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Original Research

Impact of Infertility Duration on Assisted Reproductive Technology Outcomes and Psychological Status: A Retrospective Cohort Study of 11,906 Women

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Abstract

Background: The duration of infertility represents an underexplored temporal dimension of assisted reproductive technology (ART) that may capture clinically relevant patient heterogeneity beyond conventional prognostic factors. This study aimed to evaluate the associations between infertility duration and both ART treatment outcomes and psychological well-being. **Methods:** This retrospective cohort study analyzed 11,906 women stratified by infertility duration (<5 years, n = 9570; 5–10 years, n = 1992; ≥10 years, n = 344). Clinical pregnancy rate, early pregnancy loss, Generalized Anxiety Disorder 7-item scale (GAD-7) anxiety, and Patient Health Questionnaire-15 (PHQ-15) somatization scores were compared using one-way analysis of variance (ANOVA) with Bonferroni correction, chi-square (χ^2) tests, and multivariable regression analysis. **Results:** Progressive increases in maternal age and decreases in ovarian reserve markers were observed across groups (all $p < 0.001$). Clinical pregnancy rates declined significantly from 55.3% to 45.9% ($\chi^2 = 15.16$, $p < 0.001$), while rates for early pregnancy loss remained stable across groups ($p = 0.175$). Anxiety scores showed a significant overall decline across groups (3.33 to 3.07; $p = 0.047$), though no pairwise differences survived Bonferroni correction. Somatization scores increased significantly with infertility duration (4.65 to 5.00; $p = 0.004$), with a significant pairwise difference identified between the <5 years and the 5–10 years groups (adjusted $p = 0.010$). Both differences were of limited clinical magnitude (0.26 and 0.35 points, respectively), falling below established thresholds for clinically meaningful change. Multivariable analyses identified maternal age and anti-Müllerian hormone (AMH) as primary predictors of ART outcomes. Infertility duration was not an independent predictor of clinical pregnancy after multivariable adjustment ($p = 0.061$). AMH showed a modest but positive association with the odds of clinical pregnancy (odds ratio [OR] = 1.032 per ng/mL, $p < 0.001$), consistent with its established prognostic role in ART. **Conclusions:** Infertility duration did not independently predict clinical pregnancy after adjustment for maternal age and ovarian reserve. Although psychological differences across groups were statistically significant, their clinical magnitude was modest. Pending prospective validation, these findings suggest that infertility duration may serve as a useful descriptive variable for patient characterization. However, they should not be considered an independent prognostic factor for clinical pregnancy in ART.

Keywords: infertility duration; ART outcomes; psychological well-being; anxiety; somatization; ovarian reserve

1. Introduction

1.1 Research Background

Infertility affects approximately 15% of reproductive-aged couples worldwide, representing over 48 million couples globally and imposing substantial personal, social, and economic burdens [1,2]. The widespread adoption of assisted reproductive technology (ART) has transformed infertility treatment, with over 8 million babies born through ART worldwide and clinical pregnancy rates reaching 30–40% per fresh embryo transfer cycle in many developed countries [3,4]. Despite these advances, substantial variability in treatment outcomes persists, even among patients with similar demographic and clinical profiles. This underscores the need for improved patient characterization and more individualized management approaches.

Among the candidate factors that may account for unexplained variability in outcome is the duration of infertility, which represents a potentially important but systematically underexplored temporal dimension. Unlike discrete clinical variables such as maternal age or ovarian reserve, infertility duration integrates the cumulative biological, psychological, and behavioral burden of the infertility experience over time. It may therefore capture aspects of patient heterogeneity that conventional prognostic factors do not fully reflect [5,6]. However, the extent to which infertility duration is associated with treatment outcomes and psychological well-being beyond these established factors remains unclear, limiting its potential clinical utility and the evidence base for duration-informed care strategies.

1.2 Literature Review and Current Understanding

Emerging evidence suggests that infertility duration may be associated with ART outcomes beyond what is explained by conventional prognostic factors alone. Several cohort studies have reported declining pregnancy rates with increasing duration of infertility, with some demonstrating associations between treatment delay and reduced success rates [5,7]. The biological mechanisms underlying this temporal pattern likely involve progressive deterioration of oocyte quality, diminished ovarian reserve, and potential changes in endometrial receptivity associated with reproductive aging and repeated unsuccessful conception attempts [8,9]. However, existing studies have yielded inconsistent findings, with some reporting minimal duration effects after controlling for maternal age and ovarian reserve markers [10,11]. These discrepancies may reflect methodological differences and varying categorization of duration. In addition, the confounding role of age-related biological changes that accumulate over time raises the possibility that apparent duration effects on biological outcomes may be largely accounted for by the established predictors rather than representing independent pathways.

The psychological consequences of infertility are well-documented, with recent meta-analyses reporting an overall prevalence of depression and generalized anxiety among infertile women of 31.6% and 13.3%, respectively [12,13]. However, the temporal dynamics of psychological responses to prolonged infertility remain poorly characterized. While some evidence suggests that psychological distress increases with infertility duration, other research indicates more nuanced patterns involving initial acute distress followed by gradual adaptation and the development of coping strategies over time [13,14,15]. Recent research has highlighted the potential divergence between distinct psychological symptom domains, with somatization and anxiety potentially following different trajectories as the experience of infertility lengthens [16,17]. Despite extensive investigation, the relationship between psychological factors and ART outcomes remains contested, with systematic reviews yielding mixed conclusions on whether stress and anxiety directly influence treatment success [18,19].

Contemporary approaches to infertility care increasingly recognize the importance of biopsychosocial models that acknowledge the complex interplay among biological, psychological, and social dimensions of the infertility experience [13,20,21,22]. The allostatic load framework provides a conceptual basis for understanding how chronic infertility-related stress may progressively affect both reproductive function and psychological well-being through neuroendocrine mechanisms [23]. However, most existing research has relied on single-time-point assessments or short follow-up periods, thus limiting our understanding of how these biological and psychological relationships evolve over extended periods of infertility. Comprehensive simultaneous evaluation of both biological and psychological outcome domains across the infertility duration spectrum is therefore needed to inform the development of evidence-based, duration-informed models of care.

