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REVIEW ARTICLE

Advancing embryo selection in artificial intelligence-assisted reproductive technologies: A systematic review

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Abstract

For couples encountering infertility challenges, assisted reproductive technologies (ARTs) offer a path to parenthood. ART procedures, such as *in vitro* fertilization (IVF), intracytoplasmic sperm injection (ICSI), and embryo implantation, involve the handling of sperm or embryos outside the body. However, the success of ART depends on the accurate selection of viable embryos. Artificial intelligence (AI) is a promising tool with the potential to revolutionize these procedures. This review explores the transformative potential of AI in ART, providing valuable insights into enhanced embryo selection and unlocking new possibilities for the field. Four electronic databases were systematically searched under the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. From an initial pool of 914 papers, 30 studies were selected for further evaluation. While noting the limitations inherent in the existing body of research, this review offers a broad analysis of AI's transformative role in embryo selection. It highlights the significant potential of AI to enhance precision, consistency, and efficiency in ART. This review also emphasizes the importance of addressing technical, ethical, and regulatory aspects to ensure responsible and effective integration of these technologies. The findings indicate that AI-based models, such as the iDAScore v2.0, have demonstrated promising results in accurately predicting embryo viability and evaluating the effects of maternal age on embryo viability. Specifically, Bayesian network modeling, with an accuracy rate of 91.3%, aims to optimize IVF and ICSI procedures. In summary, AI stands at the forefront of innovation in ART, offering new hope through more accurate and efficient embryo selection.

Keywords: Artificial intelligence; Machine learning; Deep learning; Embryo selection; Assisted reproductive technologies

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1. Introduction

Once considered a private matter, infertility has become a globally recognized issue, affecting millions of couples worldwide. The burden of infertility has been increasing globally and regionally for both males and females. Infertility affects one in six adults worldwide, with higher rates reported in the Americas and the Western Pacific region.[1]

The global infertility rate has shown fluctuating trends over the past few decades. In high-income and developed countries, the prevalence of primary and secondary infertility has been decreasing, potentially due to greater access to infertility treatment facilities.[2] Assisted reproductive technologies (ARTs) hold promise for struggling couples with infertility. It can be a common approach to the problem in the future.[3,4]

ART techniques, such as intracytoplasmic sperm injection (ICSI) and *in vitro* fertilization (IVF), are frequently utilized to assist infertile couples in getting pregnant. The procedures involve the retrieval of eggs, laboratory fertilization with sperm, transfer of viable embryos into the uterus, and control of ovarian stimulation. The viability of ART is highly dependent on the quality of gametes and embryos, which are conventionally evaluated subjectively by embryologists based on morphological criteria.

Since the birth of Louise Brown, the first infant conceived through IVF, ART has undergone significant advancements aimed at reducing complications and improving outcomes.[5] The integration of artificial intelligence (AI) into ART holds great promise for enhancing outcomes. AI technologies, such as computer-assisted sperm analysis and machine learning (ML) algorithms, enable the objective evaluation of semen parameters and embryo quality. By standardizing evaluations and processing large volumes of data, AI has the potential to enhance treatment outcomes and increase conception rates.[6-8] However, despite its groundbreaking breakthroughs, only 30% of ART treatments result in conception, highlighting the necessity for more accurate predictive models.[9] As the process involves manipulating human gametes or embryos *in vitro*, ART outcomes are influenced by multiple complex factors, including the cause of infertility, age, hormonal profile, and laboratory conditions. Advanced technologies, such as AI and ML, are being explored to enhance prediction accuracy and decision-making in ART,[10] with promising results in predicting IVF cycle outcomes and guiding embryo selection.[11] These systems interpret data using image-based analysis to provide clinically relevant recommendations,[12] and AI models are also being developed to classify reproductive data, such as embryonic development and semen characteristics.[13] As[4,11-13] AI continues to demonstrate potential in improving diagnostic and therapeutic processes in reproductive medicine, its adoption in fertility clinics is likely to increase.[14] Nonetheless, challenges remain regarding the generalizability and standardization of AI applications in ART.[4]

This systematic review aims to identify and map the current landscape of research on embryo selection, focusing on advancements and innovations in AI-based ARTs. In Figure 1, the flow diagram depicts the integration of AI-based ART into the embryo selection process. Key input data include genetic profiles, historical success rates, and medical histories. Using deep learning and ML methods, AI systems analyze this data to predict embryo viability. Selected embryos are then processed using AI-based ART. Pregnancy outcomes are tracked, enabling continuous refinement and optimization of the AI systems. Ethical considerations and regulatory compliance are crucial at every stage of this process. This systematic review explores the following research queries (RQs):

- RQ1. What are the current state-of-the-art AI technologies used in embryo selection for ART?
- RQ2. To what extent does ART improve the pregnancy success rate and live birth outcomes compared to traditional methods?
- RQ3. How can AI algorithms be seamlessly integrated into existing embryo selection protocols and laboratory workflows to leverage the expertise of embryologists and healthcare professionals?
- RQ4. What is the impact of AI-driven embryo selection on the psychological health and decision-making processes of prospective parents, particularly in light of ethical concerns?
- RQ5. What are the primary barriers and limitations to the clinical application of AI algorithms in embryo selection, and how are these technologies being developed and validated?

2. Research methodology

This section outlines the research design and analytical procedures used in the present study.

2.1. Overview

According to McKenzie *et al.*,[15] a systematic review is a rigorous, structured method for identifying, evaluating, and synthesizing research evidence on a specific question using predefined protocols. It minimizes bias through comprehensive literature searches and transparent processes, often incorporating meta-analysis to quantitatively combine study findings. Consequently, this systematic review was conducted to investigate the technologies utilized in AI-guided embryo selection and to map the current landscape of advancements within ART.

2.2. Objectives

The key objectives of this systematic review include:

(i) To examine current AI applications in embryo selection and analyze the success rates of various ML models used in ART

(ii) To identify potential future improvements, innovations, and existing research gaps in the application of AI for embryo selection

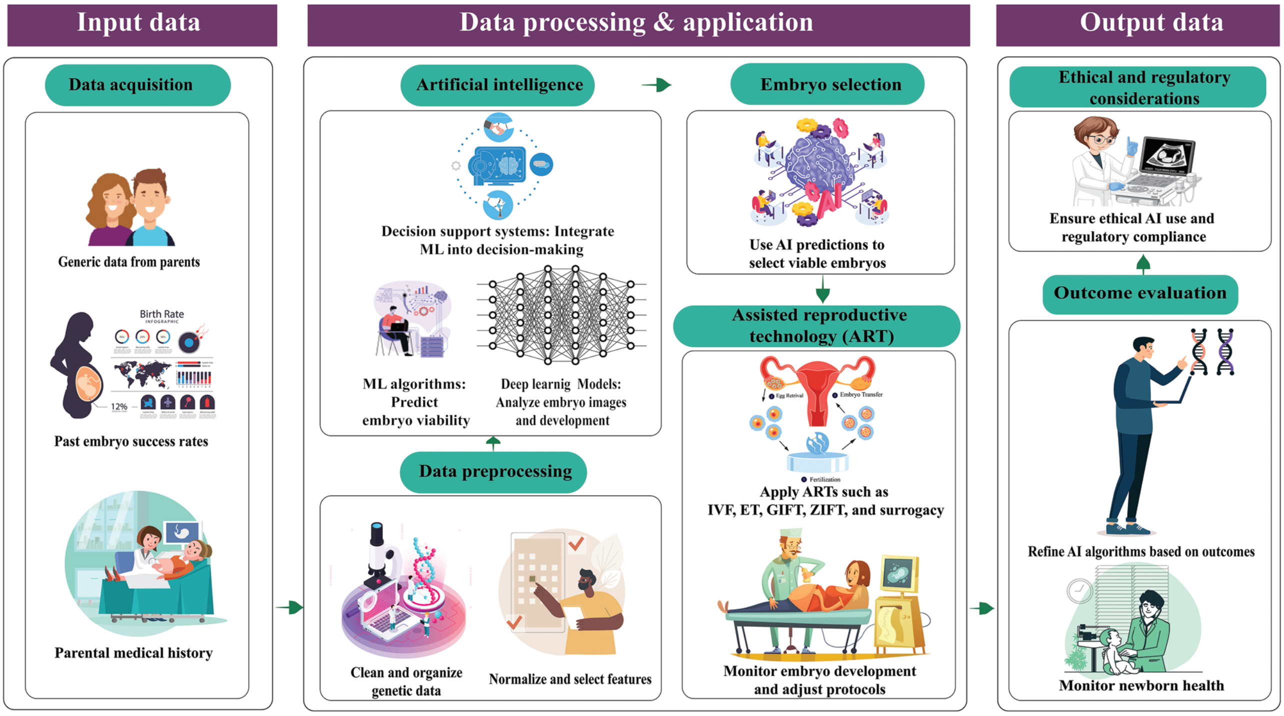

Figure 1. Flow diagram of artificial intelligence-based assisted reproductive technology

Abbreviations: ET: Embryo transfer; GIFT: Gamete intrafallopian transfer; IVF: *In vitro* fertilization; ML: Machine learning; ZIFT: Zygote intrafallopian transfer.

