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WHITE PAPER

Evidence on Fertility Treatment Standard Adherence from Commercial Insurance Claims

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Guideline-recommended diagnostic evaluation and first-line treatment are frequently incomplete at the time in vitro fertilization (IVF) is initiated, and in several cases, the care being received before IVF begins is actively contraindicated by guideline care standards. Specifically:

- In most male and female infertility presentations examined, IVF was underway in the majority of patients before recommended evaluation or first-line treatment had been completed in even a third of cases.
- For the most basic diagnostic step in male infertility evaluation, semen analysis, nearly half of patients remained untested at six months following diagnosis.
- Among men with azoospermia, over half received testosterone treatment, which ASRM and AUA guidelines explicitly identify as contraindicated in men pursuing fertility.
- Among women with PCOS, more than a quarter had initiated IVF within the first month of diagnosis, before guideline-recommended first-line therapy had been attempted in the large majority of cases.
- Among women with hyperprolactinemia, a potentially reversible cause of infertility treatable with a well-tolerated oral medication, more than half had initiated IVF by month three while fewer than 34% had received any recommended first-line treatment.

These findings are drawn from an actuarial analysis of commercial insurance claims data conducted by Axene Health Partners (AHP). The analysis used the Merative MarketScan® Commercial Claims database covering approximately five million commercially insured members from 2021 through 2024. Guideline adherence was measured against ASRM and AUA/ASRM published recommendations, including the ASRM/AUA Joint Guidelines on male-factor



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infertility¹, the 2023 International Evidence-Based Guideline for Polycystic Ovary Syndrome², ASRM committee opinions on amenorrhea³ and endometriosis⁴, and ASRM guidance on evaluation of infertile women⁵. Because claims data reflects billing activity rather than clinical confirmation, adherence rates presented in this paper should be understood as reflecting services that were billed, not services that were clinically indicated — though population-level patterns of the magnitude documented here are not adequately explained by appropriate clinical variation alone.

Male-Factor Infertility

Evaluating guideline adherence in male-factor infertility requires examining two distinct dimensions: whether the basic diagnostic workup was completed before IVF began, and whether conditions identified in that workup received appropriate treatment before escalation to IVF. AHP examined both dimensions across four male-factor diagnostic presentations: semen analysis, varicocele, azoospermia, and recurrent pregnancy loss. The analysis compared the rate of guideline-recommended services to IVF initiation rates at defined intervals following an infertility diagnosis among male infertility patients whose partners would go on to receive IVF treatment within fifteen months. The findings are consistent across all four: diagnostic evaluation and first-line treatment were substantially incomplete at the time IVF was initiated.

¹ Schlegel PN, et al. Diagnosis and Treatment of Infertility in Men: AUA/ASRM Guideline Part I. *Fertil Steril.* 2021;115(1):54–61. doi:10.1016/j.fertnstert.2020.11.015. Part II: *Fertil Steril.* 2021;115(1):62–69. doi:10.1016/j.fertnstert.2020.11.016.

² Teede HJ, et al. Recommendations from the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome. *Fertil Steril.* 2023;120(4):763–793. doi:10.1016/j.fertnstert.2023.07.025.

³ Practice Committee of ASRM. Current evaluation of amenorrhea: a committee opinion. *Fertil Steril.* 2024;122(1):52–61. doi:10.1016/j.fertnstert.2024.02.001.

⁴ Practice Committee of ASRM. Endometriosis and infertility: a committee opinion. *Fertil Steril.* 2012;98(3):591–598. doi:10.1016/j.fertnstert.2012.05.031.

⁵ Practice Committee of ASRM. Fertility evaluation of infertile women: a committee opinion. *Fertil Steril.* 2021;116(5):1255–1265. doi:10.1016/j.fertnstert.2021.08.038.