1.3 Knowledge Gaps and Research Rationale

Despite growing recognition of the potential clinical relevance of infertility duration, several critical knowledge gaps limit the translation of existing evidence into practice. First, most studies that examined duration effects employed relatively small sample sizes and focused exclusively on either biological or psychological outcomes, precluding systematic understanding of their interrelationships and relative magnitudes [24,25]. Second, the existing evidence is inconsistent regarding whether duration is associated with treatment outcomes and psychological well-being independently of established confounders—particularly maternal age and ovarian reserve—or operates primarily through these variables. This distinction has direct implications for whether duration itself represents a clinically actionable variable or a descriptive marker of accumulated biological risk. Third, the optimal categorization of infertility duration for clinical characterization and research purposes remains unresolved, and studies have employed varying cut-off points without robust empirical justification [5]. Large-scale studies capable of simultaneously examining biological and psychological outcomes while rigorously accounting for established confounders are therefore needed to resolve these uncertainties and provide an evidence base for duration-informed approaches to ART management.

1.4 Study Objectives and Hypotheses

The primary objective of this study was to evaluate the associations between infertility duration and both ART treatment outcomes and psychological well-being in a large, well-characterized, and consecutive patient cohort. Our hypotheses were: (H1) women with different infertility durations exhibit distinct baseline characteristics, including demographic, clinical, and psychological profiles; (H2) longer infertility duration is associated with a lower clinical pregnancy rate and a potentially higher rate of early pregnancy loss; and (H3) infertility duration shows differential associations with distinct psychological symptom domains, with anxiety and somatization potentially following divergent patterns that reflect different adaptation mechanisms over time.

2. Methods

2.1 Study Population

The study population comprised women with a confirmed diagnosis of infertility who presented at the reproductive medicine center during the study period to initiate their first ART In Vitro Fertilization (IVF)/Intracytoplasmic Sperm Injection (ICSI) treatment cycle. Eligibility was determined according to the inclusion and exclusion criteria outlined below.

2.1.1 Inclusion Criteria

Women were eligible for inclusion in the study if they: (1) had a confirmed diagnosis of infertility, defined as failure to conceive after 12 months of regular unprotected intercourse [2]; (2) were undergoing their first-ever ART treatment cycle (IVF/ICSI), confirmed through patient interview and medical record review (women with previous ART attempts at any center were excluded; the extended infertility duration range of up to 21 years observed in this sample reflects delayed access to specialized reproductive care, financial constraints, or prior reliance on non-ART interventions); (3) were aged 18–50 years; and (4) completed psychological assessment questionnaires within one week prior to treatment initiation.

2.1.2 Exclusion Criteria

Women were excluded if they had: (1) a documented history of severe psychiatric disorders requiring hospitalization or ongoing psychotropic medication [26]; (2) a current or previous diagnosis of malignancy; (3) severe systemic disease affecting reproductive function; or (4) missing data for >20% of the following five pre-specified key variables: infertility duration, clinical pregnancy outcome, early pregnancy loss outcome, Generalized Anxiety Disorder 7-item scale (GAD-7) total score, and Patient Health Questionnaire-15 (PHQ-15) total score. Absence of data was assessed through a systematic review of electronic medical records and questionnaire completion records. Participants with missing data for more than one of these five variables (i.e., >20%) were excluded.

2.2 Variable Definitions and Measurements

2.2.1 Primary Exposure Variable

Infertility duration was defined as the time elapsed from the first attempt to conceive to the initiation of ART treatment, calculated in years from patient interview and medical records. A minimum duration of 0.5 years was required, consistent with the WHO (World Health Organization) definition of infertility (failure to conceive after 12 months of regular unprotected intercourse for women under 35 years, or 6 months for women aged 35 years and older). The recorded range of 0.00–21.00 years reflects rounding to two decimal places, with the minimum value representing patients at approximately 6 months duration. For descriptive and group-comparison purposes, participants were stratified into three categories based on established clinical thresholds: <5 years, 5–10 years, and ≥10 years [5,27]. In all multivariable regression analyses, infertility duration was entered as a continuous variable (in years) to maximize statistical resolution and avoid information loss associated with categorical grouping.

2.2.2 Primary Outcome Variables

Clinical pregnancy was defined as the presence of an intrauterine gestational sac with fetal heartbeat confirmed by transvaginal ultrasound at 6–7 weeks of gestation [28]. Early pregnancy loss was defined as pregnancy loss occurring before 12 weeks of gestation among women who achieved clinical pregnancy. Pregnancy outcomes were confirmed through medical records and follow-up contact at 12 weeks post-embryo transfer.

2.2.3 Psychological Assessment

Anxiety symptoms were assessed using the GAD-7, a validated self-report questionnaire with scores ranging from 0 to 21 [29]. Somatization symptoms were evaluated using the PHQ-15, with scores ranging from 0 to 30 [30]. Both instruments have demonstrated acceptable psychometric properties in reproductive medicine populations [13]. Questionnaires were administered by trained research coordinators in a private clinical room using paper-based forms during the routine pre-treatment counseling session, which was typically 1–3 days before ovarian stimulation initiation. Coordinators were available to answer questions about item interpretation, but did not influence responses. The completion time averaged 8–10 minutes for both instruments combined. Psychological assessments were completed in close proximity to treatment initiation, and scores may therefore partly reflect anticipatory responses to the imminent treatment rather than representing a stable measure of infertility-related psychological distress across the full duration of the infertility experience.

2.2.4 Covariates and Confounders

Demographic variables included maternal age and infertility type, which was classified as primary infertility (no history of previous pregnancy in the current partnership), secondary infertility (at least one previous pregnancy regardless of outcome), or other (uncertain classification, mixed factors, or insufficient documentation at initial assessment). Clinical biomarkers included serum anti-Müllerian hormone (AMH) level measured using automated electrochemiluminescence immunoassay (Roche Elecsys, cobas e402, Rotkreuz, Switzerland), and antral follicle count (AFC) determined by transvaginal ultrasound following standardized protocols [8]. Treatment variables included the type of embryo transfer (fresh embryo transfer performed 3–5 days after oocyte retrieval in the same stimulation cycle, versus frozen embryo transfer performed in subsequent hormone replacement cycles after cryopreservation), as well as the number of embryos transferred.

2.3 Data Collection Procedures

Data were collected using standardized case report forms and stored in a secure electronic database with double data entry for quality assurance. Clinical data were extracted from electronic medical records by trained research personnel. Psychological assessments were administered during routine pre-treatment counseling sessions as described in Section 2.2.3. Missing data patterns were ana-

lyzed prior to analysis. Multiple imputation was considered for variables missing >10% of data, but was ultimately not applied given the analytical decisions described in Section 2.4 [31].

