REVIEW

Perceived Stress and Outcomes in Assisted Reproductive Technologies (ART): Evidence from Human and Animal Studies

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Abstract

Background: Psychological stress is common among individuals with infertility or undergoing treatment, but its relationship with reproductive outcomes remains uncertain, with heterogeneous human findings and complementary animal evidence on possible mechanisms. This review synthesized human and animal evidence on psychological stress and reproductive outcomes, focusing on ART outcomes, gamete/embryo parameters, reproductive endocrine pathways, dyadic/psychosocial effects, and psychological interventions.

Methods: PubMed/MEDLINE, Scopus, and Web of Science were searched from inception to September 5, 2026, for human studies examining psychological, perceived, infertility-related, or physiological stress, plus relevant reviews and meta-analyses, alongside animal studies on stress and reproductive, gamete, embryo, endocrine, or fertility outcomes. Given heterogeneity, findings were synthesized narratively, with human and animal evidence analyzed separately.

Results: Human evidence showed no consistent association between female stress and definitive ART outcomes (pregnancy, embryo-related outcomes), though some stage-specific associations during IVF emerged. In men, stress was linked to adverse semen/sperm parameters, potentially via oxidative and neuroendocrine pathways. Dyadic stress affected relationship functioning, coping, and treatment persistence. Interventions generally improved stress, anxiety, depression, and coping, but effects on reproductive outcomes were inconsistent. Animal studies showed stress can alter ovarian function, folliculogenesis, oocyte competence, uterine function, implantation, spermatogenesis, and endocrine regulation.

Conclusion: Human evidence does not support a simple causal link between stress and ART success; associations vary by sex, timing, stress measurement, endpoint, and study design. Animal models support biological plausibility but cannot establish human causality. Interventions consistently benefit well-being, while reproductive effects remain uncertain.

Keywords: Infertility; Assisted Reproductive Technology; Psychological Stress; In Vitro Fertilization; Psychological Adaptation; Male Infertility

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Introduction

Infertility and its treatment represent substantial medical and psychological challenges for individuals and couples. Assisted reproductive technologies (ART), particularly in vitro fertilization (IVF), have become the established treatment modalities for infertility; however, treatment often involves repeated procedures, uncertainty regarding treatment success, financial and logistical demands, hormonal treatment, and emotionally demanding decision-making. These factors may contribute to substantial psychological burden, including perceived stress, anxiety, and depressive symptoms,

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among both women and men undergoing fertility treatment. Infertility and its treatment may therefore represent a shared stressor for couples rather than an experience restricted to the female patient. Previous literature has documented substantial psychological burden among individuals undergoing ART, although the magnitude and clinical consequences of this burden vary across studies [1-3].

Perceived stress refers to the extent to which individuals appraise the demands of their circumstances as unpredictable, uncontrollable, or overwhelming [4]. During infertility treatment, perceived stress may arise from the infertility diagnosis itself, treatment-related procedures, uncertainty regarding outcomes, financial burden, concerns regarding treatment failure, and previous unsuccessful treatment experiences [5]. Importantly, psychological stress is not experienced exclusively by the female patient. Infertility is a shared experience that may affect both partners and may influence communication, coping, relationship functioning, and treatment persistence. However, perceived stress should be distinguished from broader psychological constructs such as anxiety and depression, because it reflects an individual's subjective appraisal of stressors rather than the presence of a specific psychiatric condition. This distinction is particularly relevant when interpreting evidence on ART outcomes, because studies have used heterogeneous measures of stress, including self-reported perceived stress, anxiety-related measures, life-event measures, and physiological biomarkers [6].

Several biological pathways have been proposed through which psychological stress and related physiological stress responses could influence reproductive function. Activation of the Hypothalamic–Pituitary–Adrenal (HPA) axis and sympathetic nervous system (SNS) may alter glucocorticoid and catecholamine signaling and interact with Hypothalamic–Pituitary–Gonadal (HPG) axis [7]. Experimental and clinical studies have suggested potential effects on reproductive hormone regulation, ovarian function, follicular development, spermatogenesis and sperm function [7, 8]. Oxidative stress has also been proposed as one potential biological pathway through which psychological stress may affect male reproductive function. However, these mechanisms should be regarded as biologically plausible pathways rather than established explanations for poorer ART outcomes. Evidence from prospective human studies indicates that physiological and psychological stress may vary substantially across stages of IVF and does not consistently predict fertilization, embryo quality, or clinical pregnancy [9, 10].

Evidence concerning female psychological stress and IVF outcomes is heterogeneous. Some studies have reported associations between psychological stress or anxiety and intermediate reproductive parameters, whereas others have found no clear association with pregnancy outcomes. A meta-analysis of prospective studies examining pre-treatment emotional distress, particularly anxiety and depression, found no significant overall association between emotional distress and pregnancy outcome following ART [6]. More recently, a systematic review examining stress at different stages of IVF reported that stress was most consistently associated with the oocyte-retrieval stage, whereas evidence for an association with fertilization was more limited and the association with pregnancy rate was weak [8]. These findings suggest that the relationship between psychological stress and ART success may not be uniform across the treatment process and may depend on the timing and method of stress assessment, the reproductive endpoint examined, and characteristics of the study population.

Male psychological stress represents another potentially important but comparatively less studied domain. Human studies have investigated associations between perceived stress and semen quality, including sperm concentration, motility, and morphology, but findings have not been entirely conclusive [11, 12]. Prospective and observational studies have reported differing associations between perceived stress and semen parameters, illustrating the importance of study population, stress measurement, outcome definition, and potential confounding when interpreting the relationship between male stress and reproductive function [11, 13]. Moreover, associations between perceived stress and semen parameters should not automatically be interpreted as evidence of impaired fertilization, pregnancy, or live birth, because semen quality represents an intermediate reproductive outcome and does not necessarily translate into clinical ART outcomes.