(iii) To investigate the ethical implications associated with the integration of AI in embryo selection processes.

2.3. Literature selection

This study strictly adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, including the extension for scoping reviews. Four electronic databases (Scopus, PubMed, IEEE Xplore, and Google Scholar) were systematically searched to identify relevant publications. The literature search was performed by three researchers (the authors) between December 2023 and April 2024. Duplicate entries were identified and removed using Python programming. The search results were initially compiled in an Excel file, ensuring the accuracy and uniqueness of the dataset for further analysis. Each researcher reviewed the titles and abstracts based on predefined inclusion and exclusion criteria to determine eligibility. In case of uncertainty or disagreement, a well-known academic expert was consulted to aid in the final selection of publications.

2.4. Inclusion criteria

Studies were included in this review if they met the following criteria:

(i) Studies that explore or utilize deep learning, ML, or AI to select embryos for ART
(ii) Studies that use rigorous research procedures and provide transparent data analysis and reporting
(iii) Research that tackles ethical considerations such as informed consent, data privacy, and societal implications associated with AI-based embryo selection
(iv) Studies that focus on AI applications specifically relevant to IVF techniques
(v) Publications including book chapters, conference proceedings, systematic reviews, meta-analyses, and peer-reviewed research articles are all covered
(vi) Research articles that primarily focused on human subjects
(vii) Articles published in the English language
(viii) Studies published between June 1, 2015, and January 9, 2024.

2.5. Exclusion criteria

Studies were excluded from this review if they met any of the following criteria:

(i) Studies not primarily focused on the use of AI for embryo selection or its role in ART
(ii) Studies lacking sufficient detail or clarity on the methods used for embryo selection
(iii) Research addressing ethical concerns that are unrelated to the application of AI in embryonic selection

(iv) Articles that do not meaningfully discuss AI application within IVF procedures
(v) Studies conducted on laboratory animals
(vi) Non-peer-reviewed sources, such as editorials, opinions, and non-scholarly articles
(vii) Studies not published in English; this is to ensure accessibility for analysis.

2.6. Search strategy

The search strings presented in Table 1 were used to identify all relevant articles and documents. Initially, the first search string was applied, yielding 56 results from Scopus, 98 from PubMed, and 3 from the IEEE Xplore database. Then, the search string was modified to achieve better results.

2.7. Study selection process

First, research questions were developed, followed by a search string. Three researchers (ABR, ASR, and AMS) performed the initial database search and removed duplicate entries. Two researchers (ASR and ABR) reviewed all collected abstracts using the inclusion and exclusion criteria. Senior researcher AMS assessed articles with disagreements to establish consensus on decisions.

2.8. Study selection and bias control

The selection approach utilized a combination of engineering and health science datasets to enhance reliability and minimize publication bias. Two researchers (ABR and ASR) reviewed the titles and abstracts to reduce selection bias, while senior researcher AMS meticulously analyzed a paper to identify errors and further mitigate bias.

3. Results

This section outlines the key findings and emerging patterns identified through the systematic review. It discusses the implications of these results by comparing them with previous research and highlighting recent developments in the field. Furthermore, the review examines any limitations encountered during the process and considers their potential influence on the outcomes.

3.1. Data overview

Between June 1, 2015, and January 9, 2024, two review writers (ASR and ABR) thoroughly searched across four databases: PubMed, Scopus, Google Scholar, and IEEE Xplore. A date restriction was applied to exclude outdated models from the early stages of AI development, ensuring the relevance of the technologies to the current AI landscape. The initial search yielded 656 articles from Scopus, 249 from PubMed, four from IEEE Xplore, and five from Google Scholar. After removing 85 duplicates using Microsoft Excel (Microsoft, United States of America [USA]), a total of 829 articles remained. Following a title and abstract screening, 789 articles were excluded, leaving 40 articles for eligibility assessment. Ten articles were subsequently excluded due to issues with data extraction, non-English language, lack of linkage with AI, or poor technical implementation. The study selection process is illustrated in Figure 2. Ultimately, 30 articles that met the inclusion criteria were retained for data extraction, as summarized in Table 2.

3.2. Risk of bias (RoB) assessment

The systematic review assessed the RoB in the included studies to evaluate the validity and reliability of the results. RoB was evaluated across multiple domains, such as selection bias, performance bias, detection bias, attrition bias, and reporting bias, using well-developed tools, such as the Cochrane RoB2 Tool for randomized controlled trials and the ROBINS-I tool for non-randomized studies. Most studies relied on retrospective data, which has the potential for bias due to the non-randomized selection of participants. For example, studies such as those by Theilgaard Lassen *et al.*[16] and Cimadomo *et al.*[17] employed internal validation methods, which limit generalizability. Meanwhile, several studies, such as those by Johansen *et al.*[18] and Bori *et al.*,[19] implemented AI models trained on time-lapse imaging data without clearly defined standard protocols. The absence of standardized protocols across clinics could have introduced heterogeneity in data collection and analysis, thereby affecting the results. In addition, in AI-based embryo selection, as seen in

Table 1. Keywords and search items

S. No.	Keywords and search items	Number of publications from database		
		Scopus	PubMed	IEEE Xplore
1.	((AI) AND (ART) AND (IVF))	56	98	3
2.	(((AI) OR (artificial intelligence) OR (machine learning) OR (deep learning)) AND ((embryo selection) OR (blastocyst transfer) OR (preimplantation genetic diagnosis)) AND ((assisted reproductive technologies) OR (in vitro fertilization) OR (Intracytoplasmic Sperm Injection) OR (Gamete Intrafallopian Transfer) OR (Zygote Intrafallopian Transfer))) AND ((precision medicine) OR (predictive algorithms) OR (prognosis)))	656	249	4

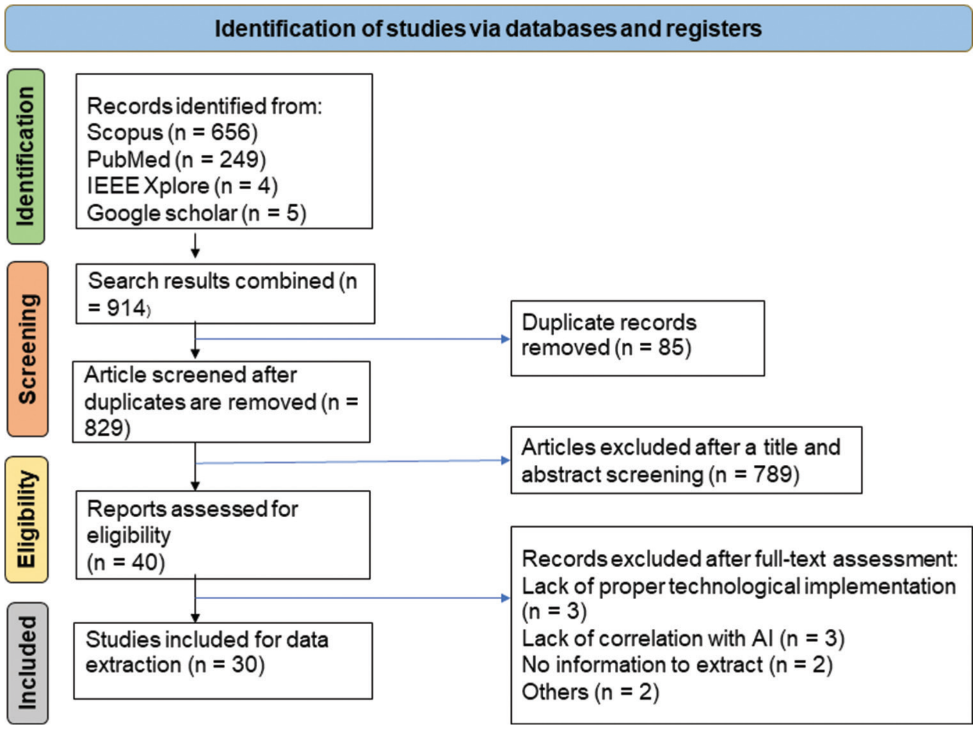

Figure 2. Flow diagram illustrating the study selection process in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses
Abbreviation: AI: Artificial intelligence.

