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Review on Emerging Diagnostic and Therapeutic Approaches for Improving Fertility Outcomes in Men and Women

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ABSTRACT

***Background**: Infertility is a prevalent global health issue, affecting a significant portion of the reproductive-aged population and driving a continuous demand for more effective interventions. While assisted reproductive technologies (ART) like in vitro fertilization (IVF) are well-established, their success rates have plateaued, necessitating a critical exploration of novel diagnostic and therapeutic approaches to improve outcomes for infertile couples. **Objective**: This narrative review aims to synthesize and evaluate the current evidence on emerging diagnostic tools and treatment strategies designed to enhance fertility outcomes in both men and women, providing a comprehensive overview of the evolving landscape of reproductive medicine. **Main Discussion Points**: The review thematically explores several key areas of innovation, including advanced molecular diagnostics for male factor infertility, such as sperm DNA fragmentation testing, and innovative sperm selection techniques for ICSI. It further examines the transformative role of artificial intelligence in embryo selection, the refined applications and ongoing controversies surrounding preimplantation genetic testing for aneuploidy (PGT-A), and novel therapeutic targets like the endometrial microbiome and receptivity. A critical analysis highlights the limitations of the existing literature, noting issues such as small sample sizes, a lack of large randomized controlled trials, and heterogeneity in outcome measures that currently temper the widespread adoption of these technologies. **Conclusion**: The field of reproductive medicine is rapidly advancing towards a more personalized paradigm. However, the evidence supporting many emerging technologies remains variable and often inconclusive. A cautious, evidence-based approach to their clinical integration is recommended, coupled with a clear need for more rigorous, long-term studies to validate their efficacy and safety, ultimately ensuring they deliver meaningful improvements in live birth rates*

Keywords
Infertility, Assisted Reproductive Technologies, Sperm DNA Fragmentation, Artificial Intelligence, Preimplantation Genetic Testing, Endometrial Receptivity

INTRODUCTION

Infertility represents a significant and often deeply personal global health challenge, affecting a substantial portion of the reproductive-aged population and carrying profound medical, social, and psychological implications. Defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse, infertility is estimated by the World Health Organization to affect millions of couples worldwide, with recent data suggesting a lifetime prevalence of approximately 17.5% (1). This condition is not gender-specific; nearly half of all infertility cases can be attributed to male factors, including conditions such as oligospermia, asthenospermia, or genetic abnormalities, while female factors, such as tubal pathologies, endometriosis, and ovulatory disorders, account for another significant portion, with the remainder being either combined or unexplained in origin (2). The desire to conceive is a fundamental aspect of life for many individuals, and the inability to do so can lead to considerable emotional distress, social stigma, and a diminished quality of life, thereby underscoring the critical need for effective and accessible interventions. The foundational pillars of fertility management have, for decades, revolved around a standardized suite of diagnostic procedures and treatment modalities. In the diagnostic realm, this has traditionally included semen analysis for the male partner, which, while informative, provides a limited snapshot of sperm concentration, motility, and morphology, often failing to capture functional deficiencies at a molecular level. For women, standard workups involve assessment of ovarian reserve via hormonal profiling, hysterosalpingography to evaluate tubal patency, and ultrasonographic monitoring of folliculogenesis (3). Therapeutically, the landscape has been dominated by controlled ovarian stimulation, intrauterine insemination, and the various iterations of in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI).

Although these Assisted Reproductive Technologies (ART) have yielded remarkable successes and have become a mainstay of clinical practice, their limitations are increasingly apparent. Success rates, often measured in terms of live birth rates per cycle, have plateaued in many regions, hovering around 20-30% for women under 35, with significant declines associated with advanced maternal age (4).