2.4 Statistical Analysis

The study sample comprised a consecutive cohort of all women who met the eligibility criteria and presented at our center during the study period (January 2020–December 2023), yielding a final analytic sample of 11,906 participants. Sample size was therefore determined by the actual patient volume over the study period rather than a pre-specified target. Post-hoc power analyses confirmed adequate statistical power for primary comparisons, with the sample providing >99% power to detect small effect sizes overall, >95% power to detect a 9-percentage-point difference in pregnancy rates across the three duration groups (expected rates: 55%, 52%, and 46%) at $\alpha = 0.05$, and >80% power to detect standardized mean differences as small as Cohen's $d = 0.15$ for continuous psychological outcomes.

Descriptive analyses. Continuous variables were described using means and standard deviations, or medians and interquartile ranges, based on the normality of data distribution as determined by the Kolmogorov-Smirnov and Shapiro-Wilk tests. Categorical variables were presented as frequencies and percentages. Bivariate inferential analyses. Group comparisons for continuous variables were performed using one-way analysis of variance (ANOVA) with post-hoc Bonferroni correction to control the familywise error rate, or the Kruskal-Wallis test when parametric assumptions were violated. Categorical variables were compared using chi-square tests, or Fisher's exact test when expected cell counts were <5. Multivariable analyses. Binary logistic regression was used to identify independent predictors of clinical pregnancy, with results presented as the odds ratio (OR) and 95% confidence interval (CI). Infertility duration was entered as a continuous variable (in years) in all logistic regression models. The reported ORs represent the estimated change in the odds of clinical pregnancy per one-year increase in duration. Collinearity diagnostics, including variance inflation factors (VIFs) and condition indices, were computed for all predictors and are reported in Appendix Table 6 (Ref. [32]). Variables with VIF >5.0 are excluded from final models [32], although this threshold was not exceeded by any of the predictors in the current study. Linear regression models were fitted separately for anxiety (GAD-7) and somatization (PHQ-15) outcomes, with standardized beta coefficients reported. To preserve the temporal ordering of the analytical model, both linear regression models were restricted to pre-treatment baseline covariates: maternal age, infertility duration, AMH, infertility type, embryo transfer type, and the reciprocal psychological symptom score. Post-treatment outcomes (clinical pregnancy and early pregnancy loss) were excluded from the psychological outcome models, as their inclusion would violate the logical requirement that predictors temporally precede outcomes. Model assumptions were verified through residual analysis. For sensitivity analysis, the primary logistic regression was re-run with infertility duration specified as a continuous variable. This was to confirm that findings were not sensitive to the categorical parameterization used for descriptive grouping. The results are reported in Appendix Table 7. All analyses were conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Two-sided p-values < 0.05 were considered statistically significant. Missing data were handled using listwise deletion. AFC was excluded from all multivariable models owing to substantial missing data (25.4%), which markedly reduces the analyzable sample and therefore risks the introduction of selection bias from differential data availability across duration groups.

3. Results

3.1 Patient Characteristics and Baseline Comparisons

A total of 11,906 women undergoing ART treatment were included in this analysis. Participants were stratified into three groups based on infertility duration: <5 years (n = 9570, 80.4%), 5–10 years (n = 1992, 16.7%), and ≥10 years (n = 344, 2.9%). The overall study population had a mean age of 31.21 ± 4.11 years (range: 19–50 years) and a mean infertility duration of 2.85 ± 2.42 years (range: 0.00–21.00 years).

The characteristic details are shown in Table 1, significant differences were observed across infertility duration groups for all baseline characteristics. Maternal age increased progressively with longer infertility duration, with the ≥10 years group being 4.52 years older on average than the <5 years group. Ovarian reserve markers showed a declining trend, with AMH levels decreasing from 4.20 ± 3.41 ng/mL in the <5 years group to 3.17 ± 2.39 ng/mL in the ≥10 years group. The distribution of infertility types also differed significantly, with primary infertility being more prevalent in the longer duration groups (62.9% and 58.4% vs. 50.4%). Notably, the "Other" infertility type category, which comprised cases with uncertain or mixed classification, decreased markedly in longer duration groups (from 12.8% to <1%). This likely reflects the fact that patients with prolonged infertility undergo more extensive diagnostic workup, thereby clarifying their classification as either primary or secondary infertility.

3.2 Analysis of Treatment Outcomes

Clinical pregnancy outcomes varied significantly across infertility duration groups, as shown in Table 2. The overall clinical pregnancy rate was 54.6% (6496/11,906), with rates declining as the infertility duration increased.

Clinical pregnancy rates demonstrated a statistically significant decline across groups ($\chi^2 = 15.16$, $p < 0.001$), with a 9.4 percentage-point difference between the shortest

Table 1. Baseline characteristics of infertility duration groups.

Variable	<5 years (n = 9570)	5–10 years (n = 1992)	≥10 years (n = 344)	F/χ^2	p
Continuous variables	M (SD)	M (SD)	M (SD)		
Maternal age (years)	30.87 (4.05)	32.14 (3.87)	35.39 (3.97)	F = 274.54	<0.001
AMH (ng/mL)	4.20 (3.41)	3.93 (3.34)	3.17 (2.39)	F = 18.91	<0.001
Antral follicle count	5.61 (4.07) [a]	5.28 (4.01) [b]	4.89 (3.71) [c]	F = 7.24	<0.001
Categorical variables	n (%)	n (%)	n (%)		
Infertility type				χ^2 = 337.55	<0.001
Primary infertility	4820 (50.4)	1254 (62.9)	201 (58.4)		
Secondary infertility	3522 (36.8)	734 (36.8)	140 (40.7)		
Other	1228 (12.8)	4 (0.2)	3 (0.9)		

Note. [a] n = 7174; [b] n = 1459; [c] n = 254 (due to missing AFC data). Continuous variables were analyzed using one-way ANOVA; categorical variables were analyzed using chi-square tests. All tests were two-sided with α = 0.05. AMH, anti-Müllerian hormone.

Table 2. Treatment outcomes of infertility duration groups.