Table 2. Bibliometric characteristics of the included studies

Characteristics	Corresponding entities	Numbers	Percentages
Publication year	2015 – 2018	1	3.33
	2019 – 2021	13	43.33
	2022 – 2024	16	53.33
Publication type	Article	23	76.67
	Review	5	16.67
	Conference proceeding	2	6.67
Quality of paper	Q1	16	53.33
	Q2	10	33.33
	Q3	1	3.33

studies by Glatstein *et al.*[20] and Salih *et al.*,[21] outcome assessors were frequently not blinded, increasing the risk of subjective determination regarding embryo viability and implantation success. Moreover, selective reporting was also an issue, with some studies failing to disclose limitations and adverse effects. For example, while Tian *et al.*[22] acknowledged the necessity for external validation, this aspect was not consistently addressed across other studies. Although the current review underscores promising progress in AI-driven embryo selection, the identified RoB highlights the need for future prospective, well-designed, and externally validated studies to confirm the reliability and generalizability of AI models in the clinical environment.

3.3. Bibliometric characteristics of the included studies

This systematic study suggests that incorporating engineering principles into the evaluation of online databases can enhance reliability and reduce publication bias. Three researchers carefully reviewed the titles and abstracts of the identified studies to reduce bias. In addition, an experienced academic expert reviewed the work to identify and address any potential inconsistencies or biases. As shown in Table 2, the selected publication types include 23 articles (77%), five review papers (17%), and two conference proceedings (6%). In terms of geographical distribution, the United Kingdom leads with 14 publications, followed by the USA (12), Switzerland (2), Japan (1), and Bosnia and Herzegovina (1).

3.4. Appraisal of the study quality

This systematic study suggests that incorporating engineering principles into online database searches can enhance reliability and reduce publication bias. Three researchers carefully reviewed the titles and abstracts of the identical studies to reduce bias. In addition, an experienced professional reviewed the work to identify and address any potential inconsistencies or biases.

Figure 3A illustrates the journal ranking of the chosen studies, showing a clear dominance of Q1 (16) and Q2 (10) journals, with a smaller representation from Q3 (1) and other categories (3). This distribution highlights a significant representation of high-quality articles in the selected literature. The dominance of Q1 and Q2 journals reflects the intent to prioritize sources known for rigorous peer-review procedures and credible academic contributions, thereby assuring the reliability of the findings. Meanwhile, Figure 3B presents the publication trends over the past decade. Notably, 25 of the selected papers were published in the past 3 years, indicating a recent increase in research efforts. In both 2022 and 2023, eight publications were published, exhibiting continuous productivity. Surprisingly, the highest point occurred in 2021 with nine publications, indicating a highly fruitful year for research in this domain.

3.5. Summary of the characteristics of the included studies

The current review thoroughly examined 30 academic publications that strictly adhere to formal academic guidelines. Each paper features a clear and distinct title and is authored by well-known researchers in the field. These articles included abstracts that briefly describe their goals, methodologies, and conclusions, as summarized in Table 3, and have been published in reputable journals and conferences. The research methods spanned surveys, case studies, and experimental studies. In addition to reporting empirical results, the current review also offers critical comments on methodological challenges, interpretative insights, and directions for further research.

3.6. Implications of the area under the curve (AUC) in embryo selection

In embryo selection algorithms, the term "area under the curve" refers to the area under the receiver operating characteristic curve, which helps in assessing the probability of successful implantation.[24] AUC is a useful statistic for evaluating the performance of embryo selection algorithms, but it has several limitations, such as its reliance on image quality, issues with generalizability, the impact of cultural conditions, sex-dependent performance, and limits related to sample size and research design. Even though AUC is frequently used to assess model performance in embryo selection, depending solely on it presents challenges due to sampling procedures and information transfer issues, which may affect the robustness and generalizability of the model. AUC provides a general measure of model performance across all thresholds but does not account for individual clinical contexts or specific requirements. Furthermore, it assumes that all misclassifications are equally important, whereas, in embryo selection, some misclassifications (e.g., false negatives) may have more severe consequences. In addition, AUC does not evaluate the calibration of predicted probabilities, which is a crucial requirement for decision-making. Thus, AUC should be complemented with additional measures and clinical judgment for a more comprehensive embryo assessment.[24,35-37]

3.7. Conventional study

Any process or therapy that involves manipulating oocytes (immature ova or egg cells) *in vitro* is referred to as ART for reproduction.[38] Couples and individuals experiencing fertility issues can benefit from this treatment option, which is characterized by individualized treatment protocols and multidisciplinary team management, both of which improve treatment outcomes and safety.[39] The field of traditional ART has significantly advanced over time. Techniques used in ART treatments include embryo

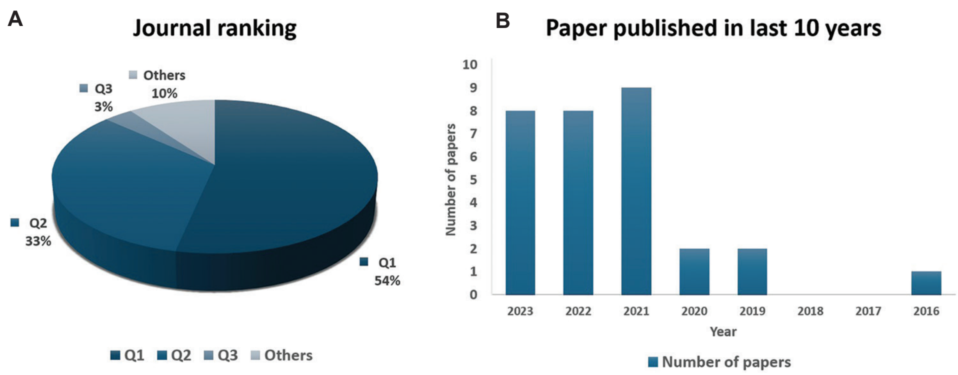

Figure 3. Quality appraisal of the included studies. (A) Ranking statistics of the journals selected for this study. (B) Number of published papers in the last 10 years.

Table 3. Summary of the characteristics of the included studies

References	Aim/research question	Dataset and data selection	Algorithm/methodology	Outcome measures	Evaluation and data processing limitations
Theilgaard Lassen *et al.*[16]	Rank embryos by likelihood of implantation	181,428 embryos from 22 IVF clinics worldwide (2011 – 2020)	Fully automated deep learning model (iDAScore v2.0)	AUC[a] range: 0.621 – 0.707; embryo ranking based on morphogenetic parameters	Only internal validation was performed; external validation is needed; there is a lack of details on sampling strategy, data imbalance, and cross-validation[c] procedures
Johansen *et al.*[18]	Assess maternal age's impact on embryo viability prediction[b]	4,805 fresh embryos from 4 clinics (2013 – 2022)	AI model based on time-lapse images with age-standardization	AUC[a] range: 0.58 – 0.69	Age density estimation may be unstable; insufficient description of sampling, data imbalance handling, and validation methods
Glatstein *et al.*[20]	Enhance embryo selection in IVF labs for improved pregnancy outcomes	The dataset is not explicitly specified	Combination of convolutional neural networks (CNN) and support vector machines	AUC[a] range: 0.63 – 0.83; some models report up to 90% accuracy	"Black box" nature of AI models; limited details on dataset selection, sampling, and cross-validation approaches
Salih *et al.*[21]	Compare the performance of AI versus that of embryologists in embryo selection	Data compiled from non-prospectively evaluated studies (2005 – 2022)	ML, deep learning, and neural networks	AI accuracy: 75.5% (range 59 – 94%) versus embryologist accuracy: 65.4% (range 47 – 75%)	Retrospective, non-clinical design; lacks explicit discussion on sampling methods, imbalance handling, and cross-validation techniques
Ueno *et al.*[23]	Evaluate the effect of increased training data on pregnancy prediction	3,960 SVBT cycles from a single Japanese clinic (2021 – 2022)	Deep learning models (iDA-V1 vs. iDA-V2) compared with Gardner grading	AUC[a]: 0.736 (iDA-V2), 0.720 (iDA-V1), and 0.702 (Gardner grading)	Retrospective design and single-center data limit generalizability; sampling details and handling of imbalance/cross-validation[c] are not fully described
Berntsen *et al.*[24]	Develop AI-based embryo selection using time-lapse images	115,832 embryos from 18 IVF centers worldwide (2011 – 2019)	Deep learning model implemented in Python/TensorFlow	AUC[a] of 0.67 for Sorted KID embryos; overall AUC reported as 0.95	No subgroup analysis for transferred euploid embryos; limited insight into data preprocessing, sampling, and validation methods
Chen *et al.*[25]	Predict the chromosomal status of blastocysts non-invasively	345 paired blastocyst culture mediums from 3 clinics in China (2017 – 2018)	Random forest ML model	Comparative clinical outcomes: A-/B-grade embryos like euploid ones; Grade C shows lower viability	Lacks a standardized threshold for CNV-based predictions; potential observer bias; minimal discussion on sampling and cross-validation[c]
Xi *et al.*[26]	Reduce IVF-associated multiple-embryo gestations	10,076 embryos from 9,211 patients at a single Chinese center (2016 – 2018)	Hierarchical model using XGBoost	AUC[a]: 0.7945 (SET), 0.8385 (DET pregnancy), 0.7229 (DET twin risk)	Single-center design limits generalizability; limited discussion on sampling strategy, imbalance handling, and cross-validation[c]
Ratna *et al.*[27]	Externally validate and update the McLernon models for live birth prediction	144,734 complete cycles from 91,035 women in the UK (2010 – 2016)	McLernon models updated via intercept adjustment, logistic recalibration, and revision	Improved agreement between live birth predictions and outcomes	High proportion of missing data and absent prior pregnancy details; limited discussion of sampling, imbalance, and cross-validation[c] practices

(Cont'd...)