Furthermore, these treatments are often associated with high financial costs, significant psychological burden, and potential medical risks such as ovarian hyperstimulation syndrome, highlighting an urgent need for more refined, efficient, and patient-specific approaches. This plateau in therapeutic efficacy is, in part, a consequence of the diagnostic inadequacies of conventional methods. The field is now recognizing that a deeper, more nuanced understanding of gamete and embryo physiology is required to break through existing barriers. Consequently, the past several years have witnessed a paradigm shift towards the exploration and integration of novel diagnostic tools and therapeutic strategies that operate at the molecular and cellular levels. In the male infertility domain, for instance, there is a growing move beyond the standard semen analysis towards advanced sperm function tests. Techniques such as sperm DNA fragmentation testing, which assesses the integrity of the paternal genetic material, are gaining traction as strong predictors of embryo quality and pregnancy outcomes, even in men with normal standard semen parameters (5). Similarly, the development of oxidative stress assays allows for the identification of a reversible cause of sperm damage, opening avenues for targeted antioxidant therapies prior to ART cycles. These advanced diagnostics promise a more etiologic understanding of male factor infertility, moving from a descriptive to a functional diagnosis. Parallel to these advancements in male infertility, the female diagnostic arena is being revolutionized by multi-omics technologies and enhanced imaging. Genomic sequencing, particularly next-generation sequencing for preimplantation genetic testing for aneuploidies (PGT-A), has become more accessible, allowing for the selection of euploid embryos and potentially improving implantation rates while reducing miscarriage risks in selected patient populations (6). Proteomic and metabolomic analyses of endometrial fluid and embryo culture media are being investigated as non-invasive methods to assess endometrial receptivity and embryo viability, potentially offering a real-time window into the critical window of implantation.

Furthermore, artificial intelligence (AI) and machine learning algorithms are beginning to be applied to vast datasets, including time-lapse imaging of embryo development, to identify subtle morphological patterns that correlate with developmental potential, thereby offering an objective and automated tool for embryo selection that may surpass traditional morphological grading (7). These emerging diagnostic modalities collectively represent a move towards a more personalized and precise medicine approach in reproductive care. The therapeutic landscape is evolving with equal fervor, driven by insights gleaned from these sophisticated diagnostics. In male infertility, the therapeutic nihilism that once prevailed is being replaced by innovative interventions. Techniques like magnetic-activated cell sorting (MACS) and intracytoplasmic morphologically selected sperm injection (IMSI) aim to select spermatozoa with superior structural and genetic integrity for use in ICSI. Moreover, the concept of treating the male to improve reproductive outcomes is being revitalized with the exploration of novel antioxidants, hormonal manipulations, and even the potential application of gene editing technologies to correct specific inherited defects in spermatogenesis (8). For female infertility, therapeutic innovation is focusing on optimizing the endometrial environment. Endometrial receptivity arrays, which generate a molecular signature to identify the personalized window of implantation, are guiding the timing of embryo transfer in frozen cycles. Immunological therapies, such as the use of intralipid infusions or corticosteroids in cases of suspected immune-mediated implantation failure, are also being actively investigated, albeit with ongoing debate regarding their efficacy (9). Perhaps one of the most groundbreaking frontiers is the emergence of in vitro gametogenesis (IVG) and mitochondrial replacement therapy, which, though still largely experimental, hold the potential to create gametes from somatic cells and prevent the transmission of mitochondrial DNA diseases, respectively.

Despite this rapid proliferation of research and technological promise, the evidence base for many emerging approaches remains fragmented, inconsistent, and sometimes controversial. The clinical integration of new tools like PGT-A and sperm DNA fragmentation testing is accompanied by vigorous debate regarding their true additive value, cost-effectiveness, and appropriate patient selection criteria. Similarly, many novel therapeutic strategies are supported by small, single-center studies or lack the robust validation from large-scale randomized controlled trials necessary to guide widespread clinical practice. This creates a significant knowledge gap for clinicians and researchers seeking to navigate this complex and rapidly shifting terrain. There is a clear need for a synthesized and critical appraisal of the current evidence to distinguish between genuine scientific advancement and premature clinical application. Therefore, the primary objective of this narrative review is to comprehensively explore and synthesize the current evidence on novel diagnostic tools and treatment strategies aimed at enhancing fertility outcomes in both men and women. The scope of this review will encompass key emerging areas, including advanced sperm and oocyte assessment techniques, AI in embryo selection, molecular diagnostics for endometrial receptivity, and innovative therapeutic interventions ranging from sperm selection methods to targeted immunomodulation. By critically evaluating the benefits, limitations, and future directions of these approaches, this review aims to provide a consolidated resource that can inform clinical decision-making, highlight areas requiring further investigation, and ultimately contribute to the advancement of a more effective, personalized, and evidence-based paradigm in reproductive medicine.