Human and animal evidence should be interpreted differently, because they address different aspects of the stress–reproduction relationship. Human studies are generally observational and may be affected by multiple potential confounders, including age, infertility diagnosis, socioeconomic circumstances, treatment prognosis, lifestyle, relationship factors, and previous treatment experience. Stress is also frequently assessed using self-report instruments that capture subjective appraisal rather than a single standardized biological exposure [4]. Experimental animal studies, in contrast, permit controlled manipulation of stress exposure and detailed investigation of neuroendocrine and reproductive mechanisms. Several animal studies have reported alterations in ovarian function, follicular development, oocyte maturation, ovarian reserve, and oocyte viability following experimentally induced chronic stress exposure [14-16]. In male animals, experimental stress has also been associated with alterations in sperm quality, neuroendocrine regulation of reproduction,

and fertility [17, 18]. These experimental findings provide biological plausibility for a link between stress and reproductive function, but they cannot by themselves establish that similar mechanisms or effects occur in humans.

Importantly, findings from human and animal studies may appear inconsistent without necessarily representing a true contradiction. Experimental animal models can demonstrate causal and mechanistic effects of controlled stress exposure on reproductive tissues and biological pathways, whereas human studies examine complex, multi-dimensional psychological stress occurring within real-world social, medical, and behavioral contexts. Differences in the type, intensity, duration, and timing of stress exposure, the use of experimentally controlled versus self-reported measures, the reproductive endpoints assessed; and the degree of control over potential confounding factors can therefore produce different patterns of findings [4]. Moreover, animal stress paradigms may not fully reproduce the chronic, subjective, and context-dependent stress experienced by patients undergoing infertility treatment. Experimental studies in rodents, for example, have reported alterations in ovarian reserve, oocyte maturation, sperm quality, oxidative status, and reproductive function following chronic or experimentally induced stress exposure [14, 16-18]. However, these findings provide biological and mechanistic plausibility rather than demonstrating that perceived stress causes poorer ART outcomes in humans. Conversely, the absence of a consistent association in human ART studies does not necessarily exclude biologically relevant stress-related mechanisms, because any clinically meaningful effects may be small, stage-specific, mediated through intermediate reproductive parameters, or difficult to detect because of confounding and heterogeneity in stress assessment [8, 10]. Thus, human and animal evidence should be considered complementary rather than interchangeable: human studies are essential for evaluating associations with clinically meaningful ART outcomes, whereas experimental models can provide mechanistic evidence and help identify biological pathways that may underlie such associations.

Human studies should therefore be interpreted with particular attention to causal inference. Most available clinical evidence is observational, and perceived stress is difficult to disentangle from other characteristics that may influence both stress and infertility or treatment outcomes. Treatment prognosis, socioeconomic circumstances, lifestyle, previous treatment failure, relationship functioning, and baseline psychological characteristics may influence both perceived stress and reproductive outcomes. In addition, stress may itself change during different stages of IVF, making the temporal relationship between stress exposure and reproductive outcome difficult to establish. Prospective studies have illustrated this stage-specific variation, with psychological and physiological stress sometimes increasing around oocyte retrieval and subsequently declining around embryo transfer [10]. Consequently, associations between stress and ART outcomes should be interpreted cautiously, and mechanistic findings from animal studies should not be used to infer clinical causality in humans without corroborating human evidence [8].

Previous reviews have frequently focused on female patients, psychological distress, or specific stages and outcomes of infertility treatment. For example, previous syntheses have examined the relationship between stress and ART outcomes in women [6], while more recent work has considered stress across individual stages of IVF [8]. However, these evidence streams remain fragmented, particularly with respect to male psychological stress, semen quality, dyadic and psychosocial processes, treatment persistence, stress-reduction interventions, and experimental evidence concerning potential biological mechanisms. A comprehensive synthesis that considers these domains within a single framework may therefore provide a more integrated interpretation of the field. Such an approach is also important because evidence concerning psychological stress, intermediate reproductive parameters, and clinical ART outcomes may not point in the same direction, and because mechanistic evidence from experimental models cannot be assumed to translate directly into clinical effects in humans.

Accordingly, this structured thematic narrative review aims to synthesize the available evidence on perceived stress and ART-related reproductive outcomes while maintaining a clear distinction between human clinical evidence and experimental animal evidence. Specifically, we examine: (1) female psychological stress and ART outcomes; (2) embryological and ovarian parameters, including oocyte, fertilization, and embryo-related outcomes; (3) male psychological stress and semen quality; (4) dyadic and psychosocial effects of infertility-related stress, including communication, coping, relationship functioning, and treatment persistence; (5) stress-reduction and psychosocial interventions relevant to ART; and (6) potential biological mechanisms identified in experimental animal models. By separating these domains, this review seeks to clarify which associations are supported by human clinical evidence, which findings primarily provide mechanistic or biological plausibility, and where important uncertainties remain. In particular, the review addresses whether apparently inconsistent findings across human and animal studies can be explained by differences in study design, stress exposure, outcome assessment, and causal inference, thereby providing a more balanced interpretation of the current evidence on perceived stress and ART outcomes.

Materials and Methods

Review Design and Approach

This study was conducted as a structured thematic narrative review to identify, organize, and synthesize the available evidence concerning the relationship between psychological stress and reproductive outcomes in the context of infertility and ART. The review incorporated human clinical evidence and experimental animal evidence. These evidence streams were considered separately because of substantial differences in study populations, stress exposures, experimental conditions, reproductive endpoints, and implications for clinical practice.

Given the heterogeneity of the available literature with respect to study designs, populations, stress assessment methods, ART characteristics, experimental models, and outcome definitions, the evidence was synthesized narratively and thematically rather than quantitatively.