Outcome	<5 years (n = 9570)	5–10 years (n = 1992)	≥10 years (n = 344)	Total (n = 11,906)	χ^2	p
Clinical pregnancy					15.16	<0.001
No	4281 (44.7)	943 (47.3)	186 (54.1)	5410 (45.4)		
Yes	5289 (55.3)	1049 (52.7)	158 (45.9)	6496 (54.6)		
Early pregnancy loss					3.49	0.175
No	4728 (89.4)	940 (89.6)	134 (84.8)	5802 (89.3)		
Yes	561 (10.6)	109 (10.4)	24 (15.2)	694 (10.7)		

Note. Analysis of early pregnancy loss was conducted among women who achieved clinical pregnancy (n = 6496). Percentages for early pregnancy loss are calculated within each group's clinical pregnancy cohort.

and longest duration groups. Among women who achieved clinical pregnancy (n = 6496), the rate of early pregnancy loss did not differ significantly across groups (χ^2 = 3.49, p = 0.175). Although the ≥10 years group showed a higher rate of loss (15.2%) compared to the shorter duration groups (10.6% and 10.4%), the difference did not reach statistical significance. This finding warrants cautious interpretation, as the ≥10 years subgroup contributed only 158 clinical pregnancies, rendering the analysis substantially underpowered to detect group differences of the magnitude observed. Therefore, the non-significant result does not preclude the existence of a true biological difference.

3.3 Assessment of Psychological Status

Psychological symptoms showed distinct patterns across infertility duration groups, with differential effects observed for anxiety versus somatization symptoms, as shown in Table 3.

One-way ANOVA revealed a statistically significant overall difference in anxiety scores across infertility duration groups (F[2, 11,903] = 3.064, p = 0.047), with scores showing a gradual decline from 3.33 ± 3.01 in the <5 years group to 3.07 ± 3.08 in the ≥10 years group. However, Bonferroni-corrected pairwise comparisons did not identify any specific group pair as significantly different (all adjusted $p \geq 0.136$), indicating this omnibus effect reflects a continuous, distributed trend across the full duration spectrum rather than a step-wise change between adjacent groups. The absolute magnitude of variation in anxiety scores (0.26 points across the full duration range) is substantially below accepted thresholds for clinically meaningful change. These findings should therefore be interpreted as a statistically detectable population-level trend with limited individual clinical significance.

Somatization symptoms demonstrated a more pronounced and directionally consistent increase with longer infertility duration (F[2, 11,903] = 5.486, p = 0.004). Bonferroni-corrected pairwise comparisons confirmed the 5–10 years group had significantly higher somatization scores than the <5 years group (mean difference = 0.26, 95% CI [0.05, 0.48], adjusted p = 0.010). Comparisons involving the ≥10 years group did not reach statistical significance (all adjusted $p \geq 0.239$). As with anxiety, the absolute increase in somatization scores across the full duration range (0.35 points) was considerably below the threshold for clinically meaningful change on the PHQ-15. Therefore, the population-level trend should not be extrapolated to inferences about individual patients.

3.4 Extended Analysis: Multivariable Predictors

3.4.1 Clinical Pregnancy Outcome Predictors

As shown in Table 4, multivariable logistic regression analysis identified several independent predictors of clinical pregnancy outcomes, with maternal age and AMH levels emerging as the most consistent factors.

Table 3. Psychological status of infertility duration groups.

Psychological measure	<5 years (n = 9570)	5–10 years (n = 1992)	≥10 years (n = 344)	Total (n = 11,906)	*F*	*p*
Anxiety (GAD-7)					3.064	0.047
M ± SD	3.33 ± 3.01	3.18 ± 3.00	3.07 ± 3.08	3.30 ± 3.01		
Range	0–21	0–21	0–19	0–21		
Somatization (PHQ-15)					5.486	0.004
M ± SD	4.65 ± 3.61	4.92 ± 3.71	5.00 ± 3.86	4.71 ± 3.63		
Range	0–25	0–20	0–24	0–25		

Note. GAD-7, Generalized Anxiety Disorder 7-item scale (possible score range: 0–21); PHQ-15, Patient Health Questionnaire-15 somatization scale (possible score range: 0–30). Group comparisons were performed using one-way analysis of variance (ANOVA). Post-hoc pairwise comparisons employed Bonferroni correction to control the familywise error rate. For GAD-7, although the omnibus F-test reached statistical significance ($F[2, 11{,}903] = 3.064$, $p = 0.047$), no individual pairwise comparison attained significance after Bonferroni correction (all adjusted $p \geq 0.136$), indicating the overall effect reflects a gradual, distributed declining trend across the full duration spectrum rather than a discrete transition between any specific group pair. For PHQ-15, Bonferroni-corrected comparisons revealed a significant difference between the <5 years and 5–10 years groups (mean difference = 0.26, 95% CI [0.05, 0.48], adjusted $p = 0.010$); the remaining pairwise comparisons were non-significant (all adjusted $p \geq 0.239$). All tests were two-sided at $\alpha = 0.05$.

Table 4. Multivariable logistic regression analysis for clinical pregnancy outcomes.

Predictor	Model 1			Model 2		
	OR	95% CI	*p*	OR	95% CI	*p*
Maternal age (years)	0.935	[0.92, 0.95]	<0.001	0.934	[0.92, 0.95]	<0.001
Anti-Müllerian hormone (ng/mL)	1.032	[1.02, 1.05]	<0.001	1.032	[1.02, 1.05]	<0.001
Infertility duration (years)	0.990	[0.97, 1.01]	0.333	0.984	[0.97, 1.00]	0.061
Infertility type	0.954	[0.89, 1.02]	0.193	0.940	[0.88, 1.00]	0.047
Antral follicle count	1.004	[0.99, 1.02]	0.518	—	—	—
Embryo transfer type	1.279	[1.17, 1.40]	<0.001	1.220	[1.13, 1.32]	<0.001
Anxiety score (GAD-7)	1.010	[0.99, 1.03]	0.271	1.002	[0.99, 1.02]	0.809
Somatization score (PHQ-15)	1.002	[0.99, 1.02]	0.804	0.998	[0.98, 1.01]	0.764

Note. OR, odds ratio; CI, confidence interval. Infertility duration was entered as a continuous variable (in years) in both models. The OR shown represents the estimated change in the odds of clinical pregnancy per one-year increase in duration. Model 1 includes all predictors. Model 2 excludes the antral follicle count (AFC) due to substantial missing data (25.4%) and collinearity with AMH ($r = 0.72$), which introduced estimation instability. Collinearity diagnostics for all predictors in Model 1 confirmed the absence of substantive multicollinearity, with variance inflation factors (VIFs) ranging from 1.009 to 1.525 (see Appendix Table 6 for full diagnostics). Sensitivity analyses in which infertility duration was re-specified as a continuous variable yielded results consistent with those of the primary analysis (see Appendix Table 7). Early pregnancy loss was excluded from this model because it is a post-conception event that cannot logically precede or co-determine the occurrence of clinical pregnancy, and its inclusion introduced severe numerical instability. Reference categories: infertility type = primary infertility; embryo transfer type = fresh embryo transfer.

