BRAIN. Broad Research in Artificial Intelligence and Neuroscience
e-ISSN: 2067-3957 | p-ISSN: 2068-0473
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2026, Volume 17, Issue 1, pages: 377-394
Submitted: January 14th, 2025 | *Accepted for publication:* March 3rd, 2026

From Statistical Regression to Explainable AI: A Synergistic Approach for Predicting Euploid Embryo Yield Based on Maternal Age, AMH, and a Visual Decision-Support System

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Abstract: ***Background:*** *Predicting the number of euploid embryos is critical for optimising IVF outcomes and managing patient expectations. While maternal age and anti-Müllerian hormone (AMH) are established markers of ovarian reserve, their combined predictive power regarding chromosomal normality remains a subject of clinical debate. Artificial intelligence is increasingly being explored in assisted reproduction as a non-invasive, data-driven approach to estimate embryo ploidy. By leveraging advanced models such as* ***convolutional neural networks (CNNs)*** *and* ***machine learning algorithms*** *to evaluate morphological and morphokinetic characteristics from time-lapse sequences, AI contributes to improving the accuracy and objectivity of embryo selection.* ***Objective:*** *This study evaluated the statistical association between maternal age, AMH levels, and fertilisation methods (IVF, ICSI, IMSI) and euploid embryo yield. A secondary objective was to translate these clinical findings into a visual* ***decision-support system (DSS)*** *grounded in an* ***Explainable AI (XAI)*** *framework.* ***Methods:*** *A retrospective observational study was conducted on 31 patients undergoing IVF with PGT-A. Statistical significance was assessed using one-way ANOVA and multiple linear regression. Building on these data, a specialised decision-support system was developed using React 19 and TypeScript, employing a binomial probability model to translate clinical biomarkers into intuitive success simulations.*
Results: *Patients younger than 35 years exhibited significantly higher AMH levels ($p = 0.033$) and a higher mean number of euploid embryos ($p = 0.032$) compared to those greater than 35. The fertilisation method did not significantly influence euploidy outcomes ($p = 0.990$). The regression model was statistically significant ($p = 0.030$), explaining 22.1% of the variance. However, none of the individual predictors reached statistical significance, suggesting that the observed effect may be driven by the combined contribution of the variables rather than by independent effects. The resulting DSS operationalises these findings in a preliminary manner through real-time attrition modelling and "Opportunity Cost" visualisations.* ***Conclusion:*** *Maternal age may represent an important factor in embryo euploidy, while AMH provides a quantitative baseline for embryo yield. By synergising retrospective data with explainable AI, the developed framework offers a transparent, data-driven approach to fertility counselling. This study indicates that integrating statistical analysis with a visual decision-support system effectively bridges the gap between raw clinical data and patient-centred practice, facilitating more objective decision-making in in vitro fertilisation.The development of a conceptual decision support system based on these findings derived a secondary objective of the paper by exploring it.*

Keywords: *IVF; AMH; maternal age; euploid embryos; fertilisation method; ICSI; IMSI; XAI; decision-support system.*

How to cite: Armeanu (Popescu), T., Popescu, D., Maftei, R., Diaconu, R., Tomita, D.-I., Novac, B., Novac, O., & Doroftei, B.(2026). From Statistical Regression to Explainable AI: A Synergistic Approach for Predicting Euploid Embryo Yield Based on Maternal Age, AMH, and a Visual Decision-Support System. *BRAIN. Broad Research in Artificial Intelligence and Neuroscience, 17*(1), 377-394. https://doi.org/10.70594/brain/17.1/26

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1. Introduction

Today, infertility represents a major clinical and social challenge (Zegers-Hochschild et al., 2017). As a response to the increased importance of infertility, various assisted reproductive technologies (ART) have become essential tools for improving reproductive outcomes (Mascarenhas et al., 2012). One of the most effective tools available is a combination of in vitro fertilisation (IVF) and preimplantation genetic testing (PGT) (Practice Committee of the Society for Assisted Reproductive Technology, and Practice Committee of the American Society for Reproductive Medicine, 2008). This combined method allows the selection of chromosomally normal embryos, thereby increasing the likelihood of implantation and reducing miscarriage rates (Forman et al., 2013). Furthermore, the introduction of next-generation sequencing (NGS) has significantly improved the precision of embryo genetic assessment and has become widely adopted in many specialised fertility centres (Mardis, 2008).

Maternal age, by its well-documented significant influence on both ovarian reserve and oocyte chromosomal competence, remains one of the strongest predictors of reproductive success (Franasiak et al., 2014). In addition, anti-Müllerian hormone (AMH) is widely used as a reliable marker of ovarian reserve (Broer et al., 2014). Furthermore, it has been demonstrated that AMH strongly correlates with the number of oocytes retrieved during IVF (La Marca and Sunkara, 2014). However, the clinical relationship between AMH and embryo euploidy is still not completely understood. While some studies suggest that elevated AMH levels may increase the likelihood of obtaining euploid embryos through a quantitative effect (Sunkara et al., 2011), other authors have reported weaker associations when age is included as a covariate in the statistical analysis (Dólleman et al., 2013).