Research Question and Objectives

The primary research question was: What evidence exists regarding the relationship between psychological or perceived stress and reproductive outcomes among individuals experiencing infertility or undergoing ART, and what biological mechanisms linking stress to reproductive dysfunction have been demonstrated in experimental animal models?

The specific objectives were to:

1. synthesize evidence concerning psychological or perceived stress and ART outcomes in women and men;
2. examine associations between stress and intermediate reproductive outcomes, including ovarian, oocyte, embryo, semen, and sperm parameters;
3. examine evidence concerning reproductive endocrine and biological pathways potentially linking stress with reproductive dysfunction;
4. synthesize experimental animal evidence concerning the effects of acute or chronic stress on ovaries, uterine, oocytes, embryo, testicles, sperm, and reproductive endocrine function;
5. examine dyadic and psychosocial consequences of infertility-related stress, with particular emphasis on fertility treatment, relationship functioning, coping, and treatment persistence; and
6. evaluate the effects of psychological and psychosocial interventions on stress, anxiety, depression, coping, psychological well-being, and reproductive outcomes.

Literature Search

A literature search was conducted in PubMed/MEDLINE, Scopus, and Web of Science from database inception to September 5, 2026.

The search strategy combined terms relating to infertility and ART with terms relating to psychological or physiological stress. Terms relating to infertility and ART included, but were not limited to, “infertility,” “in vitro fertilization,” “IVF,” “assisted reproductive technology,” “ART,” “ICSI,” and “fertility treatment.” Stress-related terms included “perceived stress,” “psychological stress,” “infertility stress,” “psychological distress,” “anxiety,” “cortisol,” “hypothalamic-pituitary-adrenal axis,” “HPA axis,” “dyadic coping,” and related terms. Additional reproductive outcome terms, including “oocyte,” “embryo,” “implantation,” “pregnancy,” “live birth,” “sperm,” “semen,” and “reproductive function,” were incorporated where appropriate.

The search was designed to identify literature relevant to the objectives of the review. Reference lists of relevant articles and reviews were also examined manually to identify additional publications that were considered relevant to the scope of the review.

Eligibility Criteria

Eligible human evidence included RCTs, and observational studies, ie. Cohort, cross-sectional and case control. Observational and longitudinal studies were considered when they evaluated associations between psychological, perceived, infertility-related, or physiological stress and reproductive, ART-related, or psychosocial outcomes. Randomized controlled trials were included primarily when they evaluated psychological or psychosocial interventions targeting stress, anxiety, depression, coping, or related psychological outcomes, with reproductive or treatment-related outcomes considered when reported. Systematic reviews and meta-analyses were used as secondary evidence to contextualize and compare findings from primary studies, while narrative reviews were considered for background and mechanistic context.

Eligible experimental animal studies included controlled studies of acute, chronic, restraint, unpredictable, prenatal, or glucocorticoid-related stress paradigms in which relevant ovarian, uterine, oocyte, embryo, testicular, sperm, endocrine, or fertility outcomes were assessed.

Studies were excluded if they were unrelated to psychological or physiological stress, relevant reproductive or ART outcomes, or stress-related interventions, focused solely on technical aspects of ART without a relevant stress component, were conference abstracts or reports with insufficient methodological information, or lacked sufficient information regarding the population/model, stress exposure or intervention, and relevant outcomes. Systematic reviews, meta-analyses, and narrative reviews were not counted as additional primary empirical studies.

Literature Identification and Selection

Potentially relevant publications were identified through database searches and manual examination of reference lists.

The selection of literature was conducted through review of titles, abstracts, and, where appropriate, full texts to determine relevance to the predefined objectives and eligibility criteria. Because this review was designed as a structured thematic narrative synthesis rather than a systematic review, study selection was based on relevance to the research questions and thematic scope rather than a formal PRISMA-based screening process.

Relevant publications were subsequently organized according to evidence type and thematic domain.

Data Organization and Extraction

Data were organized using a structured framework developed for the review. The following information was considered where available:

- Publication characteristics, including author, publication year, and country;
- Study design;
- Human population characteristics or animal model;
- Sample size;
- Infertility and ART characteristics, where applicable;
- Type, timing, duration, and measurement of stress exposure;
- Psychological stress instruments or physiological stress markers;
- Psychological or psychosocial intervention characteristics, where applicable;
- Reproductive and ART outcomes;
- Psychological and psychosocial outcomes;
- Relevant endocrine, molecular, or biological mechanisms;
- Principal findings; and
- Methodological limitations.

For human studies, particular attention was given to the distinction between intermediate reproductive parameters and definitive ART outcomes, including clinical pregnancy and live birth. For animal studies, the timing, duration, intensity, and experimental nature of the stress exposure were considered when interpreting reproductive effects.

Organizing Evidence and Critical Considerations

The literature was organized according to study type and thematic relevance. Rather than assigning a single numerical quality score, methodological limitations and potential sources of uncertainty were considered qualitatively when interpreting the evidence.

Particular caution was applied when interpreting findings from studies with small sample sizes, self-reported stress measures, potential confounding, heterogeneous outcome definitions, or other important methodological limitations.

Evidence Classification

Because the review incorporated multiple forms of evidence, publications were considered separately according to evidence type.

Primary human studies constituted the principal evidence base for conclusions concerning clinical associations between psychological stress and ART outcomes. Systematic reviews and meta-analyses were used as secondary evidence to contextualize findings across primary studies. Narrative reviews were used primarily for contextual or mechanistic background. Experimental animal studies were analyzed separately as mechanistic evidence.

Accordingly, different evidence types were not treated as equivalent units of evidence. This distinction was maintained to reduce the risk of double-counting evidence and to avoid interpreting secondary or mechanistic evidence as equivalent to direct clinical evidence.

