

Precision Nursing Interventions in Assisted Reproductive Technologies: A Systematic Review and Meta-Analysis of Fertility, Psychological, and Immunological Outcomes

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Abstract

Background: Infertility affects approximately 10–15% of couples globally, presenting significant clinical, psychological, and immunological challenges. While Assisted Reproductive Technologies (ART) have advanced, the potential of precision nursing interventions—individualized, nurse-led strategies based on patient-specific needs—to optimize outcomes remains largely unquantified. This systematic review and meta-analysis aimed to evaluate the effectiveness of these interventions on fertility outcomes (clinical pregnancy, live birth), psychological well-being, and key immunological markers in patients undergoing ART.

Methods: A systematic literature search was conducted across PubMed, Scopus, Web of Science, and the Cochrane Library from inception to July 2025. We included randomized controlled trials (RCTs) and quasi-experimental studies assessing nurse-delivered, individualized interventions in ART patients. Two independent reviewers performed study screening, data extraction, and quality appraisal using the Cochrane Risk of Bias tool. A random-effects model was employed for meta-analysis, calculating pooled effect sizes (Risk Ratios [RR] for dichotomous, Standardized Mean Difference [SMD] for continuous outcomes). Heterogeneity was assessed using the I^2 statistic.

Results: Eighteen studies encompassing 2,610 participants met the inclusion criteria. Nurse-led precision interventions demonstrated a significant positive impact on clinical pregnancy rates (RR = 1.37, 95% CI: 1.15–1.63, $p < 0.001$). A substantial improvement was also observed in patient-reported psychological well-being (SMD = 0.45, 95% CI: 0.23–0.67, $p < 0.001$), primarily driven by reduced anxiety and depression

scores. Furthermore, the interventions favorably modulated immunological markers, evidenced by a statistically significant reduction in stress-related cytokines (e.g., TNF-alpha) compared to standard care. Subgroup analysis suggested that interventions integrating personalized counseling, lifestyle modification, and stress management techniques yielded the largest effects.

Conclusion: This study highlights the innovative and clinically important role of precision nursing in the ART setting. Individualized, nurse-led interventions can significantly enhance reproductive success, improve psychological health, and beneficially modulate immune responses. These findings strongly support the integration of precision nursing into global ART clinical practice guidelines and establish a clear agenda for future research focusing on mechanism and long-term impact.

Keywords: Precision nursing, assisted reproductive technology, infertility, systematic review, meta-analysis, psychological well-being.

I. INTRODUCTION

1.1 Background and Rationale

Infertility, defined as the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse, affects approximately 10% to 15% of reproductive-aged couples worldwide [1]. The emotional and physical toll of infertility is substantial, often leading to elevated levels of anxiety, depression, and marital distress, which can negatively impact treatment adherence and outcomes [2].

Assisted Reproductive Technologies (ART), such as in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI), have revolutionized fertility treatment. However, success rates remain suboptimal, with cumulative live birth rates varying widely [3]. Beyond the clinical and laboratory factors, growing evidence points to the crucial role of psychoneuroimmunological factors—the complex interplay between psychological stress, the nervous system, and the immune response—in influencing ART outcomes [4]. Elevated stress is often associated with dysregulation of the HPA axis and increased pro-inflammatory cytokines, which may impair implantation [5].

1.2 The Role of Precision Nursing in ART

Nursing care is integral to the ART journey, providing education, medication instruction, and emotional support. Precision nursing extends this role by advocating for highly individualized, evidence-based interventions tailored to a patient's unique genetic, psychological, lifestyle, and clinical profile [6]. These interventions move beyond standardized protocols to address specific patient deficits, such as high baseline stress, poor adherence to lifestyle modifications, or specific risk factors for adverse immunological responses. Examples include personalized stress management training, tailored nutritional counseling based on patient biomarkers, and highly targeted psychological support.

1.3 Knowledge Gap and Study Objectives

Despite the theoretical promise, the current body of literature lacks a comprehensive, quantitative synthesis evaluating the cumulative effectiveness of nurse-led precision interventions across the critical domains of fertility, psychological, and immunological outcomes in ART. While individual studies exist, a high-quality meta-analysis is necessary to generate robust, generalizable evidence that can inform global clinical guidelines.

The primary objective of this systematic review and meta-analysis was to:

Quantify the effect of nurse-led precision nursing interventions on fertility outcomes (Clinical Pregnancy Rate [CPR] and Live Birth Rate [LBR]) in patients undergoing ART.

Determine the impact of these interventions on psychological well-being (e.g., anxiety and depression scores).

Evaluate the modulation of key immunological markers (e.g., inflammatory cytokines) by the interventions.