Table 3. ***(Continued)***

References	Aim/research question	Dataset and data selection	Algorithm/methodology	Outcome measures	Evaluation and data processing limitations
Cimadomo *et al.*[17]	Validate iDAScore v1.0 for ranking blastocysts in PGT-A cycles	3,604 blastocysts and 808 euploid transfers from 1,232 cycles in Italy (2013 – 2022)	Deep learning model (iDAScore v1.0)	AUC[a]: 0.60 for euploidy prediction and 0.66 for live birth prediction	Retrospective design; need for randomized controlled trials; lacks details on data sampling, imbalance handling, and cross-validation
Diakiw *et al.*[28]	Predict embryo euploidy likelihood using blastocyst images	15,192 Day-5 blastocyst images from 10 IVF clinics (USA, India, Spain, Malaysia)	AI model trained on 2D microscope images with PGT-A metadata	Accuracy: 65.3%, sensitivity: 74.6%; AUC[a]: 0.68 (uncleaned), 0.87 (cleansed test dataset)	Predictive accuracy based solely on PGT-A outcomes; limited discussion on sampling, data imbalance, and cross-validation[c] processes
Bori *et al.*[19]	Predict embryo viability and grading via image analysis	Over 3,000 embryo images (Day 2 – 3)	CNN-based model deployed on Azure	Reported>85% improvement in success rate (accuracy boost)	Limited sample size; minimal details on sampling strategies, imbalance handling, and validation methods
Sawada *et al.*[29]	Develop a self-improving ML system (DynScore[d]) to predict ART embryo fate	Training: 891 embryos (110 couples); Global: 1,186 embryos (201 couples)	ML system using statistical tests (Kolmogorov–Smirnov, ANOVA, Chi-squared) to calculate DynScore[d]	AUC[a]: ~0.634 (training) and~0.638 (global) for blastocyst formation prediction	Small sample sizes; potential bias from the inclusion of failed ART cases; limited information on sampling, data imbalance, and cross-validation[c]
Cheredath *et al.*[30]	Conduct a SWOT analysis on human-versus ML-based embryo assessments in IVF	Varied datasets ranging from 16 to 11,898 embryos	Supervised learning approach in ML	General performance trends in IVF prediction noted (no specific quantitative metric)	Lacks detailed analysis of specific ML models and processing factors, such as sampling and validation methods
Patil *et al.*[31]	Provide an overview of prediction models in ART using varied feature sets	Dataset not specified	Various machine-learning techniques	Qualitative discussion on clinical decision support potential	No external validation or detailed impact analysis; minimal information on dataset selection, sampling, and cross-validation[c]
Giscard d'Estaing *et al.*[32]	Investigate AI's potential in reproductive medicine for infertility treatment	Dataset not specified	ML algorithms	Qualitative improvements in infertility diagnosis and ART outcomes (pregnancy/live birth rates)	Lack of standardized protocols and guidelines; limited description of data selection, sampling, and validation approaches
Zaninovic *et al.*[14]	Enhance implantation/live birth prediction via an updated ASEBIR scoring system	1,044 Day-5 blastocysts from 6 clinics in Spain (2017 – 2019)	Multivariable logistic regression analysis	AUC[a]: 0.90 (trophectoderm A vs. BC) and 0.89 (trophectoderm AB vs. C)	Limited number of blastocysts analyzed; insufficient detail on sampling strategies, data imbalance handling, and cross-validation[c]
Tian *et al.*[22]	Enhance IVF processes through automation and AI integration	Dataset not specified	Integrated automation and AI (including endometrial evaluation, cryopreservation, and gamete/embryo selection)	Qualitative discussion on improved accessibility, affordability, and reduced labor intensity	Lack of specific dataset details; minimal description of sampling, data imbalance management, and validation protocols

(Cont'd...)

Table 3. *(Continued)*

References	Aim/research question	Dataset and data selection	Algorithm/methodology	Outcome measures	Evaluation and data processing limitations
Kanakasabapathy *et al.*[33]	Predict viable embryos for transfer using shallow artificial networks	654 cycles from a French cohort (2013 – 2018)	Shallow artificial networks (MLP and simple RNN)	AUC[a]>0.8 in predicting embryo viability	Retrospective observational design introduces bias; limited discussion on sampling methods, data imbalance, and cross-validation[c]
Pons *et al.*[34]	Assess maternal age's impact on embryo viability prediction[b]	4,805 fresh embryos from 4 clinics (2013 – 2022)	AI model based on time-lapse images with age-standardization	AUC[a] range: 0.58 – 0.69	Age density estimation may be unstable; insufficient description of sampling, data imbalance handling, and validation methods

Notes: [a]The area under the curve (AUC) of an AI model measures its ability to distinguish between classes, with a higher AUC indicating better performance; [b]Embryo viability prediction is an approach in which AI models evaluate different characteristics of embryos to estimate their likelihood of successful implantation; [c]Cross-validation is a statistical technique used to assess the performance and generalizability of an ML model; [d]DynScore, also known as Dynamic Scoring, is a dynamic assessment measure that is utilized in fields such as bioinformatics, finance, or AI. Abbreviations: AI: Artificial intelligence; ANOVA: Analysis of variance; ART: Assisted reproductive technology; CNV: Copy number variation; DET: Day-5 embryo transfer; IVF: *In vitro* fertilization; ML: Machine learning; MLP: Multilayer perceptron; PGT-A: Preimplantation genetic testing for aneuploidy; RNN: Recurrent neural network; SET: Single embryo transfer; SVBT: Single-voxel brain tissue; SWOT: Strengths, weaknesses, opportunities, and threats; USA: United States of America.

transfer (ET), ICSI, and IVF.[11] These methods encompass the *in vitro* manipulation of human gametes or embryos for addressing genetic disorders or sub-fertility that impede spontaneous conception.[12] Nonetheless, conventional ART success rates can vary, and ART laboratories must continually strive for refinement and implement evidence-based practices.[13] Various frequently utilized ARTs are depicted in Figure 4, depending on the specific circumstance. These ARTs are elaborately discussed in the following section.

3.7.1. IVF

The IVF technique has significantly enhanced our understanding of fertilization processes in 11 mammalian species, including humans.[40] IVF is a medically assisted reproduction method that allows infertile couples to achieve a successful pregnancy.[41] It involves the retrieval of oocytes, which are then fertilized outside the body, with the resulting embryos cultured in a laboratory setting before being transferred into a woman's uterus.[42] An IVF cycle typically lasts for 4 – 6 weeks and begins with 10 – 14 days of hormonal stimulation to produce multiple eggs. Between days 12 and 16, mature eggs are retrieved and fertilized in the laboratory using either ICSI or conventional IVF. The resulting embryos are cultivated for 3 – 5 days before being transferred into a uterus. Two weeks later, a blood test is conducted to confirm pregnancy.[43] While the overall success rate remains relatively low, interventions such as hysteroscopy with local endometrial injury before ovarian stimulation can improve implantation and pregnancy rates in women with repeated IVF failure.[44] Successful ET requires careful preparation, including minimizing uterine contractions and placing the embryo approximately 2 cm below the uterine fundus for optimal pregnancy rates.[45]

3.7.2. ICSI

ICSI is an assisted reproduction technique that treats severe male-factor infertility. It entails inserting a single spermatozoon directly into the ooplasm of a mature egg. ICSI was established in the early 1990s and has since become a widely accepted treatment option for couples facing reproductive challenges due to male factors. The method overcomes potential hurdles to fertilization, allowing fertilization to occur even with compromised sperm parameters, such as low motility and aberrant morphology. However, there are concerns regarding the safety and long-term implications of ICSI, including an increased risk of sex chromosomal abnormalities and potential developmental issues in offspring conceived through this technique.[46] During the procedure, a physician injects sperm into an oocyte, and the resulting fertilized egg is then transferred into a woman's uterus for