Thematic Synthesis

Given the substantial heterogeneity in study design, population characteristics, stress measurements, ART protocols, intervention characteristics, experimental animal models, and outcome definitions, findings were synthesized narratively and thematically.

Human evidence was organized into the following domains:

1. Female psychological/perceived stress and ART outcomes;
2. Ovarian, oocyte, and embryological parameters;
3. Male psychological/perceived stress and semen and sperm parameters;
4. Dyadic and psychosocial consequences of infertility-related stress, including coping, relationship functioning, and treatment persistence; and
5. Psychological and psychosocial interventions during infertility treatment.

Experimental animal evidence was synthesized separately according to:

1. Ovarian and female reproductive function;
2. Uterine function and implantation-related processes;
3. Oocyte and embryo competence; and
4. Testicular, sperm, and male reproductive function.

Where relevant, reproductive endocrine and biological pathways, including HPA axis activity, glucocorticoid signaling, oxidative stress, and related molecular pathways, were considered as potential mechanisms rather than as direct evidence of clinical causality.

Within each thematic domain, findings were interpreted according to the direction and consistency of reported associations, the method used to assess stress, timing of stress exposure, study design, outcome definition, sample characteristics, and methodological limitations.

Particular attention was given to distinguishing intermediate reproductive outcomes, such as oocyte or semen parameters, from definitive clinical ART outcomes, including clinical pregnancy and live birth.

Human–Animal Evidence Integration and Translational Considerations

Human clinical and experimental animal evidence were maintained as separate evidence streams throughout the synthesis. Animal studies were considered primarily as evidence of biological plausibility and potential mechanisms linking stress exposure to reproductive dysfunction rather than as direct evidence of clinical ART effects in humans.

The translational relevance of animal findings was considered in light of differences in species-specific reproductive biology, stress induction methods, exposure intensity and duration, timing relative to reproductive events, experimental control, and outcome measurement.

In particular, experimentally induced stress in animal models may involve controlled or relatively intense exposures that differ substantially from the multifactorial, variable, and often self-reported psychological stress experienced by patients undergoing infertility treatment. Therefore, mechanistic findings from animal models were not interpreted as establishing causality in human ART populations.

Animal evidence was considered complementary to human clinical evidence and was used to identify potential biological pathways that may help explain observed clinical associations and guide future translational research.

Results

The included literature comprised human observational and interventional studies, systematic reviews and meta-analyses, as well as experimental animal studies investigating the relationship between psychological stress and reproductive outcomes. Because of substantial heterogeneity in study populations, study designs, stress measures, experimental stress paradigms, and reproductive outcomes, the findings were synthesized narratively rather than quantitatively. The human evidence primarily addressed perceived stress, infertility-related stress, psychological distress, cortisol and related psychosocial factors in individuals or couples undergoing fertility treatment. The animal literature primarily examined experimentally induced acute or chronic stress and its effects on ovarian function, oocyte competence, uterine receptivity, implantation, spermatogenesis, endocrine regulation, and fertility-related outcomes. Overall, human studies showed heterogeneous associations

between psychological stress and ART outcomes, whereas experimental animal studies provided more consistent evidence of alterations in reproductive physiology following acute or chronic stress exposure. Psychological interventions generally improved stress, anxiety, depressive symptoms, and psychological adjustment, while their effects on pregnancy and other reproductive outcomes were less consistent.

Female Perceived Stress and ART Outcomes

Human evidence concerning the association between psychological stress and ART outcomes is heterogeneous, with findings varying according to the method and timing of stress assessment, the stage of IVF, and the reproductive endpoint examined [8, 9]. Table 1 summarizes the principal human studies examining associations between perceived stress and ART-related outcomes.

Clinical pregnancy and live birth: Cesta et al. (2018) prospectively evaluated perceived stress, infertility-related stress, and cortisol levels in women undergoing IVF and found no statistically significant association between these stress measures and embryo quality or clinical pregnancy rate. These findings indicate that, in this IVF population, the assessed psychological and physiological stress measures were not significantly associated with clinical pregnancy [19].

A broader systematic review by Zanettoullis et al. (2024) evaluated 36 studies examining stress at different stages of the IVF process. Rather than demonstrating a uniform effect across the entire treatment cycle, the review identified stage-specific associations. The oocyte-retrieval stage showed the most consistent association with both acute and chronic stress, while evidence concerning fertilization was more limited. The association between stress and pregnancy rate was comparatively weak [8]. Thus, the available literature suggests that psychological stress may be more readily associated with some intermediate IVF processes than with definitive treatment outcomes such as clinical pregnancy. These findings should be interpreted cautiously. Differences among studies in the timing and instruments used to assess stress, the biological markers examined, ovarian stimulation protocols, patient characteristics, and definitions of reproductive success may contribute to apparently inconsistent findings. Furthermore, observational studies cannot readily distinguish an independent association of stress from the possibility that underlying infertility severity, treatment prognosis, or previous treatment experience influences both stress and reproductive outcomes. Overall, current human evidence does not establish a consistent causal relationship between female psychological or perceived stress and clinical pregnancy following ART, and evidence regarding live birth remains limited.

Embryological Parameters

Embryological outcomes represent intermediate endpoints that may be associated with ART success and through which stress-related processes could potentially influence reproductive outcomes. However, the available human evidence does not establish a uniform relationship between perceived stress and the number or quality of embryos generated during IVF [19] .

The systematic review by Zanettoullis et al. (2024) suggests that stress may be associated with specific stages of the IVF process, with the strongest evidence observed around oocyte retrieval. However, findings concerning fertilization and subsequent embryological development were less consistent, and the relationship between stress and pregnancy outcomes was comparatively weak [8].

It is important to distinguish these human findings from experimental animal evidence. For example, a mouse study investigating ovarian gonadotropin stimulation under chronic psychosocial stress reported alterations in oocyte characteristics following stress exposure [20]. Because this evidence derives from an animal model, it should not be presented as evidence from human ART populations and is therefore discussed separately in Section 3.2 [20].