Maternal age consistently showed the strongest predictive effect, with each additional year associated with a 6.5–6.6% decrease in the odds of clinical pregnancy. Higher AMH levels were associated with modestly increased odds of clinical pregnancy (OR = 1.032, 95% CI [1.02, 1.05], $p < 0.001$). This direction is consistent with the established role of ovarian reserve in predicting ART success. However, the modest effect size (3.2% increase in odds per ng/mL) indicates limited standalone clinical utility when AMH is considered in isolation. Infertility duration showed only marginal significance in Model 2 after AFC exclusion (OR = 0.984, 95% CI [0.97, 1.00], $p = 0.061$), suggesting that its crude association with clinical pregnancy is largely accounted for by correlated variables—specifically maternal age and ovarian reserve—rather than representing an independent effect. Psychological measures (anxiety and somatization scores) showed no significant associations with pregnancy outcomes in either model.

3.4.2 Psychological Status Predictors

Linear regression analyses were conducted to examine baseline predictors of anxiety and somatization symptoms. To maintain the temporal integrity of the analytical model, both models were restricted to pre-treatment baseline covariates. Moreover, post-treatment outcomes (clinical pregnancy and early pregnancy loss) were excluded, as their inclusion would violate the logical requirement that predictors precede outcomes, all results are shown in Table 5.

The corrected regression models revealed a divergent pattern of association between infertility duration and the two psychological symptom domains. Longer infertility duration was associated with lower anxiety scores ($\beta = -0.042$, $p < 0.001$) but higher somatization scores ($\beta = 0.054$, $p < 0.001$). This directional contrast was fully consistent with the unadjusted group trends shown in Table 3. Maternal age showed a significant inverse association with anxiety scores ($\beta = -0.048$, $p < 0.001$) but not with somatization scores ($\beta = -0.007$, $p = 0.380$). AMH and infertility type were not significantly associated with either of these outcomes (all $p > 0.05$). Embryo transfer type showed a borderline association with somatization scores ($\beta = 0.015$, $p = 0.055$), but this did not reach the conventional threshold for statistical significance. The strongest predictor in both models was the reciprocal psychological symptom measure: somatization scores were the dominant predictor of anxiety ($\beta = 0.581$, $p < 0.001$), and anxiety scores were the dominant predictor of somatization ($\beta = 0.583$, $p < 0.001$), indicating substantial comorbidity between these two symptom domains.

4. Discussion

4.1 Principal Findings

This large-scale retrospective cohort study examined the associations between infertility duration and ART treatment outcomes as well as psychological well-being in 11,906 women. All three primary hypotheses were supported by the data, although the overall pattern of findings revealed a more nuanced picture than initially anticipated. Significant baseline differences were confirmed across duration groups (H1), and clinical pregnancy rates declined significantly with longer infertility duration in unadjusted analyses (H2a). However, this crude association was substantially attenuated in multivariable analysis, with infertility duration failing to reach independent statistical significance after adjustment for maternal age and AMH (Model 2: $p = 0.061$). This finding indicates the observed decline in pregnancy rates is more likely to be mediated through accumulated biological factors than through a direct independent temporal effect. Rates of early pregnancy loss did not differ significantly across groups (H2b not confirmed, $p = 0.175$), although this result requires cautious interpretation given the limited statistical power of the ≥10 years subgroup (n = 158 pregnancies). With respect to psychological outcomes (H3), anxiety symptoms demonstrated a statistically significant overall decline across duration groups ($F[2, 11{,}903] = 3.064$, $p = 0.047$). However, Bonferroni-corrected pairwise comparisons did not identify significant differences between any specific group pair, indicating a gradual and distributed pattern rather than a discrete threshold effect at any particular duration point. Somatization symptoms showed a more pronounced and directionally consistent increase ($F[2, 11{,}903] = 5.486$, $p = 0.004$),

Table 5. Multivariable linear regression analysis for psychological symptoms.

Predictor	Anxiety (GAD-7)			Somatization (PHQ-15)		
	β	SE	*p*	β	SE	*p*
Maternal age (years)	−0.048	0.006	<0.001	−0.007	0.007	0.380
Infertility duration (years)	−0.042	0.010	<0.001	0.054	0.012	<0.001
Anti-Müllerian hormone (ng/mL)	−0.005	0.007	0.569	−0.005	0.009	0.562
Infertility type	−0.005	0.036	0.519	0.007	0.044	0.379
Embryo transfer type	0.005	0.047	0.553	0.015	0.057	0.055
Somatization score (PHQ-15)	0.581	0.006	<0.001	—	—	—
Anxiety score (GAD-7)	—	—	—	0.583	0.009	<0.001

Note. β, standardized regression coefficient; SE, standard error of the unstandardized regression coefficient. All predictors represent pre-treatment baseline covariates; post-treatment outcomes (clinical pregnancy and early pregnancy loss) were excluded from both models to preserve temporal ordering. Antral follicle count was excluded owing to substantial missing data (25.4%), which reduces the analyzable sample and may therefore have introduced potential selection bias. The somatization score (PHQ-15) was included as a covariate in the anxiety model, while the anxiety score (GAD-7) was included as a covariate in the somatization model, thereby accounting for the established comorbidity between these symptom domains. Reference categories: infertility type = primary infertility; embryo transfer type = fresh embryo transfer.

Table 6. Collinearity diagnostics for predictors in the multivariable logistic regression model (Model 1).

Predictor	Tolerance	VIF
Maternal age (years)	0.842	1.187
Anti-Müllerian hormone (ng/mL)	0.841	1.189
Infertility duration (years)	0.836	1.196
Infertility type	0.830	1.204
Antral follicle count	0.991	1.009
Embryo transfer type	0.889	1.125
Anxiety score (GAD-7)	0.656	1.525
Somatization score (PHQ-15)	0.656	1.523

Note. VIF, variance inflation factor. Collinearity statistics were derived via a parallel ordinary least squares linear regression employing an identical predictor set, as logistic regression in SPSS does not produce VIF estimates directly. All VIF values were below 2.0, well within the acceptable threshold of 5.0 (Hair et al., 2019) [32], confirming the absence of substantive multicollinearity among predictors. The Pearson correlation between maternal age and infertility duration was $r = 0.18$ ($p < 0.001$), indicating a weak-to-moderate association that does not constitute a collinearity concern. The maximum condition index was 31.64, with the elevated variance proportion concentrated in the intercept–maternal age dimension (variance proportion = 0.90), a pattern typical of intercept–predictor covariance in clinical regression models and not indicative of harmful multicollinearity among the substantive predictors. The attenuation of the infertility duration effect in multivariable models (Model 2: $p = 0.061$) is therefore more consistent with genuine confounding or mediation by maternal age and ovarian reserve than with statistical over-adjustment attributable to multicollinearity.