THEMATIC DISCUSSION

1. Advanced Molecular Diagnostics in Male Infertility

The evaluation of male infertility is undergoing a profound transformation, moving beyond the conventional semen analysis to embrace a new era of molecular diagnostics. The limitations of standard parameters are well-documented, as they often fail to explain cases of idiopathic infertility or reliably predict outcomes in assisted reproduction. In response, the focus has shifted towards assessing the functional competence of spermatozoa, particularly the integrity of their nuclear material. Sperm DNA fragmentation (SDF) has emerged as a critical biomarker, with a growing body of evidence linking high SDF levels to impaired fertilization, poor embryo quality, increased miscarriage rates, and reduced live birth rates following both natural conception and ART (5). Techniques like the sperm chromatin structure assay (SCSA) and terminal deoxynucleotidyl transferase dUTP nick end labelling (TUNEL) are now utilized in clinical settings to identify males who may benefit from targeted interventions, even when their semen analysis appears unremarkable.

The clinical utility of SDF testing, however, is not without controversy. While numerous meta-analyses confirm its negative correlation with pregnancy outcomes, the establishment of a universal, clinically applicable threshold for intervention remains elusive. Discrepancies between different testing methodologies contribute to this challenge, making it difficult to standardize results across laboratories (10). Furthermore, the question of how to best manage patients with elevated SDF is an area of active investigation. Although strategies such as testicular sperm

aspiration—which retrieves spermatozoa that have undergone less oxidative damage—and the use of oral antioxidants are commonly employed, robust evidence from large-scale randomized controlled trials (RCTs) to definitively support one approach over another is still needed. This gap highlights the transition of SDF from a research tool to a clinical parameter that requires further refinement for optimal integration into patient care pathways.

2. Innovations in Sperm Selection for Assisted Reproduction

Parallel to advancements in diagnostics, significant innovation has occurred in the realm of therapeutic sperm selection during ICSI, a procedure pivotal for treating severe male factor infertility. The conventional method of selecting sperm based on morphology and motility under high magnification (up to 400x) is now being superseded by more sophisticated technologies. Intracytoplasmic morphologically selected sperm injection (IMSI), which employs high-magnification (over 6000x) microscopy to examine sperm vacuoles and organelle integrity, was initially met with enthusiasm. Some studies suggested that avoiding sperm with large vacuoles could lead to improved embryo development and reduced miscarriage rates (11). However, more recent and methodologically rigorous RCTs have tempered this optimism, reporting no significant difference in live birth rates between IMSI and standard ICSI, thereby questioning the cost-effectiveness and added clinical value of this more labor-intensive technique.

In contrast, physiological sperm selection methods are gaining traction based on a more biologically relevant premise. The PICSI (Physiological ICSI) technique involves selecting spermatozoa that bind to hyaluronic acid, a major component of the oocyte's extracellular matrix. This binding is indicative of sperm maturity, plasma membrane integrity, and lower rates of aneuploidy and DNA fragmentation. A systematic review and meta-analysis concluded that PICSI is associated with a significant reduction in the rate of miscarriage, though a corresponding significant increase in live birth rate has been more difficult to consistently demonstrate (12). Another promising technology is sperm selection based on surface charge using electrophoretic separation. This method efficiently isolates sperm with lower levels of DNA damage and has shown promise in improving pregnancy rates in some studies, though its adoption into routine practice awaits further validation (13). The evolution of sperm selection strategies underscores a broader shift towards selecting functionally superior gametes, even if the most clinically effective and efficient methodology is still being defined.

3. The Role of Artificial Intelligence in Embryo Selection

One of the most dynamic and rapidly evolving frontiers in reproductive medicine is the application of artificial intelligence (AI) to embryo selection. The subjective nature of traditional morphological embryo grading has long been recognized as a limitation in optimizing IVF success. Time-lapse imaging systems provided the first major step forward by allowing uninterrupted observation of embryo development and the identification of dynamic morphokinetic markers. Now, AI and deep learning algorithms are being trained on vast datasets of time-lapse images and corresponding clinical outcomes to identify complex, often subvisual, patterns that correlate with implantation potential. These systems can provide a standardized, objective, and continuous assessment of embryo quality, potentially outperforming even experienced embryologists in predicting blastocyst formation and pregnancy likelihood (14).

The potential benefits of AI are multifold: reducing inter-observer variability, automating the labor-intensive process of embryo assessment, and potentially identifying the single best embryo for transfer with higher precision. This could directly contribute to increasing the efficiency of single embryo transfer (SET) policies, thereby reducing the risks associated with multiple pregnancies. Nevertheless, the integration of AI into clinical practice is accompanied by significant challenges. A primary concern is the "black box" nature of some complex algorithms, where the specific morphological features driving the selection decision are not transparent to the clinician, potentially raising ethical and medico-legal questions (15). Furthermore, the generalizability of AI models trained on specific patient populations and using particular laboratory equipment to other, more diverse clinical settings requires extensive external validation. As these technologies mature, the focus will shift from proving their predictive accuracy to establishing robust clinical workflows and addressing the ethical implications of algorithmic decision-making in human reproduction.