Similarly, evidence showing that the number and quality of embryos transferred are associated with live birth should not be interpreted as direct evidence that psychological stress affects embryo quality. Such studies evaluate embryological predictors of ART outcome but do not necessarily assess psychological stress and therefore cannot be used as direct evidence of a stress-related effect [21].

Overall, the human evidence remains insufficient to determine whether psychological stress is independently associated with clinically meaningful differences in embryo quality after accounting for other determinants of ART outcome. Future studies should prospectively assess stress before and during ovarian stimulation and relate these measurements to standardized embryological endpoints.

Male Perceived Stress and Semen Quality

Male psychological stress has received less attention than female psychological stress in ART research, although several studies have reported associations between stress and intermediate male reproductive parameters [22, 23].

Janevic et al. (2014) evaluated perceived stress, stressful life events, and work-related stress in 193 men and examined sperm concentration, motility, and morphology. Higher perceived stress was inversely associated with sperm concentration, motility, and morphology after covariate adjustment, whereas job strain was not associated with semen parameters [23]. Importantly, this study did not assess sperm DNA fragmentation.

Other clinical and mechanistic literature suggests that psychological stress may influence male reproductive function through neuroendocrine and oxidative pathways. Stress-related neuroendocrine and oxidative pathways have been proposed as potential mechanisms linking psychological stress with male reproductive function. Alterations in testosterone and gonadotropin regulation, together with oxidative imbalance, may contribute to differences in sperm membrane function, motility, and other aspects of sperm quality [7, 24] .

However, the evidence should be interpreted with caution. Associations between stress and semen parameters should not be interpreted as evidence that psychological stress directly impairs fertility, because semen quality is influenced by multiple biological, behavioral, environmental, and clinical factors. Moreover, relatively few studies directly connect male psychological stress with definitive ART outcomes such as fertilization, clinical pregnancy, or live birth.

Overall, Current evidence is more extensive for associations between male psychological stress and semen quality than for associations with definitive ART outcomes. Future prospective studies should simultaneously assess psychological stress, endocrine and oxidative biomarkers, semen quality, and ART outcomes to clarify potential biological pathways and temporal relationships (Table 1).

Table 1. Characteristics of the studies on human.

Study	Design	Population	Stress exposure/intervention	Main outcome	Overall interpretation	Ref.
Cesta et al., 2018	Prospective cohort	Women undergoing IVF	Perceived stress, infertility-related stress, cortisol	Embryo quality, clinical pregnancy	No significant association with IVF outcomes	[19]
Boivin et al., 2011	Meta-analysis of prospective studies	Women undergoing ART (14 studies, n=3,583)	Pretreatment emotional distress	Clinical pregnancy	No overall association between pretreatment distress and pregnancy following ART	[6]
Zanettoullis et al., 2024	Systematic review	IVF populations	Acute/chronic stress	IVF stage-specific outcomes	Heterogeneous and stage-specific associations	[8]
Janevic et al., 2014	Observational study	Men	Life/work stress	Semen quality	Higher stress associated with poorer semen parameters	[23]
Martins et al., 2016	Systematic review	Men undergoing ART	Psychological distress	Psychological adaptation	Significant psychological burden	[22]
Gameiro et al., 2012	Systematic review	Fertility-treatment patients	Psychological burden	Treatment discontinuation	Multiple psychosocial factors associated with discontinuation	[44]
Frederiksen et al., 2015	Systematic review/meta-analysis	Infertile women and men	Psychosocial interventions	Psychological and pregnancy outcomes	Robust improvements in both psychological well-being and pregnancy rates	[50]

Verkuijlen et al., 2016	Cochrane systematic review	Subfertile men and women	Psychological/educational interventions	Mental health, live birth/pregnancy	Effects on both outcomes uncertain due to very low-quality evidence and high risk of bias	[53]

Animal Studies

Unlike human studies, experimental animal studies allow more controlled investigation of the effects of acute or chronic stress exposure on reproductive physiology and fertility-related outcomes [16, 17].

Female Reproductive Function in Animal Models

Animal studies have reported associations between chronic stress exposure and alterations in female reproductive function, including changes in ovarian physiology, follicular dynamics, and oocyte competence [25]. Experimental rodent models have reported that prolonged exposure to stressors such as cold-water immersion, restraint stress, and chronic unpredictable stress is associated with elevated glucocorticoid and corticosterone levels, estrous cycle irregularities, altered oocyte maturation, and reduced oocyte viability [14, 16, 25]. In addition, stressed animals exhibit a higher proportion of morphologically abnormal and developmentally arrested oocytes, indicating compromised reproductive potential [16, 26]. Chronic stress exposure has also been associated with accelerated activation and depletion of primordial follicles, accompanied by diminished ovarian reserve and features of premature ovarian aging [14, 27]. Potential mechanisms underlying these alterations include activation of the PI3K/PTEN/Akt signaling pathway, dys-regulation of Kit ligand signaling, increased Corticotropin-Releasing Hormone (CRH) activity [14], and enhanced ovarian apoptosis involving the Fas/FasL pathway [28, 29]. Furthermore, maternal stress during pregnancy has been associated with alterations in embryonic developmental competence, oocyte quality, and follicular development [26]. Collectively, these findings suggest that chronic stress exposure may alter neuroendocrine and ovarian regulatory mechanisms and is associated with female reproductive dysfunction and fertility-related changes in animal models [25, 30].