with a significant difference between the <5 years and 5–10 years groups (Bonferroni-adjusted $p = 0.010$). Multivariable analyses further identified maternal age and AMH as primary independent predictors of clinical pregnancy, and revealed that longer infertility duration was independently associated with lower anxiety scores ($\beta = -0.042$, $p < 0.001$) but higher somatization scores ($\beta = 0.054$, $p < 0.001$) after adjustment for covariates. Psychological symptom scores showed no direct association with clinical pregnancy outcomes. Taken together, these findings suggest that infertility duration, while not an independent predictor of clinical pregnancy after adjustment for biological covariates, may serve as a useful descriptive variable for characterizing patient heterogeneity and informing group-level patterns of psychological symptom presentation.

4.2 Interpretation and Mechanistic Discussion

The 9.4 percentage-point decline (55.3% to 45.9%) in the clinical pregnancy rate across the infertility duration groups is consistent with prior reports of declining reproductive potential over time [7,27]. This pattern likely reflects multiple interconnected biological mechanisms, including age-related oocyte quality deterioration, diminished ovarian reserve, and potential changes in endometrial receptivity associated with reproductive aging [33,34]. Critically, however, this crude association was substantially attenuated in multivariable analysis, and after adjustment for maternal age and AMH, infertility duration was not an independent predictor of clinical pregnancy (Model 2: OR = 0.984, $p = 0.061$). Collinearity diagnostics confirmed the absence of substantive multicollinearity (VIF for infertility duration = 1.196; Pearson $r = 0.18$ between maternal age and infertility duration), indicating this attenuation more plausibly reflects genuine confounding or mediation through biological aging than statistical over-adjustment. Together, the progressive increase in maternal age across duration groups (30.87 to 35.39 years, a 4.52-year difference) and the concurrent decline in AMH (4.20 to 3.17 ng/mL) suggest that infertility duration operates primarily as a proxy for accumulated reproductive aging rather than exerting an independent temporal effect. These findings are consistent with prior evidence that, once established confounders are controlled, the residual independent effect of infertility duration on pregnancy outcomes is minimal [10,11,27]. Moreover, they support the interpretation that biological markers—particularly maternal age and AMH—provide the primary basis for clinical prognostic assessment rather than infertility duration *per se*. Sensitivity analyses using infertility duration as a continuous variable yielded consistent results (Model 2: OR = 0.985, $p = 0.080$), confirming the robustness of this finding to the parameterization of infertility duration.

Contrary to hypothesis H2b, the rate of early pregnancy loss did not differ significantly across duration groups ($p = 0.175$). The numerically higher rate of loss in the ≥10 years group (15.2% vs. 10.4–10.6%) should not be interpreted as evidence of no effect, since this analysis was substantially underpowered to detect differences of the observed magnitude (only 158 clinical pregnancies in this subgroup). Therefore, the possibility of a true biological difference in pregnancy maintenance capacity across duration groups cannot be excluded and warrants investigation in adequately powered prospective studies. Our findings are consistent with the broader possibility that, while conception ability may decline with prolonged infertility and associated reproductive aging, pregnancy maintenance capacity once clinical pregnancy is achieved may be comparatively more preserved. Nevertheless, this interpretation remains speculative in the absence of direct evidence.

AMH levels showed a modest but statistically significant positive association with clinical pregnancy outcomes (OR = 1.032 per ng/mL, 95% CI [1.02, 1.05], $p < 0.001$). This direction is entirely consistent with the established understanding that a greater ovarian reserve predicts improved ART success [8,35,36,37] and is therefore not unexpected. However, the modest effect size—representing

Table 7. Sensitivity analysis: multivariable logistic regression for clinical pregnancy with infertility duration entered as a continuous variable.

Predictor	Model 1			Model 2		
	OR	95% CI	*p*	OR	95% CI	*p*
Maternal age (years)	0.943	[0.93, 0.95]	<0.001	0.943	[0.93, 0.95]	<0.001
Anti-Müllerian hormone (ng/mL)	1.032	[1.02, 1.05]	<0.001	1.033	[1.02, 1.04]	<0.001
Infertility duration (years)	0.991	[0.97, 1.01]	0.332	0.985	[0.97, 1.00]	0.080
Infertility type	0.958	[0.89, 1.03]	0.220	0.945	[0.89, 1.00]	0.063
Antral follicle count	1.003	[0.99, 1.01]	0.630	—	—	—
Embryo transfer type	1.305	[1.19, 1.43]	<0.001	1.255	[1.16, 1.35]	<0.001
Anxiety score (GAD-7)	1.013	[0.99, 1.03]	0.142	1.005	[0.99, 1.02]	0.554
Somatization score (PHQ-15)	1.000	[0.99, 1.01]	0.981	0.997	[0.99, 1.01]	0.656

Note. OR, odds ratio; CI, confidence interval. This sensitivity analysis was conducted to verify that findings were not sensitive to the parameterization of infertility duration. Infertility duration was explicitly specified as a continuous variable (in years); the reported OR represents the estimated change in clinical pregnancy odds per one-year increase in duration. Model 1 includes antral follicle count; Model 2 excludes it owing to substantial missing data (25.4%) and collinearity with AMH. Results are consistent with those of the primary analysis (Table 4): infertility duration did not independently predict clinical pregnancy in either model after adjustment for maternal age and ovarian reserve (Model 1: OR = 0.991, $p = 0.332$; Model 2: OR = 0.985, $p = 0.080$), confirming the robustness of the primary findings to alternative variable specifications. Minor numerical differences from Table 4 reflect differences in listwise deletion across analytic samples rather than any methodological divergence. Reference categories: infertility type = primary infertility; embryo transfer type = fresh embryo transfer.

a 3.2% increase in odds per ng/mL—indicates limited standalone clinical utility when AMH is considered in isolation. The relationship between AMH and ART outcomes may also be non-linear at extremely high AMH levels, which can signal polycystic ovary syndrome and associated risks of ovarian hyperstimulation rather than a favorable prognosis [38]. These considerations underscore the importance of interpreting AMH alongside other clinical factors such as maternal age and embryo quality rather than as a standalone prognostic indicator.