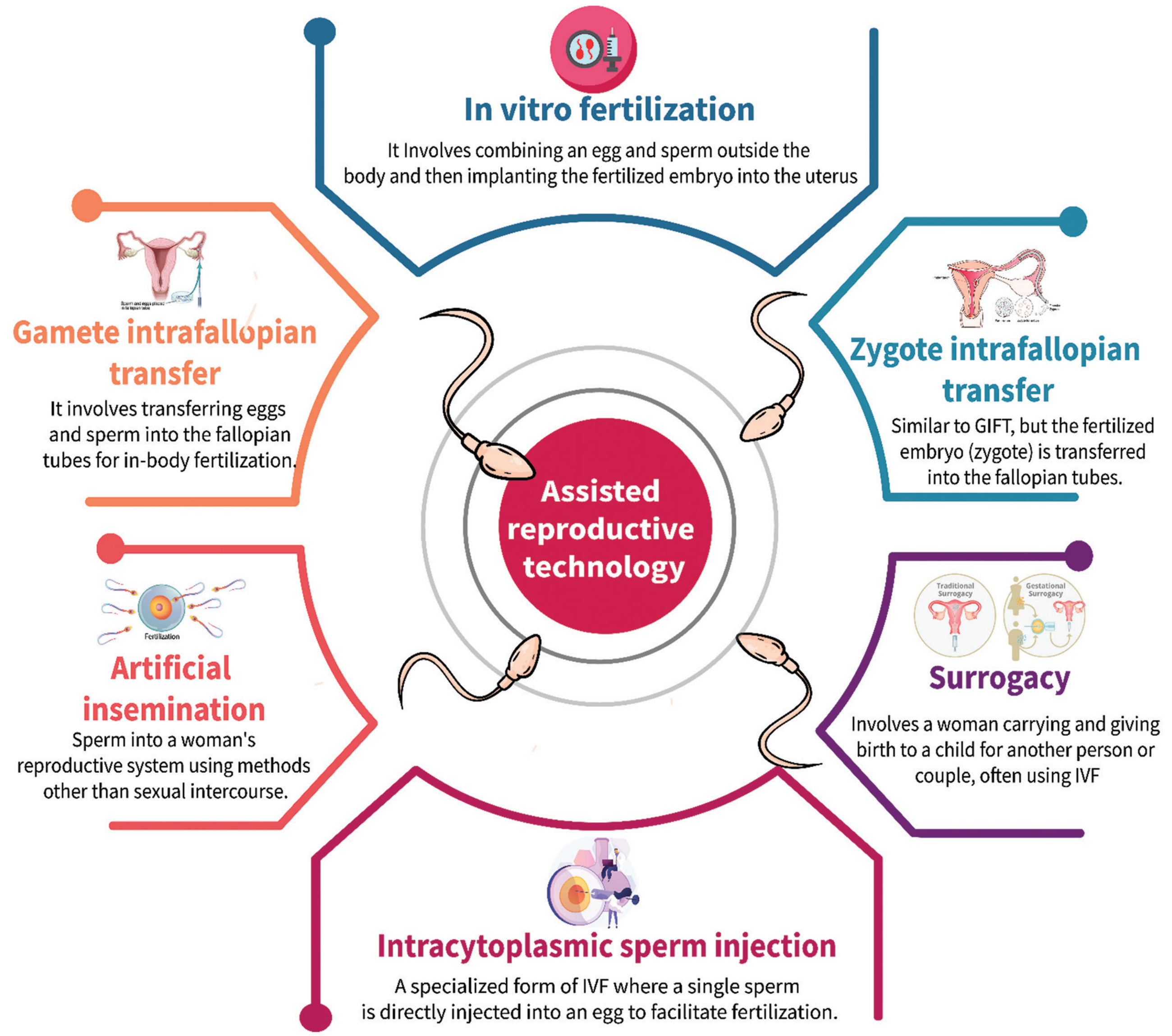

Figure 4. Different types of assisted reproductive technologies
Abbreviations: GIFT: Gamete intrafallopian transfer; IVF: *In vitro* fertilization.

implantation.[47] Although originally developed for cases of severe male infertility, ICSI is now also being utilized in clinical practice for mild male infertility or unexplained infertility.[48] Looking ahead, future advancements in ART may involve the use of immature spermatozoa, spermatids, and spermatocytes for ICSI, as well as further research into gene expression and genomic imprinting during spermatogenesis.

3.7.3. Surrogacy

Surrogacy is an assisted reproduction option often chosen by intended parents due to infertility, health concerns, same-sex parenting dynamics, or broader family diversity. In this method, another woman, known as the surrogate mother, carries and delivers a child on behalf of the intended parents.[49] While parental vetting and counseling are required to ensure parental responsibility and minimize future complications, surrogacy can be a good alternative for starting a family.[50] Despite its potential benefits, surrogacy raises complex ethical and legal concerns, such as fostering inequality, violating human rights, and commodifying children.[51] To mitigate these risks, robust legislation is required to safeguard the rights of intended parents, surrogate mothers, and the resulting child.[52] Increasing public awareness about the advantages of surrogacy, as well as addressing infertility, advancing age, health limitations, and adoption barriers, can contribute to broader acceptance and responsible practices.[53] Legal and ethical concerns about surrogacy differ considerably among nations. Countries such as the USA, France, Germany, and Austria predominantly impose restrictions on surrogacy, whereas nations such as India, Russia, and Kazakhstan hold more permissive legislation. Ethical discussions frequently classify nations as either advocates or adversaries, highlighting concerns over the possible exploitation of women in poor economic circumstances. Moreover, surrogacy prompts concerns regarding parental rights and acknowledgment. The identification of the legal mother – be it genetic or gestational – differs by jurisdiction, further complicating the legal status of both the child and the surrogate. Certain nations, such as Israel, have established extensive legal systems that may function as a model for international standards. Furthermore, the commercialization of surrogacy engenders ethical dilemmas about treating reproduction as a commercial process, possibly abusing women in economically precarious circumstances. In addition, ethical issues focus on the moral repercussions of surrogacy as a type of contemporary slavery.[54,55] The role of the gestational surrogate is typically underestimated, which can lead to ethical oversights, such as those found in adoption and donor-assisted conception. Therefore, understanding the gestational connection is essential for ensuring ethical surrogacy activities. On the other hand, the absence of international agreement on surrogacy legislation has led to the phenomenon of "surrogacy tourism," where individuals pursue surrogacy services in nations with more advantageous regulations. This situation underscores the urgent need for internationally recognized standards to safeguard the rights and well-being of all parties involved.[55,56]

3.7.4. Gamete intrafallopian transfer (GIFT)

GIFT is used to address infertility or genetic issues that may prevent spontaneous conception. Through GIFT, sperm and eggs are inserted into the fallopian tubes, allowing internal fertilization. Along with other treatments, including IVF and ET, GIFT is a part of the ART spectrum.[13] Several variables, including the quality of gametes and the physical and psychological conditions in which the operation is conducted, affect the outcomes of GIFT.[6] Couples seeking reproductive treatment still have the option of GIFT, even though it is less prevalent than IVF and ET.[57] For women with healthy fallopian tubes, GIFT is an easier and more effective assisted conception approach that provides higher successful rates than IVF.[58] It is also an effective treatment for non-tubal infertility, with a 32% rate of continued pregnancy and options for ovum donation, diagnostic IVF, and embryo freezing.[59] GIFT has an improved version known as "New GIFT," which has evolved from its earlier form referred to as "Old GIFT." The New GIFT approach is more effective than the Old GIFT, with the formation of pregnancy primarily dependent on sperm motility and oocyte count. The New GIFT approach, which involves preincubation of oocytes, has a lower abortion rate (19%) and a higher pregnancy rate (37% each cycle and 42% per patient) than the Old GIFT method (24% per cycle, 29% per ovum pick-up, and 22% abortion rate). It is more effective overall because it highlights the significance of mature oocytes and sperm motility, as well as benefits from improved luteal support.[60,61]

3.7.5. Zygote intrafallopian transfer (ZIFT)

ZIFT combines the natural environment of the fallopian tubes with IVF. In this method, zygotes are placed into fallopian tubes 24 h after fertilization in the lab following ICSI. The transfer is carried out using a catheter during laparoscopy, allowing the zygotes to travel through the fallopian tubes naturally to the uterus. ZIFT is typically considered by patients with fallopian tube issues or those seeking a more natural method for embryo implantation.[61] A 2-year study reported that ZIFT has a 40.4% clinical pregnancy rate and a delivery/ongoing rate of 34.2%.[62] While IVF-ET has the highest cumulative take-home baby and pregnancy rates for treating male infertility, both GIFT and ZIFT show comparable rates of pregnancy but are associated with higher rates of miscarriage.[63] In IVF-ET cycles, ZIFT has proven particularly beneficial for patients experiencing repeated implantation failure. Research indicates that ZIFT considerably increases the likelihood of pregnancy and implantation in these individuals compared to further IVF-ET cycles. For example, patients with repeated implantation failures had pregnancy rates of 34.2% with ZIFT compared to 17.1% with IVF-ET.[64,65] Despite these advantages, ZIFT is more invasive than conventional IVF-ET due to the requirement of laparoscopy. Moreover, studies have shown that, especially in cases involving male-factor infertility or non-tubal infertility, the added complexity of ZIFT does not always result in improved outcomes.[66,67]

