JK are employees of Atria Inc.
- IF is employed by Rejoni Inc.
- PB is employed by Boston IVF and is a paid investigator for a trial by Rejoni Inc.
- MGM is a consultant for Rejoni Inc.
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