II. METHODS

A. Review Design and Registration

This systematic review and meta-analysis was conducted and reported in strict accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [7].

B. Search Strategy

A comprehensive, pre-defined search strategy was developed in consultation with a medical librarian. The following electronic databases were searched from their inception to July 30, 2025: PubMed, Scopus, Web of Science (Core Collection), and the Cochrane Central Register of Controlled Trials (CENTRAL).

The search combined terms related to the population, intervention, and setting using Boolean operators (AND/OR). Key search terms and their synonyms included:

Population/Setting: ("Assisted Reproductive Technology" OR "ART" OR "In Vitro Fertilization" OR "IVF" OR "Infertility" OR "Subfertility").

Intervention: ("Precision Nursing" OR "Personalized Nursing Care" OR "Individualized Intervention" OR "Nurse-led Care" OR "Tailored Intervention" OR "Specialized Nursing").

Study Design: ("Randomized Controlled Trial" OR "RCT" OR "Controlled Clinical Trial" OR "Quasi-experimental Study").

The search strategy for PubMed was: (("Assisted Reproductive Technology"[MeSH] OR "Infertility"[MeSH] OR "IVF") AND ("Precision Nursing" OR "Personalized Nursing Care" OR "Individualized Intervention") AND ("Randomized Controlled Trial"[Publication Type] OR "Quasi-experimental")). Citation tracking of included studies and review articles was also performed to identify additional relevant reports.

C. Inclusion and Exclusion Criteria

Studies were considered for inclusion if they met the following PICO criteria:

Population: Adult women (or couples) undergoing any form of ART (IVF, ICSI, frozen embryo transfer, etc.).

Intervention: A nurse-led, individualized, or tailored intervention (e.g., counseling, education, lifestyle modification, stress management) delivered during the ART cycle.

Comparison: Standard nursing care, routine care, or another non-individualized control intervention.

Outcomes: Reported at least one primary or secondary outcome of interest (Fertility, Psychological, or Immunological).

Study Design: Only Randomized Controlled Trials (RCTs) and well-conducted Quasi-experimental Studies published in English were included.

Studies were excluded if they: were conference abstracts, editorials, review articles without original data, involved non-human subjects, or focused solely on pharmacologic or surgical interventions without a distinct, nurse-led behavioral component.

D. Study Selection and Data Extraction

Two independent reviewers (Reviewer 1, Reviewer 2) screened the titles and abstracts of all retrieved records. Disagreements were resolved through consensus or consultation with a third reviewer (Reviewer 3). Full texts of potentially eligible studies were retrieved and assessed against the inclusion criteria.

Data extraction was performed using a standardized, pre-piloted data extraction form. Extracted data included:

Study characteristics: Author(s), year of publication, country, study design.

Participant characteristics: Sample size (Intervention/Control), age, cause of infertility, type of ART.

Intervention details: Specific components, duration, delivery mode, frequency.

Outcome data: Mean, standard deviation (SD), sample size for continuous outcomes; event counts for dichotomous outcomes (e.g., number of pregnancies/live births).

For studies reporting multiple time points, the outcome closest to the end of the ART cycle (e.g., clinical pregnancy) or immediately post-intervention (e.g., anxiety scores) was prioritized.

E. Quality Appraisal / Risk of Bias Assessment

The methodological quality and risk of bias (RoB) for all included RCTs were assessed independently by two reviewers using the Cochrane Risk of Bias (RoB) tool (version 2) [8]. The domains assessed were: RoB arising from the randomization process, RoB due to deviations from intended interventions, RoB due to missing outcome data, RoB in measurement of the outcome, and RoB in selection of the reported result. Each study was categorized as 'Low RoB,' 'Some Concerns,' or 'High RoB.'

F. Statistical Analysis

All statistical analyses were conducted using Review Manager (RevMan) Version 5.4 and R software (version 4.2.1) with the 'meta' package.

- *Data Synthesis*

Dichotomous Outcomes (Clinical Pregnancy Rate, Live Birth Rate): Effect sizes were calculated as Risk Ratios (RR) with 95% Confidence Intervals (CI).

Continuous Outcomes (Psychological Scales, Immunological Markers): Since different scales were used (e.g., HADS, STAI for anxiety), the effect size was calculated as the Standardized Mean Difference (SMD) with 95% CI. A negative SMD indicated an improvement (reduction) for scales like anxiety/depression, while a positive SMD indicated a beneficial increase for immunological factors (e.g., regulatory T-cells) or reduced inflammation-related markers (e.g., TNF-alpha).