3.7.6. Artificial insemination

Artificial insemination involves the use of a syringe and an artificial insemination catheter to inject semen into a woman's uterus. This medical treatment is performed in conjunction with homologous insemination, particularly in cases of oligospermia or when sexual intercourse becomes difficult. In more complicated situations, donor sperm can be surgically inserted into a female's oviduct through laparoscopic surgery; however, this method is more invasive, costly, and technically demanding than vaginal insemination. Despite its complexity, artificial insemination may be necessary for specific infertility treatments or breeding initiatives. It allows for the conservation of genetic lines, acceleration of line extension, or the synchronization of embryo development by enabling one male's sperm to inseminate multiple females.[68] This method addresses the issue of male-factor infertility and can be used with various species, including gorillas, lions, bears, and tuna fish. Infertility in both males and females can be successfully treated using artificial insemination, with a success rate of up to 18.2% every cycle and 58.4% after 6 months of treatment.[69]

3.8. Relationship between ART and AI

A significant portion of people worldwide experience infertility, which is defined as the inability to achieve a clinical pregnancy following 12 months of regular, unprotected sexual intercourse.[10] Treatment for subfertility, infertility, or genetic disorders that hinder natural conception is referred to as ART. Common ART methods include ET, IVF, ICSI, and GIFT.[4] Recent technological advancements aim to automate processes such as sperm selection, fertilization, and embryo culture, which could enhance consistency and reduce the stress caused by manual manipulation.[13] The integration of AI with ART enhances the effectiveness and success rates of ART treatments. AI algorithms can assess and predict the quality of gametes and embryos, which are vital to the success of ART. At present, morphological examinations, which are prone to subjectivity and human error, are the primary method used by embryologists to manually assess the quality of gametes and embryos.[70] By eliminating inter-observer and inter-objective variations, AI algorithms may provide a more standardized and objective evaluation.[71] This integration enhances reproductive health outcomes by increasing implantation success rates, reducing the incidence of multiple pregnancies, and improving single-ET.[72] Moreover, AI can predict embryos' viability and oocytes' developmental capability using ML algorithms and morphokinetic parameter analysis. By selecting the most viable embryos, this method can increase the chances of implantation and successful pregnancy.[73] In addition, AI can aid in automating tedious and repetitive ART laboratory duties, thereby increasing productivity and minimizing errors.[23] However, to achieve extensive integration into clinical practice, ethical considerations and the imperative for transparency in AI algorithms must be duly acknowledged and resolved.

3.9. Advancements in AI and ML in ART

AI and ML are two related yet distinct disciplines within the field of computer intelligence. ML is a subset of AI that focuses on algorithms enabling computers to learn from data, while AI is a vast field that aims to replicate human intelligence through reasoning, problem-solving, and learning. Although AI is widely used in many sectors, ML is essential for enhancing decision-making and prediction skills in these applications.[74] AI and ML have the potential to revolutionize basic science, clinical practice, healthcare administration, and medicinal economics.[70] In reproductive medicine, predictive modeling using AI can accurately predict fertility outcomes. However, challenges such as managing large-scale data, identifying valuable features, and validating models with gold-standard study designs remain.[75] Further precision, standardization, and automation in the field of reproductive medicine could be achieved using AI-guided procedures.[76] For example, AI-based ART software can reduce interobserver variability, personalize drug doses, and improve clinical and operational efficiency, particularly in sperm selection and oocyte quality assessment.[77] Most importantly, AI has shown potential in reproductive urology by predicting semen parameters, identifying candidates for genetic testing, and automating sperm detection.[7] In addition, AI in ART improves efficiency by identifying patients at risk for conditions such as endometriosis, detecting gamete production values, and optimizing controlled ovarian stimulation by calculating ideal starting drug doses and trigger timing using deep learning algorithms.[73] Recently, Levenberg–Marquardt neural networks trained on local binary patterns have demonstrated promising outcomes in terms of oocyte and embryo quality prediction, offering potential improvements in ART, especially in nations with restricted embryo selection practices.[68]

3.10. Integration of AI in embryo selection

In the past, doctors have utilized ML algorithms to assist in selecting embryos for human-assisted reproduction. The challenges of embryo selection have gained significant attention with the advent of ART. Invasive techniques, including preimplantation genetic screening, as well as transcriptome and proteome analyses of biopsied embryonic tissue, were initially emphasized and are currently being explored to obtain direct insights into embryonic development. In ART, a variety of deep learning and ML models are applied to enhance embryo selection processes. For example, AI models such as ERICA use blastocyst images to estimate euploidy in embryos.[78] To enhance embryo selection processes in IVF, AI analyzes complex data, identifies trends, and provides an objective evaluation of embryos.[79] Furthermore, AI is used to determine the optimal quantity of metaphase II oocytes required for ART to produce viable blastocysts and embryos.[73]

3.11. Transformative algorithms in enhancing embryo selection

Within the field of ART, a wide range of ML and AI methods have been utilized to improve embryo selection and predict the likelihood of successful implantation during IVF procedures. These technologies aim to enhance the precision, consistency, and efficiency of evaluating embryo viability. One prominent approach involves the use of deep learning models, such as iDAScore v1.0, for the objective ranking of blastocysts, introduced by Cimadomo *et al.*[17] Its successor, iDAScore v2.0, developed by Theilgaard Lassen *et al.*,[16] incorporated morphokinetic parameters into embryo ranking, and achieved an AUC ranging from 0.621 to 0.707. Ueno *et al.*[23] further demonstrated that increasing training data with Gardner grading for both IDA-V1 and V2 significantly enhanced predictive performance, with an AUC value of 0.736 for ongoing pregnancy predictions. Moreover, studies by Bori *et al.*[19] and Johansen *et al.*[18] introduced AI models using time-lapse images to evaluate embryo viability. Benchaib *et al.*[80] employed shallow artificial networks (e.g., multilayer perceptron and recurrent neural network) based on morphokinetic time-lapse parameters to predict viable embryos for transfer. Berntsen *et al.*[24] employed a deep-learning AI model based on Python and TensorFlow to sort 115,832 embryos from 18 IVF centers, achieving AUC values between 0.63 and 0.69. In another approach, Chen *et al.*[25] used a random forest model on 345 paired blastocyst cultures, demonstrating transplant suitability for A- and B-grade embryos comparable to euploid ones. Glatstein *et al.*[20] used convolutional neural networks and support vector machines to predict live birth probabilities, with AUC values of 0.63 – 0.83 and achieving up to 90% accuracy in some models. Salih *et al.*[21] showed that ML outperformed embryologists in predicting embryo morphology, with an accuracy of 75.5% compared to the embryologists' 65.4%. Meanwhile, Pons *et al.*[34] applied logistic regressions to update the ASEBIR system for predicting blastocyst implantation and live birth. To predict fertilization failure probabilities (Logistic Regression Function and Threshold Fertilization Failure) in ART cycles, Tian *et al.*[22] utilized Bayesian network modeling and achieved an accuracy of 91.3%, aiming to optimize IVF and ICSI treatments.

Recent deep learning models show significant advancements in performance. For example, the Embryo2live model outperformed traditional morphology grading by increasing live birth rates from 23.0% to 71.3% for top embryo selections.[81] The Esava model, developed for the quantitative evaluation of IVF embryos, reported high rates for precision (0.9940), recall (0.9121), and mean average precision (0.9531), demonstrating superior blastomere detection compared to previous computational methods.[82] Similarly, the CHLOE model revealed no significant bias between XX and XY embryos (U = 204621, p=0.208). In contrast, manual morphological grading and the KIDScore algorithm, a tool to support embryologists in decision-making, tended to favor male embryos, with XY embryos receiving higher scores than XX embryos (U = 207604, p=0.0182; χ^2 = 19.843, p<0.00001). These findings suggest that deep-learning approaches may help mitigate sex-selection bias.[83] However, deep learning is not always superior to manual methods. In a recent double-blind non-inferiority trial involving 1,066 patients, 533 were assigned to the iDAScore group and 533 to the morphological grading group. The iDAScore group showed a clinical pregnancy rate of 46.5% (248 of 533 patients), compared to 48.2% (257 of 533 patients) in the morphological grading group (risk difference = −1.7%; 95% CI = −7.7, 4.3; p=0.62).[84]

4. Discussion

This comprehensive analysis of the systematic review aims to address the RQs, assess the quality of the review, and propose directions for future study.