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Figure 1. Male Factor Guideline Adherence Rates and IVF Initiation Rates (6 Months After Condition Diagnosis)

Condition	Guideline Measure	Adherence Rate	IVF Initiation Rate
Semen Analysis	≥1 semen analysis by month 6	56.0%	65.1%
	≥2 semen analyses by month 6	7.5%	
Varicocele	Scrotal ultrasound	52.4%	52.4%
	Varicocelectomy	11.9%	
Azoospermia	Karyotype + Y-deletion testing	19.6%	62.7%
	CFTR testing	9.8%	
	Testosterone treatment received (contraindicated)	41.2%	
Recurrent Pregnancy Loss	Karyotype testing by month 6	22.4%	65.6%
	DNA fragmentation testing by month 6	3.0%	

Semen analysis, the lowest-cost, most foundational diagnostic step in male infertility evaluation, and the starting point for all subsequent treatment decisions, was not completed in nearly half of patients before IVF was underway². This matters because semen analysis is not merely confirmatory; it characterizes the nature and severity of the underlying condition, and that characterization directly determines what treatment is appropriate. Without it, treatment selection is occurring in a diagnostic vacuum.

For conditions affecting semen production and quality including varicocele, azoospermia, and the genetic abnormalities associated with recurrent pregnancy loss the adherence picture is similarly incomplete. Varicocele is one of the most common correctable causes of male infertility, and varicocelectomy is a routine outpatient procedure with documented improvements in semen parameters and pregnancy rates⁶. Yet fewer than one in seven eligible patients received it before IVF was initiated in over 80% of the cohort. The argument that azoospermia explains this gap is not supported by the literature; reported azoospermia rates in varicocele patients are only 4–13%.⁷ For azoospermia specifically, recommended genetic evaluations, including karyotype and Y-chromosome microdeletion testing, were received by fewer than a quarter of patients, despite carrying implications for the patient's broader health beyond fertility alone².

An additional clinically significant finding in the male-factor cohort is not a gap in recommended care but the presence of contraindicated care: over half of men coded with azoospermia received testosterone treatment, which ASRM and AUA guidelines explicitly identify as contraindicated in men pursuing fertility². Exogenous testosterone suppresses gonadotropins and can reduce or eliminate spermatogenesis, potentially compounding the very condition for

⁶ Baazeem A, et al. Varicocele and male factor infertility treatment: a new meta-analysis and review of the role of varicocele repair. *Eur Urol.* 2011;59(5):796–808. doi:10.1016/j.eururo.2011.01.014

⁷ Hamada A, et al. Unexplained male infertility: diagnosis and management. *Int Braz J Urol.* 2012;38(5):576–594. doi:10.1590/S1677-55382012000500002



which the patient is being evaluated.⁸ For patients with recurrent pregnancy loss, DNA fragmentation testing was completed in only 3.4% of cases by month six despite a direct guideline recommendation, while approximately 75% had initiated IVF. Sperm DNA fragmentation is a known driver of recurrent miscarriage that standard IVF does not address⁹; for patients in this cohort whose losses are attributable to fragmentation abnormalities, the underlying cause of their pregnancy losses was not identified before IVF began.

Female-Factor Infertility

Female-factor infertility encompasses a wide range of presentations, from ovulatory disorders driven by endocrine conditions to structural pathology to idiopathic causes. For several of the most common presentations, including PCOS, hyperprolactinemia, endometriosis, hypothyroidism, and amenorrhea, ASRM has identified recommended evaluation and first-line treatment that should precede IVF. AHP examined adherence to those recommendations across all five presentations, comparing the rate of recommended services to IVF initiation rates at defined intervals. As with the male-factor findings, the pattern is consistent: recommended care is frequently incomplete when IVF begins, and IVF begins quickly.

Figure 2. Female Factor Guideline Adherence Rates and IVF Initiation Rates (6 Months After Condition Diagnosis)

Condition	Guideline Measure	Adherence Rate	IVF Initiation Rate
PCOS	Letrozole	28.6%	62.7%
	Metformin	19.4%	
	Gonadotropins	28.5%	
Hyperprolactinemia	Cabergoline	24.7%	71.4%
Endometriosis (<35)	IUI Before IVF	11.1%	65.9%
Dysmenorrhea	Laparoscopy	10.4%	62.6%
Hypothyroidism	Levothyroxine	59.3%	60.7%
Amenorrhea	FSH Testing	42.9%	51.8%
	LH Testing	44.9%	
	AMH Testing	13.5%	

For conditions where infertility is driven by a specific, potentially reversible endocrine abnormality, principally PCOS and hyperprolactinemia, the data show that IVF is being initiated at high rates before the targeted medical treatment that guidelines recommend as first-line has been attempted. PCOS is the most common cause of anovulatory infertility, and ASRM is explicit that ovulation induction with letrozole should precede IVF for most patients with this

⁸ Schlegel PN, et al. AUA/ASRM Guideline Part I. Fertil Steril. 2021;115(1):54–61. See also Crosnoe LE, et al. Transl Androl Urol. 2013;2(2):106–113.