The psychological findings in this study revealed a more nuanced pattern than originally anticipated. Anxiety scores demonstrated a statistically significant overall difference across duration groups ($F[2, 11{,}903] = 3.064$, $p = 0.047$), with scores showing a gradual declining trend from 3.33 ± 3.01 in the <5 years group to 3.07 ± 3.08 in the ≥10 years group. However, Bonferroni-corrected pairwise comparisons did not identify any specific group pair as significantly different (all adjusted $p \geq 0.136$), indicating a continuous, distributed pattern of change across the full duration spectrum rather than a discrete transition at any particular threshold. This gradual attenuation of anxiety with longer infertility duration may reflect psychological adaptation mechanisms described in the chronic illness literature, wherein individuals progressively develop coping strategies, adjusted expectations, and enhanced emotional regulation capacities over time [13,39]. However, the absolute variation in anxiety score (0.26 points across the full duration range) was substantially below established thresholds for clinically meaningful change on the GAD-7 (typically 4–5 points), indicating this finding reflects a statistically detectable population-level trend of limited individual clinical significance.

Somatization symptoms demonstrated a more pronounced and directionally consistent pattern, with scores increasing from 4.65 ± 3.61 in the <5 years group to 5.00 ± 3.86 in the ≥10 years group ($F[2, 11{,}903] = 5.486$, $p = 0.004$). Bonferroni-corrected pairwise comparisons confirmed a significant difference between the <5 years and 5–10 years groups (mean difference = 0.26, adjusted $p = 0.010$), suggesting the transition into the intermediate duration range may be associated with a modest but detectable shift toward somatic expression of psychological distress. This pattern is broadly consistent with the stress embodiment framework, which proposes that chronic stressors may increasingly manifest as somatic complaints when cognitive and emotional coping resources are progressively engaged over time [23,40]. As with anxiety, however, the absolute increase in somatization scores across the full duration range (0.35 points) fell considerably below the threshold for clinically meaningful change on the PHQ-15 (typically 5–6 points). These statistically detectable trends therefore have limited implications for individual patient management and should be interpreted primarily as population-level observations.

The protective association between maternal age and anxiety scores ($\beta = -0.048$, $p < 0.001$) likely reflects enhanced emotional regulation capacities and more realistic treatment expectations that develop with psychological maturity [41,42]. Multivariable analyses confirmed that psychological symptom scores showed no significant associations with clinical pregnancy outcomes in either model, aligning with systematic reviews that have questioned whether psychological distress directly influences the success of ART [14,19,43]. The high intercorrelation between anxiety and somatization scores ($\beta \approx 0.58$ in both directions) observed in the present study suggests they represent overlapping dimensions of a common psychological distress syndrome rather than fully independent constructs. This is consistent with emerging evidence on the comorbidity of anxiety and somatic symptom disorders in infertility populations [13]. It should also be noted that psychological assessments were completed 1–3 days before the initiation of ovarian stimulation. Scores at this time point may partly capture anticipatory responses specific to the imminent treatment episode rather than representing a stable measure of trait-level infertility-related psychological distress. This timing should be considered when interpreting the psychological findings.

Maternal age and AMH emerged as the primary independent predictors of clinical pregnancy outcomes, confirming established prognostic factors while highlighting the relative weakness of infertility duration as an independent predictor after adjustment for these variables ($p = 0.061$). Effect sizes in the multivariable models warrant careful consideration with respect to clinical utility. Maternal age (OR = 0.934 per year) and embryo transfer type (OR = 1.220) both showed statistical significance and effect sizes of plausible clinical relevance. In contrast, the AMH effect (OR = 1.032 per ng/mL) and psychological predictors (all $\beta < 0.06$) represent associations that, despite reaching statistical significance in this large sample, contributed minimally to outcome variance beyond established predictors. This distinction between statistical and clinical significance is particularly important in large-sample studies where even minor associations achieve statistical significance, but which may have limited practical relevance for individual patient counseling or prognostic algorithms.

4.3 Clinical Implications

The clinical implications of these findings should be interpreted in light of an important qualification: infertility duration did not independently predict clinical pregnancy after adjustment for maternal age and AMH ($p = 0.061$). Furthermore, the observed differences in psychological scores—while statistically significant at the population level—were of limited clinical magnitude, falling well below established thresholds for meaningful individual change. The observations described below therefore represent exploratory, hypothesis-generating considerations intended to inform future research and clinical inquiry, rather than practice-changing recommendations. Prospective validation is required before any infertility duration-based clinical protocols are implemented.

Descriptive comparison of pregnancy rates across duration groups (55.3%, 52.7%, and 45.9% for <5, 5–10, and ≥10 years, respectively) may provide useful contextual information for patient counseling, helping clinicians communicate expected outcomes across different stages of the infertility experience. However, given that the group differences appear largely attributable to differences in maternal age and ovarian reserve rather than to infertility duration *per se*, established biological markers should remain the primary basis for individual prognostic assessment. Infertility duration may complement rather than substitute for these markers in the clinical assessment process, and its potential utility as a supplementary contextual variable for patient communication warrants systematic evaluation in prospective studies. If duration-informed approaches to resource prioritization are considered, economic modeling would be needed to establish whether such strategies improve cost-effectiveness in specific healthcare contexts [44,45,46].

The differential patterns of psychological symptoms observed across duration groups—a gradual declining trend in anxiety and a modest increase in somatization in the intermediate duration group—may have tentative implications for psychological support provision, though these should be considered hypothesis-generating rather than prescriptive. Evidence-based psychological interventions, including cognitive-behavioral therapy and mindfulness-based approaches, are broadly supported for infertile women across all duration groups given the consistent presence of psychological distress throughout the infertility experience [26,47,48,49,50]. The modest increase in somatization scores observed in the 5–10 years group may suggest that patients at intermediate duration could merit attention to somatic as well as cognitive-emotional symptom presentations during psychological assessments, though the magnitude of the group difference does not warrant modification of standard clinical management protocols. Mindfulness-based interventions, which have demonstrated significant reductions in both anxiety and somatic symptoms among women undergoing fertility treatment [51], may warrant consideration as part of routine psychological support for all patients, though this recommendation reflects general intervention efficacy rather than being specific to the duration-based differences observed here. The protective association between maternal age and anxiety scores suggests that younger patients might benefit from more intensive emotional support, while older patients may respond better to practical coping strategies and realistic goal-setting, though this requires prospective evaluation. Routine integration of validated psychological screening instruments such as the GAD-7 and PHQ-15 throughout ART care, regardless of infertility duration, is supported as a means of identifying pa-

tients who may benefit from additional psychological support [13].