4.1. General discussion

The term "ART" is gaining significant recognition in the context of infertility treatment. ART refers to any procedure involving the *in vitro* manipulation of oocytes (immature ova or egg cells) for reproductive purposes.[38] Common ART procedures include IVF, ICSI, ET, and luteal phase assistance, although these techniques may cause perinatal complications and outcomes.[85] Primarily used for infertility treatments, ART includes techniques such as artificial insemination, IVF, surrogacy, and the use of fertility medication.[86] The implementation of individualized treatment protocols and multidisciplinary team management significantly improves treatment outcomes and safety, making ART a viable option for couples and individuals facing fertility issues. The ART process encompasses several critical stages, including controlled ovarian stimulation, pituitary downregulation, oocyte retrieval, fertilization, ET, embryo selection, and luteal phase support.[39] In recent years, AI has been integrated into ART to enhance and automate embryo selection by analyzing microscopy images and identifying optimal embryos for transfer or cryopreservation.[77] AI is also used to reduce interobserver variability, optimize drug dosing, enhance sperm selection and oocyte quality evaluation, and increase overall clinical efficiency.[87] By enhancing outcomes and decision-making processes through sophisticated algorithms and data analysis, AI is transforming the landscape of ART.[29] This exploratory review examines recent developments in embryo selection and related AI-driven innovations within ART.

4.2. Strength of the systematic review

The strength of this systematic review lies in its thorough analysis of the correlation between AI and ART, particularly those concerning embryo selection. The review thoroughly explains the opportunities, challenges, and future directions in using AI to improve ART outcomes by analyzing a wide range of literature from the past 10 years. This paper is the first to highlight the need for external validation of prediction models, an aspect that requires significant improvement in the reviewed studies. Most of the scientific papers used retrospective and anonymized data, which may introduce biases and limit the generalization of findings. Therefore, this systematic review combines an in-depth analysis of various documents from several countries, thus reducing bias and highlighting its potential to transform the field of ART. It also highlights ethical considerations and emphasizes the significance of responsible implementation in clinical practice. With its in-depth analysis and interdisciplinary approach, the review provides valuable insights for researchers, clinicians, and policymakers, facilitating informed decision-making. In addition, four key parameters have been identified – ethical concerns, clinical and regulatory constraints, discussion of AI techniques, and the potential applications of AI in ART – to illustrate the strength of this review (Table 4).

4.3. Addressing the RQs

In subsequent sections, comprehensive responses are provided to address the RQs.

4.3.1. RQ1: What are the current state-of-the-art AI technologies used in embryo selection for ART?

In ART, recent developments in AI have significantly improved embryo selection procedures. These cutting-edge AI tools use ML, deep learning, and computer vision to increase the precision, reliability, and efficiency of embryonic health evaluation. AI technologies are transforming IVF laboratories by automating the assessment of embryo morphology and leveraging synthetic data. The primary AI tools currently employed in embryo selection are listed below:

(i) Computer vision and deep learning: Computer vision and deep learning are used by AI systems to automatically examine images of embryo morphology and extract important aspects that are essential for determining the survival of the embryo. The accuracy of embryo selection is improved, and the subjectivity associated with manual assessments by embryologists is reduced.[92] For example, deep learning algorithms that have been trained on both synthetic and actual embryo images have shown excellent accuracy in predicting the stages of embryo cells, reaching up to 97% accuracy when synthetic data is included.[93]

(ii) Time-lapse imaging: AI systems use time-lapse imaging to improve predictions from fertilization to the blastocyst stage, thereby increasing IVF success rates by identifying viable embryos more accurately than human experts.[94]

(iii) ML Techniques: Several ML techniques, such as neural networks, naive Bayes, support vector machines, and random forests, are used to predict treatment outcomes and enhance IVF results. The average AUC rating for these models is 0.91, indicating high accuracy, sensitivity, and precision.[94]

Table 4. A thorough comparative analysis of relevant studies and the current review

References	Ethical concerns	Regulatory and clinical barriers	AI techniques discussed	Prospects of AI in ART
Kragh and Karstoft[87]	✓	✓	✓	✗
Merican *et al.*[88]	✗	✗	✓	✓
Raef and Ferdousi[4]	✗	✗	✓	✓
Medenica *et al.*[89]	✓	✓	✗	✓
Afnan *et al.*[9]	✓	✓	✗	✗
Fernandez *et al.*[13]	✗	✗	✓	✗
Curchoe[90]	✓	✓	✗	✓
Tran *et al.*[91]	✓	✓	✓	✗
Abdullah *et al.*[3]	✗	✓	✓	✓
Current study	✓	✓	✓	✓

Abbreviations: AI: Artificial intelligence; ART: Assisted reproductive technology.

(iv) Generative models for synthetic data: Images of synthetic embryos are produced using generative models, such as diffusion models and generative adversarial networks. Combining these artificial images with actual data enhances AI model training and improves classification performance.[93]
(v) AI-powered embryo ranking systems: Deep learning is used by platforms such as the Embryo Ranking Intelligent Classification Algorithm to rank embryos according to their expected genetic state and implantation potential. These systems enable clinicians to select embryos with the highest potential for successful implantation and pregnancy.[95]
(vi) Automated morphological feature extraction: AI solutions reduce subjectivity and unpredictability in assessments by automating the measurement of important morphological parameters from embryo images.[96]

4.3.2. RQ2: To what extent does ART improve the pregnancy success rate and live birth outcomes compared to traditional methods?

The performance of ART may be improved using AI and ML approaches. These techniques also hold a promise for the advancement of medical technology in the future.[5] AI-guided ARTs offer enhanced accuracy, uniformity, and automation compared to traditional ARTs.[76] AI can accurately identify embryos' inner cell mass, blastocoel, trophectoderm, and zona pellucida. Deep learning methods are employed to accomplish this capability and reduce the workload of embryologists, thereby improving the efficiency of ARTs.[97] In general, factors such as maternal age, the underlying cause of infertility, and the ovarian stimulation protocols significantly influence the probability of achieving successful pregnancies and live births.[22]

4.3.3. RQ3: How can AI algorithms be seamlessly integrated into existing embryo selection protocols and laboratory workflows to leverage the expertise of embryologists and healthcare professionals?

AI algorithms can enhance embryo selection protocols by leveraging data from time-lapse imaging, proteomic profiles, and morphological features to predict live birth outcomes and embryo viability.[73,79,98] Although ML systems are used to predict the results of frozen ETs in early pregnancy, their accuracy is limited, and additional predictors are required to improve predictive performance.[99] By utilizing ML models and computer vision, AI can analyze vast amounts of image data to automate embryo selection processes.[100] Nevertheless, issues such as the interpretability of AI models and the requirement for open, and peer-reviewed research remain to be resolved. The application of AI as a quality control tool post-thawing or for continuous monitoring of embryo culturing systems optimizes laboratory workflows. This application allows for a synergistic approach, integrating the strengths of AI algorithms with the expertise of embryologists and healthcare professionals to improve ART outcomes. AI can streamline laboratory workflows by automating time-consuming tasks, such as embryo evaluation, allowing professionals to focus on critical decision-making.[87]

4.3.4. RQ4: What is the impact of AI-driven embryo selection on the psychological health and decision-making processes of prospective parents, particularly in light of ethical concerns?

It is necessary for ethical considerations to maintain public trust and improve both psychological and clinical results in ART.[101] The use of AI technologies in embryo selection raises ethical concerns regarding deskilling, transparency, accountability, and fairness. The absence of transparency in AI models, which are frequently referred to as "black-box" systems, creates uncertainty and undermines trust.[98] Furthermore, the potential repercussions of AI failures in embryo selection, which could lead to anomalies or undesired outcomes, underline the significance of responsibility and fairness in the utilization of AI in this sensitive field.[71] To address these issues and preserve the trust of the public, it is essential to prioritize the development of AI models that can be interpreted, carry out thorough evaluations through randomized controlled trials, and establish regulatory oversight for the application of these algorithms.[102] If these recommendations are followed, the integration of AI in embryo selection may enhance psychological and therapeutic results while upholding ethical standards in ART.

4.3.5. RQ5: What are the primary barriers and limitations to the clinical application of AI algorithms in embryo selection, and how are these technologies being developed and validated?

AI-based ARTs can reduce inconsistencies, increase clinical and client outcomes, and improve sperm testing and oocyte quality assessment.[103] Obstacles to applying AI algorithms arise due to the lack of transparency in ML models, ethical concerns about selection errors, and the fact that current embryo-selection algorithms lose diagnostic value when applied externally to many known implantation embryos.[104] These limitations are exacerbated by the black-box nature of AI models, leading to ethical and epistemic issues, such as unclear responsibility for treatment success and biases with unintended consequences.[105] To address these challenges, efforts are being made to increase the generalizability of AI models by diversifying training data and developing clinic-specific models.[9] Ethical considerations in adopting AI for embryo selection include transparency, interpretability, and collaborative decision-making to ensure the well-being of prospective parents and uphold ethical standards in assisted reproduction.[21] In addition, there is growing support for more rigorous clinical testing, including larger sample sizes, balanced datasets, and improved performance metrics, to ensure the reliability and effectiveness of AI algorithms for embryo selection.