- *Heterogeneity and Model Selection*

Statistical heterogeneity among studies was assessed using the Cochran's Q test (with $p < 0.10$ indicating significance) and the I^2 statistic (with $I^2 < 40\%$ indicating low heterogeneity, 40%-60% moderate, and $>60\%$ substantial) [9]. Given the anticipated clinical and methodological diversity across precision nursing interventions, a random-effects model (DerSimonian-Laird method) was pre-specified for all meta-analyses.

- *Subgroup and Sensitivity Analyses*

Pre-planned subgroup analyses were conducted to explore potential sources of heterogeneity based on: (a) Intervention type (e.g., psychological counseling focus vs. combined lifestyle/counseling), (b) Intervention duration (short-term ≤ 4 weeks vs. long-term > 4 weeks), and (c) Type of ART cycle (fresh vs. frozen transfer). Sensitivity analyses, including the "leave-one-out" method, were performed to test the robustness of the pooled effect sizes.

- *Publication Bias*

Publication bias was assessed visually using funnel plots for outcomes with ten or more included studies. Egger's regression test was used to statistically determine the asymmetry of the funnel plot, with $p < 0.10$ indicating potential bias.

III. RESULTS

A. Study Selection and Characteristics

The initial search yielded 3,145 records. After removal of duplicates, 2,152 unique articles were screened by title and abstract. A total of 158 full-text articles were assessed for eligibility. Ultimately, 18 studies (15 RCTs and 3 quasi-experimental studies) meeting all inclusion criteria were included in the systematic review and meta-analysis, involving a total of 2,610 participants (Intervention $n=1,315$; Control $n=1,295$). The study selection process is detailed in the PRISMA 2020 Flow Diagram.

B. Quality Assessment and Risk of Bias

The quality assessment, summarized in Table 2, showed that 12 of the 15 included RCTs had an overall 'Low Risk of Bias,' primarily due to adequate methods for sequence generation and allocation concealment. Three RCTs were assessed as having 'Some Concerns,' mainly due to insufficient detail on blinding of outcome assessment (performance bias) or incomplete reporting of missing data. The three quasi-experimental studies were assessed using the JBI checklist and were considered to be of high methodological quality.

C. Quantitative Synthesis (Meta-Analysis)

- *Primary Fertility Outcome: Clinical Pregnancy Rate (CPR)*

Data from 18 studies were pooled for Clinical Pregnancy Rate (CPR). The meta-analysis revealed a statistically significant benefit of nurse-led precision interventions compared to standard care.

The pooled Risk Ratio (RR) was 1.37 (95% CI: 1.15–1.63, $p < 0.001$).

This indicates that patients receiving precision nursing interventions had a 37% higher likelihood of achieving a clinical pregnancy.

Heterogeneity was moderate: $I^2 = 48\%$ ($p = 0.02$).

- *Secondary Fertility Outcome: Live Birth Rate (LBR)*

Thirteen studies reported Live Birth Rate (LBR). The pooled effect size showed a positive trend, though the result was marginally non-significant at the $\alpha = 0.05$ level.

The pooled Risk Ratio (RR) was 1.21 (95% CI: 0.99–1.48, $p = 0.06$).

Heterogeneity was low: $I^2 = 32\%$ ($p = 0.15$).

- *Psychological Outcomes*

Twelve studies reported psychological outcomes (anxiety and/or depression) using various validated scales. The pooled Standardized Mean Difference (SMD) demonstrated a significant improvement in overall psychological well-being (reduced negative scores).

The pooled SMD was 0.45 (95% CI: 0.23–0.67, $p < 0.001$). This represents a moderate-to-large beneficial effect.

Heterogeneity was substantial: $I^2 = 68\%$ ($p < 0.001$), prompting subgroup analysis.

- *Immunological Outcomes*

Seven studies provided data on immunological markers, primarily stress-related pro-inflammatory cytokines (e.g., TNF-alpha, IL-6) measured pre-embryo transfer. The pooled analysis of these markers indicated a favorable modulation towards reduced inflammation.

The pooled SMD for reduced cytokine levels was 0.51 (95% CI: 0.19–0.83, $p = 0.002$).

Heterogeneity was high: $I^2 = 75\%$ ($p < 0.001$).

D. Subgroup Analysis

Subgroup analysis on psychological outcomes (where heterogeneity was substantial) identified the most effective intervention characteristics:

Intervention Content: Interventions integrating personalized counseling, lifestyle modification, AND stress management (SMD = 0.65, 95% CI: 0.42–0.88) showed a significantly larger effect than those focusing only on education (SMD = 0.20, 95% CI: -0.05–0.45).

Intervention Duration: Long-term interventions (> 4 weeks) demonstrated a larger beneficial effect (SMD = 0.58) compared to short-term interventions (4 weeks) (SMD = 0.31).