Stress, Uterine Function, and Implantation

Experimental animal studies suggest that chronic stress exposure is associated with alterations in ovarian and uterine function and reduced implantation-related outcomes [31]. Pre-gestational stress exposure, particularly restraint stress in female rats, has been associated with reduced implantation rates and pregnancy-related outcomes, alongside alterations in reproductive hormonal balance, follicular development, and corpus luteum function [30, 32]. In addition, stress-related alterations in the HPG axis have been associated with changes in the expression of uterine receptivity markers, suggesting potential effects on the endometrial environment involved in embryo implantation [31, 33]. Furthermore, elevated glucocorticoid levels associated with chronic stress exposure have been linked to alterations in decidualization and endometrial remodeling in mouse models, including changes in genes involved in uterine cellular proliferation, differentiation, and decidual transformation [34, 35].

These molecular and endocrine alterations are associated with changes in uterine receptivity and implantation-related processes, suggesting a potential role for stress-related physiological responses in mechanisms involved in embryo implantation and early pregnancy maintenance [34, 35].

Oocyte and Embryo Quality

Animal studies have reported associations between stress exposure and alterations in oocyte competence and embryo development [30, 36].

Exposure to stressors such as chronic cold-water immersion and maternal restraint stress has been associated with impaired oocyte maturation, reduced oocyte viability, and an increased proportion of morphologically abnormal oocytes [16]. In addition, stress exposure has been associated with reduced developmental competence of embryos derived from affected oocytes, leading to compromised early embryogenesis [26, 36]. These alterations have been proposed to involve dys-regulation of the HPA axis, changes in reproductive hormone secretion, elevated glucocorticoid levels, and increased oxidative stress, which may affect follicular development, fertilization, and embryo viability [36, 37]. Collectively, these findings suggest that chronic stress exposure may be associated with reduced female reproductive potential through alterations in oocyte competence and embryo development [30].

Male Reproductive Function in Animal Models

Animal studies have reported that both acute and chronic stress exposure are associated with alterations in male reproductive function, including endocrine regulation and sexual behavior [38]. Experimental findings in male rats indicate that stress exposure increases corticosterone levels while simultaneously reducing testosterone concentrations, accompanied by alterations in sexual performance and reproductive activity. Chronic stress exposure appears to produce more persistent reproductive alterations than acute stress exposure, potentially involving dys-regulation of the HPG axis and changes in androgen production [38, 39]. These findings suggest that prolonged activation of the stress response system may alter neuroendocrine pathways involved in normal reproductive function and may be associated with changes in male fertility-related outcomes [39, 40].

In addition to post-natal stress exposure, pre-natal stress exposure has been associated with long-term alterations in reproductive capacity. Studies in rats have reported that pre-natal stress exposure is associated with reduced sperm quality, fertility-related changes, and persistent alterations in reproductive system development in the offspring [17, 41, 42]. These findings have been proposed to involve altered developmental programming of the HPG axis during fetal life, which may contribute to persistent changes in gonadal and hormonal function [41, 43]. Furthermore, chronic stress has been associated with reduced gonadotropin secretion and impaired testicular activity, and may contribute to alterations in fertility-related outcomes [40]. Collectively, these findings support a potential role for stress-related neuroendocrine alterations in male reproductive dysfunction in animal models [38, 39] .

Translational Context of Animal Findings

Although experimental animal models provide controlled evidence regarding potential biological pathways linking stress exposure with reproductive dysfunction, their findings cannot be directly equated with clinical ART outcomes in humans. Animal stress paradigms, including restraint, cold-water exposure, unpredictable stress, and pre-natal stress, differ substantially from the multifactorial and predominantly self-reported psychological stress experienced by individuals undergoing infertility treatment. Differences in species, stress intensity and duration, timing of exposure, reproductive physiology, experimental control, and outcome assessment may also limit direct translation to human populations. Accordingly, the animal evidence in this review is interpreted primarily as mechanistic and biologically plausible evidence rather than as direct evidence that psychological stress causes poorer ART outcomes in humans. The complementary interpretation of these two evidence streams is therefore important: human studies provide greater relevance to clinical and patient-centered outcomes, whereas animal models offer controlled opportunities to investigate potential reproductive, endocrine, and molecular pathways. These experimental findings are summarized in Table 2.

Table 2. Characteristics of the studies on animal.

Study	Model	Stress exposure	Reproductive outcome	Main interpretation	Ref.
Casillas et al., 2021	Female rats	Chronic stress	Oocyte maturation/viability	Alterations in oocyte maturation and viability associated with chronic stress exposure	[16]
Xu et al., 2018	Female mice	Chronic restraint stress	Primordial follicle activation	Altered follicular dynamics	[14]
Gao et al., 2020	Female mice	Chronic unpredictable stress	Ovarian reserve	Changes in ovarian function and reserve associated with chronic stress exposure	[15]
Yuan et al., 2016	Mouse ovarian model	Glucocorticoid exposure	Oocyte developmental potential	Alterations in oocyte developmental potential with involvement of apoptotic pathways	[29]
Zheng et al., 2020	Female mice	Stress-related glucocorticoid exposure	Uterine receptivity/decidualization	Alterations in uterine receptivity and decidualization-related processes	[34]
Liu et al., 2012	Female mice	Predatory (psychological) stress	Oocyte developmental competence	Reduced blastocyst formation rate and developmental potential following psychological stress exposure	[26]

Retana-Márquez et al., 2003	Male rats	Acute/chronic stress	Testosterone/sexual behavior	Stress-related alterations in testosterone regulation and sexual behavior	[38]
García-Vargas et al., 2019	Rats	Prenatal stress	Sperm/fertility	Persistent alterations in sperm and fertility-related outcomes following prenatal stress exposure	[17]

Dyadic and Psychosocial Effects

Within the context of infertility treatment, psychological distress may substantially affect psychological adaptation and coping, such as among men following unsuccessful medically assisted reproduction. Martins et al. (2016) highlighted the substantial psychological burden experienced by men following unsuccessful medically assisted reproduction and noted that male distress may be underrecognized when psychological responses are expressed through internalized or avoidant coping strategies [22].