4.4. Limitations of this study

The studies included in this review focused on deep learning, ML, or AI for embryo selection, providing a general overview rather than a detailed statistical data analysis, which could limit the depth of insights provided. Furthermore, the absence of critical appraisal may induce uncertainty regarding the robustness of the evidence synthesized in the review. The selection was determined through an exhaustive search of numerous databases, which may have resulted in bias. Due to limited access, some databases, such as Web of Science and PsycINFO, were not included in the study. The inclusion and exclusion criteria were meticulously defined to ensure a thorough search. Only publications that were written in the English language were considered. The studies spanned from June 1, 2015, to January 9, 2024, considering that older studies might not reflect recent technological advancements.

4.4.1. Factors influencing analytical results

One of the most concerning limitations of this reviewed study is sampling imbalance. Some papers in this study do not adequately represent the diverse population undergoing ART, creating potential bias. Some AI models were trained using datasets of a limited number of clinics, thereby lacking generalizability. Another limitation is the variation of validation techniques used across studies. Differences in validation techniques can influence performance matrices. Without external validation, these models may demonstrate high accuracy on training data but perform poorly in real-world applications. Furthermore, variability in model predictions, influenced by various characteristics of the dataset provided, raises concerns about clinical reliability. AI models are often trained on retrospective data (data collected from past events or historical records), and their performance in real-world clinical settings raises concerns. In addition, some AI models lack interpretability (black-box algorithms). This further complicates the integration of AI models into ART.

4.5. Future scope of ART

Throughout the years, ART has made an extraordinary contribution to the endeavor to resolve the infertility issues that couples have been facing. ART, spanning from its traditional to contemporary iterations, has played a pivotal role in enhancing birth rates and facilitating conception through ET, GIFT, and other procedures. It has increased the birth rate by surmounting barriers to conception and augmenting the probability of a successful pregnancy. There is significant potential for ART advancements through the implementation of AI-based algorithms. AI possesses the capability to assist in antiretroviral therapy by addressing therapeutic challenges.[71] To enhance the outcomes of ART, prediction models can be developed by implementing ML methodologies, which encompass a diverse array of feature sets and numerous algorithms.[4] Future advancements in soft robotics, telesurgery, and the integration of AI with robotics may potentially lead to an ART procedure that is fully automated and intelligent.[73]

The potential impacts of AI on ARTs are shown in Figure 5, highlighting seven key areas:

(i) Personalized treatment plans: AI customizes care based on patient data, taking specific health profiles into account to maximize success rates
(ii) Real-time decision support: AI offers clinicians timely insights during critical procedures, such as ET, enhancing accuracy and efficacy
(iii) Predictive analytics: AI accurately predicts treatment outcomes, enabling proactive adjustments to optimize success rates
(iv) Automated laboratory processes: AI automates tasks such as sperm and embryo analysis, enhancing efficiency and reducing errors
(v) Remote monitoring and teleconsultation: AI-powered systems enable continuous patient monitoring and teleconsultation, extending ART accessibility
(vi) Genomic analysis: AI identifies genetic risks, aiding informed decisions on embryo selection and genetic screening for better outcomes
(vii) Enhanced quality control: AI ensures optimal laboratory conditions, minimizing variability and enhancing success rates.

The integration of AI into these areas promises personalized, efficient, and accessible reproductive healthcare solutions, revolutionizing the field of reproductive medicine. Furthermore, robust regulatory frameworks are essential to guarantee the ethical and safe application of AI in ART, highlighting the requirement for policies and supervision to promote ethical AI adoption in reproductive medicine.[89] Moreover, the utilization of AI in

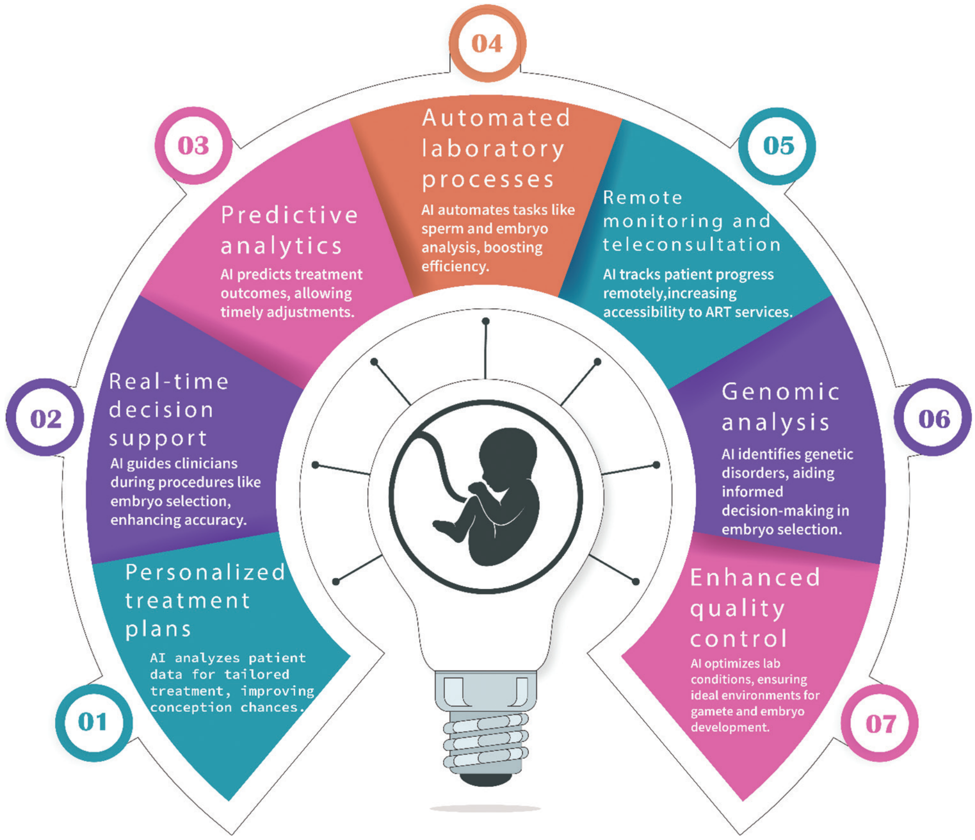

Figure 5. Future scope of assisted reproductive technology using artificial intelligence

the field of reproductive health is advancing significantly, as indicated by the proliferation of AI-related conference abstracts and the commercialization of numerous AI models.[3] As an illustration, in countries with embryo selection restrictions, Levenberg–Marquardt neural networks that have been trained to utilize local binary patterns have exhibited promising outcomes in predicting the quality of oocytes and embryos.[68] This could improve the technology used in assisted reproduction. It is crucial to address AI's shortcomings, such as algorithmic bias and the need for future research and clinical trials, to ensure its successful integration into ART.[90] Employing large training datasets and robust models is recommended to surmount these challenges.

5. Conclusion

Despite the extensive literature on AI applications in embryo selection, our study specifically focuses on addressing existing gaps in this area. The endeavor to revolutionize ART is at a critical turning point where the convergence of AI and precision in embryo selection intersects. This study explores AI applications in embryo selection, highlighting advancements, challenges, and opportunities. AI technologies, such as automatic embryo scoring algorithms (e.g., KIDScore D5 v3), Bayesian networks, and shallow artificial neural networks (e.g., multilayer perceptron and recurrent neural network), have been applied in ART for embryo selection. These AI models have demonstrated various levels of accuracy, with some achieving up to 90% prediction accuracy for live birth probabilities. However, the reviewed studies are often retrospective and conducted in single centers, limiting their generalizability. In addition, the lack of comprehensive datasets and previous pregnancy information poses challenges to model performance. Throughout this paper, we demonstrate that AI has the potential to enhance embryo viability, improve live birth prediction accuracy, personalize treatment plans, minimize human errors, and standardize IVF practices. To make advancements in the field of ART, future research must focus on creating AI models that are transparent, interpretable, and thoroughly verified through randomized controlled trials. To overcome current limitations, the generalizability of AI models can be improved by diversifying training datasets and tailoring models to different clinical settings. Integrating AI-driven predictive analytics and real-time decision support systems into clinical practices can enhance treatment outcomes. Furthermore, it is essential to implement individualized treatment plans based on patient-specific information, streamline laboratory procedures through automation, and establish strong ethical guidelines to enhance ART effectiveness and maintain public trust in ART. Future research should focus on developing AI algorithms to address challenges such as algorithmic bias and the need for extensive clinical validation, incorporating robust statistical approaches. Successful integration of AI into clinical practice necessitates close collaboration between clinicians, researchers, and policymakers to ensure ethical and effective implementation. By leveraging interdisciplinary methodologies and emerging technologies, we can establish a pathway toward a future where infertile couples can fulfill their aspirations.

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Ethics approval and consent to participate

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Consent for publication

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