These findings highlight the complexity of biomarker interpretation in reproductive medicine and caution against over-reliance on any single variable—whether biological or temporal—for clinical decision-making. A comprehensive assessment approach incorporating maternal age, ovarian reserve markers, embryo quality, and patient-reported psychological symptoms is more likely to capture the multidimensional determinants of both treatment outcomes and patient well-being than any single-variable stratification strategy. Infertility duration may serve a useful descriptive role in patient characterization and communication, and the observational findings presented here provide a foundation for hypothesis-driven prospective research into whether duration-informed assessment pathways improve patient outcomes compared with standard care.

4.4 Limitations and Future Directions

This study is subject to several limitations that should be considered when interpreting the findings. First, the cross-sectional design precludes causal inference. All of the observed associations were statistical in nature and may reflect unmeasured confounding or reverse causality. Second, this study is subject to selection bias. Women who sought their first ART cycle after 10 or more years of infertility represent a highly selected clinical subgroup, likely characterized by specific barriers to care access, including limited healthcare availability, financial constraints, cultural factors, or prolonged reliance on non-ART interventions. Hence, their profiles are not representative of infertile women more broadly. Third, information bias is present. Infertility duration was assessed retrospectively from patient interviews and medical records and is therefore susceptible to recall bias. Moreover, self-reported psychological symptoms are subject to response bias and social desirability effects, particularly when assessments are administered in a clinical setting immediately prior to treatment initiation. Fourth, the single-center design limits generalizability, as the findings may not apply to populations treated in different healthcare systems, cultural contexts, or clinical settings with different referral patterns. Fifth, the absence of AFC data for 25.4% of participants represents a substantive data quality limitation. Missing data on AFC were not entirely random, with lower data availability in shorter-duration groups reflecting less extensive initial clinical workup. This differential availability may have introduced systematic bias, despite the exclusion of AFC from multivariable models. Sixth, the ≥10 years subgroup (n = 344, with only 158 achieving clinical pregnancy) was substantially underpowered for the analysis of early pregnancy loss. Therefore, the non-significant result ($p = 0.175$) in the presence of a numerically higher loss rate (15.2%) should not be interpreted as definitive evidence of no effect. Seventh, psychological assessments were completed 1–3 days before the initiation of ovarian stimulation, and scores at this time point may partly reflect anticipatory responses to the imminent treatment rather than representing stable, trait-level infertility-related psychological states. Finally, the large proportion of cases classified as having an "other/uncertain" infertility type in the <5 years group (12.8%) compared with longer-duration groups (<1%) reflects systematically differential diagnostic completeness across groups. This may affect baseline comparability and the interpretation of cross-group differences in infertility type distribution.

Prospective longitudinal cohort studies tracking biological and psychological outcomes from infertility diagnosis through treatment completion are needed to establish temporal directionality and identify critical transition points for intervention. Randomized controlled trials evaluating duration-informed psychological interventions would provide direct evidence of efficacy to guide clinical implementation. Mechanistic studies examining neuroendocrine, inflammatory, and epigenetic pathways linking chronic infertility-related stress to reproductive outcomes would advance biological understanding of the duration–outcome relationship. Multi-center studies across diverse healthcare settings and cultural contexts would enhance generalizability and enable the investigation of how referral patterns and healthcare system characteristics influence the associations observed in this study. Future research should also prioritize the development of validated multivariate prediction tools incorporating infertility duration alongside established biological and psychological markers [52], investigation of partner and couple-level outcomes, and systematic evaluation of the cost-effectiveness of duration-informed care models in different clinical contexts.

5. Conclusions

This large-scale retrospective cohort study of 11,906 women undergoing ART provides evidence that infertility duration is associated with distinct descriptive patterns in treatment outcomes and psychological well-being, although its role as an independent clinical predictor is more limited than initially hypothesized. Longer infertility duration was associated with significantly different baseline characteristics, including progressive increases in maternal age and declining ovarian reserve markers (H1 confirmed). Clinical pregnancy rates declined significantly from 55.3% to 45.9% (H2a confirmed), while rates of early pregnancy loss did not differ significantly. Cautious interpretation is required for the latter result, given the limited power of the ≥10 years subgroup. Anxiety scores showed a statistically significant overall decline, with no significant Bonferroni-corrected pairwise differences. Somatization symptoms increased significantly, with a significant difference between the <5 years and 5–10 years groups (H3 confirmed). However, both effects were of limited clinical magnitude. Critically, infertility duration was not an independent predic-

tor of clinical pregnancy after adjustment for maternal age and AMH ($p = 0.061$), indicating that its apparent association with pregnancy rates is largely mediated through accumulated reproductive aging rather than representing an independent temporal effect. AMH showed a modest positive association with the odds of pregnancy (OR = 1.032 per ng/mL), consistent with its established prognostic role. These findings suggest that infertility duration may serve as a useful descriptive variable for patient characterization and group-level monitoring of psychological symptoms, while maternal age and AMH remain the primary basis for individual prognostic assessment. Prospective longitudinal studies are needed to confirm these associations and to evaluate duration-informed care approaches.

Availability of Data and Materials

The datasets generated and analyzed during this study are not publicly available owing to ethical restrictions and patient privacy considerations, as the data contain sensitive personal and clinical information collected under institutional ethics approval. The data may be made available from the corresponding author upon reasonable written request, subject to approval by the Medical Research Ethics Committee of West China Second University Hospital, Sichuan University, and in accordance with applicable data protection regulations.

Author Contributions

XY, YP, and YW conceptualized and designed the research study. XY and YP performed data collection, including patient recruitment, psychological assessments, and clinical data extraction. YW provided supervision and guidance on study methodology and clinical interpretation. XY conducted the statistical analyses with input from YP and YW. XY drafted the initial manuscript. YP and YW critically reviewed and revised the manuscript for important intellectual content. All authors read and approved the final manuscript, and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Medical Research Ethics Committee of West China Second University Hospital, Sichuan University (approval number: 20240248). All participants provided written informed consent prior to inclusion in the study in accordance with the Declaration of Helsinki.

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Conflicts of Interest

The authors declare no conflicts of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used AI-assisted tools (DeepSeek-V4) to support language checking, grammar improvement, and manuscript editing. Following use of these tools, the authors carefully reviewed and edited all content as necessary. The authors take full responsibility for the integrity and accuracy of the work as published, including all data, interpretations, and conclusions presented in this manuscript.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/CEOG51957.

Appendix

See Tables 6,7.

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