⁹ Tan J, et al. Int J Mol Sci. 2019;20(20):5038. See also Practice Committee of ASRM. Fertil Steril. 2012;98(5):1103–1111



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presentation.¹⁰ Many PCOS patients will conceive with ovulation induction alone. Yet fewer than one-third had received letrozole by month six, while 71% had initiated IVF. The pattern is similar for hyperprolactinemia, where restoring normal prolactin levels with a well-tolerated oral dopamine agonist can restore ovulation without assisted reproduction⁴, yet more than half of patients had initiated IVF by month three while fewer than 34% had received any recommended treatment.

For conditions where the diagnosis is itself uncertain or incomplete, such as dysmenorrhea, amenorrhea, and related endocrine presentations, a different but equally significant issue emerges: IVF is being initiated before the underlying cause of infertility has been established. Dysmenorrhea is a symptom, and laparoscopy is the recommended procedure to determine whether endometriosis or other structural pathology is present⁵. Over 70% of patients with dysmenorrhea and infertility proceeded to IVF while fewer than 12% had received that diagnostic evaluation. Similarly, amenorrhea is a symptom with a broad differential (e.g., ovarian insufficiency, hypothalamic dysfunction, hyperprolactinemia, and structural abnormalities, among others), and ASRM recommends a structured workup including FSH, LH, estradiol, and AMH before treatment is selected⁴. AMH testing, which directly characterizes ovarian reserve and informs whether IVF is likely to be effective, was documented in only 17.1% of amenorrhea patients. Estradiol and ultrasound rates appear higher but are likely inflated, as these tests cannot be distinguished from IVF cycle monitoring in claims data. The same diagnostic gaps are present for oligomenorrhea, anovulation, and androgen excess, where targeted endocrine evaluation rates were similarly low across all measures examined.

Hypothyroidism represents the one area of comparatively better adherence in this study, with approximately 60% of patients receiving levothyroxine treatment by month six. Even here, however, approximately 40% of patients with overt hypothyroidism proceeded toward IVF without documented levothyroxine treatment, a condition that carries independent risks for pregnancy outcomes, including elevated miscarriage risk, that IVF itself does not mitigate.¹¹

¹⁰ Legro RS, et al. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. *N Engl J Med*. 2014;371(2):119–129. doi:10.1056/NEJMoa1313517. This landmark RCT documents live birth rates with letrozole monotherapy and forms the basis for ASRM's letrozole-first recommendation for PCOS-related anovulatory infertility.

¹¹ Practice Committee of ASRM. Subclinical hypothyroidism in the infertile female population: a guideline. *Fertil Steril*. 2015;104(3):545–553. Note: ASRM's guidance distinguishes between overt hypothyroidism, for which treatment before conception is clearly supported, and subclinical hypothyroidism, for which the evidence is more equivocal



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Conclusions

AHP's analysis of commercial insurance claims data covering approximately five million members from 2021 through 2024 produces the following findings regarding fertility treatment sequencing relative to ASRM and AUA guidelines.

Among men coded with male-factor infertility who subsequently underwent IVF, guideline adherence was consistently low across all conditions examined. For the most basic diagnostic step, semen analysis, the lowest-cost and most foundational evaluation in male infertility workup, nearly half of patients remained untested at six months following diagnosis, and fewer than one in ten received the guideline-recommended repeat testing at any point through fifteen months². For conditions affecting semen production and quality, including varicocele and azoospermia, adherence to recommended evaluation and treatment was similarly limited: varicocelectomy was received by only 13.9% of eligible patients within nine months, and recommended genetic evaluations for azoospermia were completed in fewer than a quarter of patients. In no male-factor condition examined did guideline-recommended care reach even 30% completion by month six in the population that went on to receive IVF. The single most notable finding is not a gap in recommended care but the presence of contraindicated care: over half of men coded with azoospermia received testosterone treatment, which ASRM and AUA guidelines explicitly identify as contraindicated in men pursuing fertility. For couples with recurrent pregnancy loss, DNA fragmentation testing, the most directly relevant evaluation for miscarriage risk, was completed in only 3.4% of cases by month six while approximately 75% had initiated IVF.