4. Preimplantation Genetic Testing: Refinements and Controversies

Preimplantation genetic testing for aneuploidies (PGT-A) has been one of the most widely adopted and debated innovations in reproductive medicine over the past decade. The fundamental premise of PGT-A is to identify and transfer only euploid embryos, thereby increasing implantation rates per transfer and reducing miscarriage rates. The technology itself has evolved significantly from fluorescence in situ hybridization (FISH) to comprehensive chromosome screening using next-generation sequencing (NGS), which provides a full karyotype of the embryo from a trophectoderm biopsy. There is a general consensus that PGT-A is most beneficial for specific patient groups, such as women of advanced maternal age and those with a history of recurrent implantation failure or recurrent pregnancy loss, where the prevalence of embryonic aneuploidy is high (16).

Despite its widespread use, PGT-A remains a subject of intense controversy. Critics point to large, well-designed RCTs, such as the STAR trial, which failed to show a significant improvement in cumulative live birth rates in a general IVF population when compared to morphology-based selection without PGT-A (17). The procedure carries inherent limitations, including the cost of genetic analysis, the technical skill required for biopsy, and the biological concern of embryo mosaicism—where the biopsied cells may not be fully representative of the entire embryo, potentially leading to the discarding of viable embryos. The ongoing debate forces clinicians to carefully weigh the potential benefit of a higher implantation rate per transfer against the possibility of no improvement in the ultimate goal of a take-home baby per cycle started, and to engage in thorough patient counseling about the realistic expectations, limitations, and financial implications of this technology.

5. Novel Therapeutic Avenues: From the Endometrium to the Microbiome

Therapeutic innovation is increasingly looking beyond the gametes and embryo to the maternal environment, particularly the endometrium. The concept of the "window of implantation" (WOI) has been revolutionized by the endometrial receptivity array (ERA), a molecular diagnostic tool that uses transcriptomic analysis to determine whether an endometrium is receptive or non-receptive at the time of biopsy. The premise of personalized embryo transfer (pET), timed according to the ERA result, is particularly appealing for patients with recurrent implantation failure

(RIF). Initial studies reported promising increases in pregnancy rates in this challenging patient subgroup when the transfer was personalized based on a displaced WOI (18). However, more recent large-scale RCTs have failed to demonstrate a significant benefit of ERA-guided pET over conventional timing in unselected RIF populations, suggesting its utility may be confined to a very specific, yet-to-be-clearly-defined subset of patients.

Simultaneously, the role of the endometrial microbiome in implantation is an area of burgeoning research. The traditional view of the uterine cavity as a sterile environment has been overturned, with studies using sophisticated molecular techniques revealing the presence of a unique microbial community. A pivotal finding has been the association of a non-Lactobacillus-dominated endometrial microbiome with significantly decreased implantation, pregnancy, and live birth rates (19). This has sparked interest in therapeutic modulation of the endometrial microbiome, potentially through the use of probiotic or antibiotic regimens. However, the field is still in its infancy, with questions regarding the optimal timing for sampling, the definition of a "healthy" microbiome, and the efficacy of interventional strategies remaining largely unanswered. These emerging themes highlight a critical expansion of the diagnostic and therapeutic focus towards a more holistic, system-wide understanding of the factors governing reproductive success.

Critical Analysis and Limitations

While the reviewed literature on emerging fertility diagnostics and therapeutics paints a picture of a rapidly advancing field, a critical analysis reveals significant limitations that temper the enthusiasm for immediate and widespread clinical application. A predominant issue across many studies, particularly those investigating novel sperm selection techniques like PICSI or electrophoretic separation and those exploring the endometrial microbiome, is the reliance on small sample sizes and a notable scarcity of large, multi-center randomized controlled trials (RCTs). These methodological constraints inherently limit the statistical power and increase the risk of type II errors, where a truly beneficial effect may be missed. For instance, while some meta-analyses on PICSI suggest a reduction in miscarriage, the individual studies pooled are often underpowered to detect a significant difference in the ultimate outcome of live birth, leading to clinical uncertainty (12, 13). Furthermore, many trials exhibit short follow-up durations, primarily reporting on early pregnancy outcomes without long-term data on the health of children born from these advanced technologies, which remains a critical gap in the safety profile of interventions like AI-driven embryo selection or PGT-A.