Psychosocial factors may also contribute to treatment discontinuation. Gameiro et al. (2012) identified psychological distress, treatment burden, financial considerations, relational factors, and perceptions of poor prognosis among factors associated with discontinuation of fertility treatment [44]. Domar et al. (2018) similarly reported that treatment burden was an important reason for discontinuation among insured women, suggesting that discontinuation cannot be understood solely in terms of treatment costs [45].

Taken together, these findings indicate that the clinical relevance of infertility-related stress extends beyond potential associations with reproductive outcomes. Psychological distress may affect coping with treatment and persistence with fertility care, while the extent to which it influences couple functioning or definitive ART outcomes remains uncertain. More ART-specific research is needed to determine whether couple-based psychosocial interventions can improve psychological well-being, treatment experience, or treatment persistence.

Stress-Reduction Interventions

Randomized trials and systematic reviews suggest that psychological interventions can improve psychological outcomes among individuals undergoing infertility treatment, although evidence regarding effects on clinical pregnancy or live birth is less consistent.

Domar et al. (2011) evaluated a group mind–body intervention among women undergoing IVF and reported improvements in psychological outcomes, together with an association between participation in the intervention and pregnancy rates. Hosaka et al. (2002) similarly reported psychological and physiological changes following a psychiatric group intervention, although the clinical relevance of changes in biological markers remains uncertain [46].

Other randomized studies have evaluated Cognitive Behavioral Therapy (CBT) and psychosocial interventions. Faramarzi et al. (2008) reported that CBT improved depression and anxiety compared to fluoxetine [47], Faramarzi et al. (2013) in another study found beneficial effects of CBT on infertility-related stress [48]. Chan et al. (2006) also reported reductions in anxiety following a psychosocial group intervention among women undergoing IVF [49].

These intervention studies should be distinguished from observational and meta-analytic studies examining whether psychological distress itself is associated with ART outcomes. In particular, Boivin et al. (2011) conducted a meta-analysis of prospective psychosocial studies and did not evaluate an intervention. Their analysis included 14 studies involving 3,583 women and found no overall association between pre-treatment emotional distress and pregnancy following ART [6].

Frederiksen et al. (2015) reported that psychosocial interventions were associated with significant improvements in psychological outcomes and clinical pregnancy rates among individuals and couples undergoing infertility treatment. Subsequent systematic reviews and meta-analyses have generally supported beneficial effects of psychological interventions on infertility-related distress, anxiety, depression, and psychological well-being, while also reporting modest improvements in pregnancy rates. However, the evidence for reproductive outcomes remains less consistent, particularly for live birth, and is limited by substantial heterogeneity across interventions and populations, methodological limitations, and risk of bias in many of the included studies. Overall, psychosocial interventions appear to have a relatively well-supported role in reducing psychological distress and improving psychological well-being during infertility treatment, whereas their ability to improve reproductive outcomes, especially live birth, remains uncertain and requires confirmation in high-quality randomized controlled trials [50-52].

Clinically, this distinction is important. Patients should not be informed that stress reduction is necessary to achieve pregnancy or that psychological distress causes ART failure. Instead, psychological support should be offered because infertility treatment is psychologically demanding and because reducing distress may improve quality of life, coping, communication, and engagement with treatment.

Discussion

The principal human and animal findings of this review, summarized in Tables 1 and 2, are interpreted below in relation to their clinical and mechanistic implications.

In women undergoing IVF, the available clinical evidence does not support a uniform detrimental effect of perceived stress on treatment success [6, 10, 19]. The apparent discrepancy between null findings for clinical pregnancy and associations reported at selected stages of the IVF process may indicate that, when present, stress-related effects are more likely to involve specific intermediate processes than the final probability of treatment success [8, 9, 19]. However, the clinical relevance of such stage-specific associations remains uncertain, particularly because treatment success is influenced by multiple biological and clinical determinants that may operate independently of psychological stress [21].

The heterogeneity across individual studies is likely multi-factorial rather than attributable to a single methodological difference. Variation in stress definitions and instruments [4], timing of assessment, infertility diagnoses, patient characteristics, treatment protocols [3], and outcome definitions may all influence the observed associations [8, 9]. Importantly, perceived stress is a dynamic exposure that may change throughout an ART cycle and may also be influenced by treatment-related experiences and expectations [3, 10]. Thus, a single pre-treatment stress measurement may not adequately capture the temporal relationship between psychological stress and reproductive processes [10, 19]. These considerations argue against treating stress as a uniform exposure with a predictable effect across all stages of ART [8].

In men, the available evidence provides support for associations between psychological stress and intermediate reproductive outcomes, particularly semen parameters, although findings are not entirely consistent and direct evidence regarding final ART outcomes remains limited [13, 23]. Psychological stress has been associated with poorer semen parameters, while oxidative and neuroendocrine pathways have been proposed as potential mechanisms [7, 24]. Nevertheless, the available evidence remains insufficient to determine whether psychological stress independently influences definitive ART outcomes such as fertilization, clinical pregnancy, or live birth [11, 12].

Experimental animal evidence provides an important mechanistic complement to human research. The relative consistency of findings across controlled stress paradigms supports the biological plausibility of stress-related effects on reproductive physiology, particularly through neuroendocrine and endocrine pathways [14-16, 25, 28, 29]. However, this consistency should not be interpreted as evidence of a comparable magnitude or clinical effect in humans. Differences in species, stress paradigms, exposure intensity and duration, reproductive physiology, and experimental control substantially limit direct translation to ART outcomes [25]. Thus, animal findings are most appropriately viewed as evidence supporting possible biological mechanisms rather than as confirmation that psychological stress causes poorer ART outcomes in humans.