E. Publication Bias

Publication bias was assessed for the Clinical Pregnancy Rate ($n=18$). Visual inspection of the funnel plot suggested

minimal asymmetry. Egger's regression test yielded a non-significant result ($p = 0.18$), suggesting that publication bias is unlikely to be a major threat to the validity of this outcome.

IV. DISCUSSION

A. Summary of Main Findings and Interpretation

This systematic review and meta-analysis provides strong, evidence-based support for the integration of nurse-led precision interventions into the care pathway for patients undergoing ART. Our primary finding is that these individualized interventions significantly increase the likelihood of achieving a clinical pregnancy (RR = 1.37). This positive effect suggests that tailored care, which addresses specific patient-centric barriers (e.g., personalized stress management, targeted diet advice, and mental health support), effectively supplements the standard medical protocol.

Crucially, the beneficial effect on reproductive outcomes is paralleled by significant improvements in psychological well-being (SMD = 0.45) and favorable modulation of immunological markers (SMD = 0.51). This simultaneous positive impact across clinical, psychological, and immunological domains supports the psychoneuroimmunological hypothesis [4]. By reducing stress and improving emotional resilience, precision nursing appears to mitigate the adverse effects of stress hormones and pro-inflammatory cytokines, which are known to be detrimental to endometrial receptivity and embryo implantation [5]. The substantial heterogeneity in psychological and immunological outcomes was largely explained by subgroup analysis, which underscored the superiority of multi-component interventions (counseling + lifestyle + stress management), suggesting that a holistic, personalized approach is key to clinical efficacy.

B. Comparison with Previous Literature

Our findings align with earlier systematic reviews that have pointed to the general benefits of psychosocial interventions in ART [10]. However, this study uniquely focuses on the precision and nurse-led aspects, distinguishing the effectiveness of a highly individualized, integrated approach from generic psychosocial support. The significant pooled effect on CPR is a stronger and more definitive finding than reported in many prior meta-analyses, which often found only marginal or non-significant effects on pregnancy rates [11]. This difference may be attributed to the inclusion of more contemporary studies that specifically utilize precision-based diagnostics and interventions (e.g., biomarker-guided counseling), which represent a higher standard of care than historical generic counseling.

C. Implications for Clinical Practice and Policy

The evidence generated here has immediate and profound implications for clinical practice:

Protocol Integration: ART centers should integrate formalized, nurse-led precision intervention protocols. These protocols should extend beyond basic education to include

personalized psychological screening and management, and individualized lifestyle coaching.

Resource Allocation: Investment in specialized training for fertility nurses is warranted to equip them with the advanced skills necessary to deliver tailored interventions (e.g., cognitive behavioral techniques, motivational interviewing, health coaching).

Holistic Care Standard: The findings establish a new standard of care, recognizing that optimal ART outcomes are achieved when clinical, psychological, and immunological factors are addressed via a unified, personalized strategy.

D. Strengths and Limitations

Strengths: This review adhered strictly to the PRISMA 2020 guidelines and utilized the Cochrane RoB tool, maximizing methodological rigor. The inclusion of three distinct outcome domains (fertility, psychological, immunological) provides a holistic and powerful narrative of the interventions' efficacy. The use of a random-effects model accounts for anticipated clinical and methodological heterogeneity.

E. Limitations:

Heterogeneity: Substantial heterogeneity was observed in psychological and immunological outcomes, likely due to the variety of intervention components and measurement instruments used. While subgroup analysis was informative, residual heterogeneity remains a consideration.

Blinding: Due to the behavioral nature of the interventions, complete blinding of participants and intervention providers was impossible, potentially introducing performance bias, although most RCTs had low overall risk of bias.

Live Birth Rate: Data for LBR was marginally non-significant, suggesting that while clinical pregnancy is improved, the long-term impact on a live baby needs further investigation and larger sample sizes.

F. Recommendations for Future Research

Future research should focus on:

Mechanism-Based Trials: Trials should explicitly test the mechanisms of action, for example, by correlating specific changes in immunological biomarkers with subsequent clinical pregnancy outcomes.

Cost-Effectiveness: Studies are needed to assess the long-term cost-effectiveness of implementing comprehensive precision nursing programs.

Standardized Reporting: Future trials must adopt standardized reporting metrics, especially for psychological

and immunological outcomes, to reduce heterogeneity and strengthen future meta-analyses.

V. CONCLUSION

This systematic review and meta-analysis of 18 studies unequivocally supports the effectiveness of nurse-led precision interventions in ART. These individualized strategies significantly enhance reproductive success by increasing the clinical pregnancy rate, substantially improve the patient's psychological health, and beneficially modulate key inflammatory immune responses. These findings position precision nursing as an indispensable component of modern ART care, warranting its incorporation into global clinical protocols to optimize patient experience and outcomes.

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