The methodological robustness of existing research is further compromised by various forms of bias. Selection bias is a pervasive concern, as many studies are conducted in single, academically affiliated tertiary care centers with patient populations that may not be representative of the broader infertile community. This limits the generalizability of findings to different ethnicities, socioeconomic groups, or less specialized clinical settings. Performance and detection bias are also frequent limitations, as blinding is often challenging or impossible in trials comparing intricate laboratory techniques like IMSI to conventional ICSI, potentially influencing both embryologists' and patients' expectations (2).

In the realm of diagnostic tests, such as the endometrial receptivity array (ERA), a critical limitation lies in the lack of a universally accepted gold standard for defining a displaced window of implantation, making validation circular and dependent on the very pregnancy outcomes the test is meant to predict (19). This fundamental methodological issue complicates the interpretation of both positive and negative trial results. Publication bias presents another substantial threat to the validity of the collective evidence. There is an inherent tendency for journals to publish studies with positive findings, while those demonstrating no significant benefit for a new and expensive technology, such as certain RCTs on PGT-A and ERA, may remain in the file drawer or face greater difficulty in publication (18). This skews the literature, creating an inflated perception of efficacy that does not align with the more nuanced reality. When systematic reviews and meta-analyses are conducted, they may consequently overestimate the true effect size of an intervention if negative studies are missing from the pooled analysis. This creates a challenging environment for clinicians and guideline-developing bodies who strive to make evidence-based recommendations. Adding to the complexity is the considerable heterogeneity in how studies define and measure success. The primary outcome of "live birth rate" is the most clinically relevant endpoint, yet many studies, often due to funding constraints or short timelines, resort to reporting surrogate markers such as implantation rate, blastulation rate, or reduction in DNA fragmentation index. While these biomarkers are mechanistically interesting, their correlation with a sustained live birth is not always linear or guaranteed. For example, a significant reduction in sperm DNA fragmentation following antioxidant therapy does not invariably translate into a proportional increase in the chance of a couple achieving a live birth (2).

This variability in outcome reporting makes direct comparisons between studies arduous and meta-analyses less reliable. Similarly, in AI research for embryo selection, different algorithms are trained on different datasets with varying outcome labels (e.g., blastulation vs. implantation vs. euploidy), making it nearly impossible to perform a head-to-head comparison of different AI systems (15). The field would benefit immensely from the widespread adoption of a core outcome set for infertility research to ensure consistency and clinical relevance. Finally, the generalizability of many groundbreaking findings is highly questionable. The data driving the development of AI models for embryo selection are often derived from specific patient cohorts using particular culture media and time-lapse incubators, raising concerns about how these algorithms will perform in external validation across diverse laboratory conditions and patient populations (14, 15). The same applies to the emerging data on the endometrial microbiome; initial seminal studies have defined a "dysbiotic" state, but what constitutes a healthy microbiome may vary across different geographical and ethnic populations, and the efficacy of any potential intervention to modulate it remains largely unknown (19). In conclusion, while the trajectory of innovation in reproductive medicine is undoubtedly promising, the current evidence base is marred by methodological limitations, biases, and inconsistencies that necessitate a cautious and critical approach. Future research must prioritize large, pragmatic RCTs with live birth as the primary outcome, strive for greater methodological rigor including blinding where feasible, and ensure that the exciting promise of these novel tools is validated in real-world, diverse clinical settings before they become the standard of care.

Implications and Future Directions

The synthesis of current evidence on emerging fertility technologies carries profound implications for the contemporary clinical practice of reproductive medicine. For the clinician at the frontline, these advancements necessitate a shift from a one-size-fits-all approach to a more nuanced, personalized strategy. The findings suggest that while tools like sperm DNA fragmentation testing and the endometrial receptivity array may not be warranted for all patients, they hold significant value in specific clinical scenarios, such as unexplained infertility or recurrent implantation failure (2, 19). This calls for a more discerning use of diagnostics, where tests are ordered based on a patient's unique history and clinical profile rather than as a blanket protocol. Therapeutically, the evidence supporting physiological sperm selection methods like PICSI, particularly for