Among female patients, the same pattern of low guideline adherence and rapid IVF initiation was observed across all conditions examined. For endocrine conditions where infertility is potentially reversible with targeted medical treatment, principally PCOS and hyperprolactinemia, first-line therapy completion rates did not exceed one-third by month six in either condition, while IVF initiation exceeded 70% over the same window. For conditions where the diagnosis itself is uncertain without a structured workup, dysmenorrhea, amenorrhea, oligomenorrhea, anovulation, and androgen excess, adherence to recommended diagnostic evaluation was similarly low, with no individual test exceeding 65% completion by month six and most falling well below 50%. Hypothyroidism showed the highest relative adherence of any condition examined, with approximately 60% of patients receiving levothyroxine by month six, the only condition in this study where guideline-recommended treatment was documented in a majority of patients before IVF was initiated.

Across both male-factor and female-factor presentations, IVF initiation rates at six months consistently and substantially exceeded guideline adherence rates. In most conditions, IVF was

underway in the majority of patients before recommended evaluation or first-line treatment had been completed in even a third of cases.

Background and Purpose

Infertility has many causes. Male-factor conditions account for roughly half of all cases, either alone or in combination with female-factor causes.¹² The remainder involve female-factor diagnoses — ovulatory disorders, endocrine conditions, structural abnormalities — or a combination of these. Matching treatment to etiology is the foundation of evidence-based fertility care, and the clinical societies most directly responsible for fertility care standards have published detailed guidance describing what evaluation and treatment should occur before escalating to IVF.

The American Society for Reproductive Medicine (ASRM) and the American Urological Association (AUA) have issued joint guidelines for male-factor infertility and clinical recommendations for female-factor infertility describing, for most common presentations, the diagnostic workup and first-line treatments that should precede IVF. These documents reflect a clinical consensus that IVF is appropriate for specific indications and patient profiles, not as a universal first-line response to an infertility diagnosis.

AHP was commissioned by the Women's Reproductive Health Foundation to examine adherence to these guidelines in a commercially insured population. This paper presents the findings of that study.

Data and Methodology

AHP conducted this analysis using the Merative MarketScan® Commercial Claims and Encounter database, which covers approximately five million commercially insured members and includes adjudicated inpatient, outpatient, professional, and retail pharmacy claims. The study window runs from January 1, 2021, through December 31, 2024.

IVF and IUI episodes were identified using ICD-10-CM diagnosis codes, CPT and HCPCS procedure codes, and NDC-based pharmacy therapeutic classes. Guideline adherence was measured by examining the rate at which patients received specific diagnostic and treatment services, identified by CPT, ICD-10, and NDC codes, within defined windows following an infertility diagnosis, and comparing those rates to the rate at which the same patients had initiated IVF over the same periods.

¹² Agarwal A, et al. A unique view on male infertility around the globe. *Reprod Biol Endocrinol*. 2015;13:37. doi:10.1186/s12958-015-0032-1



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Guideline sources for male-factor infertility are the jointly authored AUA/ASRM guidelines on diagnosis and treatment of male infertility. Formal ASRM guidelines for female-factor infertility do not yet exist; ASRM committee opinions and international evidence-based guidelines were used in their place. Specifically, female-factor adherence measures were derived from the 2023 International Evidence-Based Guideline for Polycystic Ovary Syndrome³, the ASRM committee opinion on current evaluation of amenorrhea⁴, the ASRM committee opinion on endometriosis and infertility⁵, and the ASRM committee opinion on fertility evaluation of infertile women⁶. Measures were selected on the basis that each guideline or committee opinion provides sufficiently direct and operationalizable recommendations to support consistent measurement of whether potentially reversible causes of infertility were evaluated or treated before IVF initiation.

Several data limitations should be noted. Claims data reflects billing activity rather than clinical confirmation; the presence of a diagnosis or procedure code indicates that a service was billed, not that the underlying condition was clinically validated or that the service was clinically indicated for that patient's specific presentation. It is possible that some patients did not receive a recommended service because it was clinically inappropriate for their individual circumstances. Population-level patterns of the magnitude documented here are not, however, adequately explained by appropriate clinical variation alone. Additionally, the underlying data have not been audited or independently verified by AHP.

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