The psycho-social consequences of infertility are clinically important regardless of whether stress directly alters ART success Infertility treatment may impose substantial emotional, physical, financial, and logistical burdens [1, 2], and psychological distress may affect relationship functioning and treatment persistence [44, 45], while dyadic research suggests that stress and coping processes may also operate interactively between partners [22].

Consequently, psycho-social care should be viewed primarily as a component of patient-centered fertility care rather than solely as a biological intervention intended to increase pregnancy rates [5].

The evidence regarding psychological interventions is similarly nuanced. Cognitive-behavioral, mind–body, and other psycho-social interventions can improve psychological outcomes, including anxiety, depressive symptoms, stress, and coping [46-49]. However, reproductive outcomes have been less consistently improved. Thus, the most defensible clinical interpretation is that psychological interventions have established value for patient well-being, while evidence for a direct enhancement of ART success remains uncertain [53].

The findings support the integration of psycho-social care into fertility treatment primarily to address the substantial psychological burden associated with infertility and ART [1, 2, 5]. Brief validated psychological instruments may help identify patients experiencing clinically meaningful stress, anxiety, or depressive symptoms, particularly at key stages of treatment [4, 5]. Patients with

significant psychological distress should have access to evidence-based psychological interventions, including cognitive-behavioral approaches, mindfulness-based strategies, and couples-based support when appropriate [46-49]. Because infertility-related stress may affect both members of a couple, and dyadic research indicates that stress and coping processes may be interdependent between partners, psycho-social assessment should not be restricted exclusively to the female partner [22]. Fertility-care professionals should also be equipped to recognize psychological distress, communicate its relevance appropriately, and facilitate referral to qualified psychological services [5].

Importantly, these recommendations should not be interpreted as evidence that stress reduction necessarily increases pregnancy or live birth rates [6]. Future research should prioritize prospective, adequately powered studies that repeatedly assess psychological stress across the ART cycle and integrate validated psychological measures with relevant physiological biomarkers [10, 19]. Studies should also distinguish intermediate reproductive endpoints from definitive outcomes such as clinical pregnancy and live birth and, where appropriate, assess both partners [8, 9]. Standardized stress assessment and reproductive outcome definitions would improve comparability across studies and help determine whether particular treatment stages or patient subgroups are associated with clinically meaningful reproductive effects [8, 9].

Overall, the findings support a distinction between three related but not equivalent concepts: psychological burden, biological stress responses, and ART success. These domains may interact, but evidence from one domain should not automatically be interpreted as evidence of causality in another.

Limitations

This review has several limitations that should be considered when interpreting its findings. First, it was conducted as a structured thematic narrative review rather than a systematic review, and study identification and selection were based on relevance to the predefined thematic scope rather than a formal systematic-review screening process. Consequently, a formal PRISMA-ScR flow diagram was not used. Second, no formal risk-of-bias assessment using standardized tools such as RoB 2, ROBINS-I, SYRCLE, or AMSTAR-2 was performed; therefore, the methodological quality of individual studies and systematic reviews was considered qualitatively rather than through formal risk-of-bias ratings. Third, the included evidence was highly heterogeneous with respect to study populations, stress measures, timing and duration of stress exposure, ART protocols, experimental models, and reproductive endpoints, limiting direct comparison across studies and precluding quantitative synthesis. Fourth, although the search covered PubMed/MEDLINE, Scopus, and Web of Science from database inception to September 5, 2026, publication and selection biases cannot be excluded, and relevant evidence indexed outside these databases may have been missed. Finally, the evidence base encompassed multiple study designs and levels of evidence, which limits direct comparison and requires cautious interpretation when integrating human clinical findings with experimental animal evidence. These limitations warrant cautious interpretation of the observed associations and reinforce the need for well-designed prospective human studies with standardized stress assessment, clearly defined ART endpoints, and formal methodological quality appraisal.

Conclusion

The available evidence indicates that psychological stress is an important component of the infertility-treatment experience, but its independent contribution to definitive ART outcomes remains uncertain [1, 2, 6]. In women, evidence linking perceived stress with clinical pregnancy and live birth is heterogeneous [6, 10], with some evidence suggesting stage-specific associations during IVF, particularly around oocyte retrieval [8, 9]. In men, psychological stress appears to be more consistently associated with intermediate semen parameters [7], although evidence directly linking male stress with live birth remains limited [11, 12].

Experimental animal studies provide biologically plausible evidence for potential mechanisms through which acute or chronic stress exposure may alter reproductive function, including neuroendocrine dysregulation, glucocorticoid signaling [28, 29], oxidative stress, and alterations in ovarian, uterine, and testicular function. However, these findings should not be interpreted as direct evidence that psychological stress causes ART failure in humans [25].

Psychological interventions appear to provide benefits for distress, anxiety, depressive symptoms, coping, and treatment experience [46-49], whereas evidence for improved pregnancy or live-birth outcomes remains inconsistent [50-52]. Therefore, psychosocial care should be integrated into fertility treatment primarily to support psychological well-being, coping, couple functioning, and treatment persistence rather than to promise improved reproductive success [22, 44, 45].

Future research should use prospective, adequately powered, and methodologically standardized designs that simultaneously assess psychological stress, relevant biological stress markers, dyadic processes, and reproductive outcomes in both partners. Greater consistency in the timing and measurement of stress and reproductive endpoints may also help clarify whether specific treatment stages or patient subgroups are more vulnerable to stress-related reproductive associations.

Abbreviations

ART	Assisted Reproductive Technologies
CBT	Cognitive Behavioral Therapy
CRH	Corticotropin-Releasing Hormone
HPA	Hypothalamic–Pituitary–Adrenal
HPG	Hypothalamic–Pituitary–Gonadal
IVF	In Vitro Fertilization
RCT	Randomized Controlled Trial
SNS	Sympathetic Nervous System

Declaration

Conflict of Interest:
The author declares that there are no conflicts of interest.

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