reducing miscarriage risk, implies that embryologists should consider integrating these techniques into laboratory practice for selected cases of male factor infertility (13). Conversely, the plateau in success rates with some technologies, such as IMSI, underscores the importance of cost-effectiveness analyses in daily practice, steering resources towards interventions with more robust evidence. Ultimately, the most immediate implication is the paramount need for thorough and balanced patient counseling. Practitioners must communicate not only the potential benefits of these novel tools but also their limitations, controversies, and financial costs, enabling couples to make truly informed decisions in the context of their individual values and circumstances. From a broader perspective, these clinical implications directly inform policy and guideline development. The current landscape, characterized by rapid commercialisation and variable evidence, creates an environment where practice patterns can diverge significantly. Professional societies and health technology assessment bodies face the critical task of developing clear, evidence-based guidelines to standardize care and prevent the premature adoption of technologies whose clinical and cost-effectiveness remains unproven. For instance, the conflicting data on PGT-A strongly indicates that policy statements should clearly delineate the specific patient subgroups for which its use may be considered, rather than endorsing its application across the general infertility population (19). Similarly, the emergence of AI in embryo selection presents a new frontier for regulatory bodies, who must establish frameworks for the clinical validation and ongoing monitoring of these algorithm-based tools to ensure their safety and efficacy (17). The development of such policies must be dynamic, capable of evolving alongside the evidence base, and should explicitly address the issue of financial coverage, as out-of-pocket costs can create significant disparities in access to these advanced technologies.

To build a more robust evidence base that can reliably guide both practice and policy, future research must be strategically directed towards the most pressing unanswered questions. A primary gap lies in understanding the long-term health outcomes of offspring conceived through these novel interventions. While techniques like AI selection or electrophoretic sperm sorting aim to choose the most viable gametes and embryos, longitudinal studies tracking the cardiometabolic, neurological, and developmental health of these children are imperative (14, 15). Furthermore, the biological mechanisms underlying many of these technologies require deeper investigation. For instance, a clearer understanding of why a non-Lactobacillus-dominated endometrial microbiome is associated with implantation failure could reveal more targeted therapeutic approaches beyond broad-spectrum antibiotics (19). The role of the sperm epigenome and its influence on embryonic development and long-term health is another fertile area for exploration, potentially opening entirely new diagnostic and therapeutic avenues in male fertility. Addressing these complex questions will require a concerted effort to implement superior study designs. The field has an urgent need for large, multi-center, pragmatic randomized controlled trials that are adequately powered to detect differences in the most patient-centered outcome: sustained live birth. These trials should prioritize head-to-head comparisons of emerging technologies against current standard practices and should be designed with longer follow-up periods to capture not only initial pregnancy success but also the health of the resulting children. For diagnostic tools, future studies must focus on validating biomarkers against clinical outcomes rather than other intermediary laboratory parameters, and should rigorously assess their impact on clinical decision-making and patient prognosis (2). Given the personalized nature of infertility, research methodologies should also evolve to incorporate principles of precision medicine. This could involve using adaptive trial designs or machine learning on large, multi-modal datasets to identify which specific patient phenotypes are most likely to benefit from a given intervention, moving beyond the broad-stroke conclusions of past studies. By embracing these rigorous and forward-thinking approaches, future research can translate the promising potential of emerging fertility technologies into tangible, reliable, and equitable improvements in patient care.

CONCLUSION

In conclusion, this review underscores a period of significant transition in reproductive medicine, marked by the emergence of sophisticated diagnostic and therapeutic strategies that promise a more personalized approach to infertility care. The key findings reveal a field moving beyond traditional paradigms, with advanced sperm DNA integrity assessments, AI-driven embryo selection algorithms, and molecular analyses of endometrial receptivity and microbiome offering new avenues to understand and overcome barriers to conception. However, the strength of the evidence supporting the routine clinical application of these technologies is decidedly heterogeneous, often tempered by methodological limitations including small sample sizes, a lack of robust multi-center RCTs, and unresolved controversies regarding their true impact on the paramount outcome of live birth rates. Consequently, the most prudent recommendation for current clinical practice is a stance of cautious and selective adoption, where these novel tools are employed judiciously within well-defined patient subgroups rather than as universal panaceas, always coupled with comprehensive patient counseling that transparently addresses the existing uncertainties. The undeniable promise held by these innovations ultimately serves to reinforce an urgent call for more rigorous, longitudinal, and clinically focused research to solidify their role, ensure their safety, and fully realize their potential in improving fertility outcomes for the diverse population of individuals struggling to build their families.

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