Another important variable to consider when analysing IVF outcomes is the fertilisation method. The three most important fertilisation methods are conventional IVF, intracytoplasmic sperm injection (ICSI), and intracytoplasmic morphologically selected sperm injection (IMSI) (De Vos et al., 2013). These three distinct methods differ in their technical approaches and indications, but their differential impact on the embryo's chromosomal status remains unclear (Palermo, Neri, and Rosenwaks, 2015). Current evidence suggests that fertilisation techniques do not directly modify euploidy rates; however, the current number of available randomised controlled trials comparing their direct effect is limited (Broekmans, Soules, and Fauser, 2009).

Therefore, given the lack of consensus in the literature, a clearer understanding of how the relationship between maternal age, AMH values, and fertilisation method influences the number of euploid embryos is clinically relevant. Furthermore, identifying significant predictors of the number of euploid embryos may help improve patient counselling, optimise treatment strategies, and refine expectations regarding IVF success.

The aim of this study was to evaluate whether AMH levels, maternal age, and fertilisation method are significantly associated with the number of euploid embryos obtained in IVF cycles. Additionally, using a multiple linear regression, we assessed whether AMH values and maternal age could independently predict the number of euploid embryos.

Beyond the statistical validation of these biomarkers, this research seeks to address a critical gap in clinical practice: the challenge of communicating complex, multi-variable probabilities to patients. Therefore, a significant component of this work involves the development and prototype implementation of an explainable AI-driven decision-support system (DSS). This system integrates the quantitative insights from our regression model with an interactive, visual interface designed to simulate embryo attrition and age-related chromosomal decline.

By synergising retrospective clinical data with modern computational frameworks, we aim to provide a transparent tool for fertility forecasting. This approach moves towards a more personalised model of care, where high-dimensional data is transformed into an intuitive "success roadmap," ultimately enhancing both clinical decision-making and the informed consent process in assisted reproduction.

2. Methods

Study design:

Our retrospective observational study was conducted from January 2023 to date at Origyn Fertility Center, Iași, Romania. All clinical, embryological, and laboratory data were collected from patients undergoing in vitro fertilisation (IVF). All procedures followed institutional protocols and were performed by the same clinical team to ensure consistency in the data

Participants:

The sample of our study consisted of 31 women undergoing IVF treatment. The inclusion criteria were straightforward: available data regarding the serum anti-Müllerian hormone (AMH) levels, documented fertilisation method (IVF, ICSI, or IMSI), and at least one blastocyst biopsied for PGT-A. Patients with incomplete data or without PGT-A results were excluded from the study.

For each patient, the following variables were recorded in our database: maternal age, AMH levels (ng/mL), fertilisation method, and number of euploid embryos obtained per cycle.

Outcome measures:

The primary predictor variables of our study was the number of euploid embryos per IVF cycle. In addition, secondary variables included maternal age, AMH levels and fertilisation method.

Statistical analysis:

All statistical analyses were performed using IBM SPSS Statistics version 26.

Group comparisons:

For group comparisons, separate one-way ANOVAs were conducted to evaluate whether AMH levels and the number of euploid embryos differed significantly in the three fertilisation method groups (IVF, ICSI, IMSI). When the independent variable had more than two levels, LSD post-hoc tests were used to assess pairwise differences,given the exploratory nature of the study.

Regression analysis:

To determine whether AMH values and maternal age could significantly predict the number of euploid embryos, we used a multiple linear regression model. Model performance was evaluated using R, R^2, adjusted R^2, F-statistics, and p-values. Unstandardised coefficients (B), standard errors, and 95% confidence intervals were also reported in the Results section.

Graphical analysis: Unstandardised predicted values from the regression model were saved and used to generate scatterplots. The scatterplots illustrated the relationship between observed and predicted euploid embryo counts.

The significance threshold was set at $p < 0.05$ for all analyses.

3. Results

Descriptive analysis

The sample of our study consisted of 31 patients. The participants were all women, maternal age ranged from 32 to 43 years, with a mean age of 37.1 years (SD = 3.7). Most patients were ≥35 years old (58.1%), while 41.9% were younger than 35 years. AMH values ranged from 0.60 to 5.40 ng/mL, with a mean of 2.47 ng/mL (SD = 1.39). The number of euploid embryos per cycle ranged from 0 to 5. The mean number of euploid embryos in our sample was 1.61 per IVF cycle (SD = 1.38).

ANOVA for AMH values by Maternal Age Group

To examine maternal age as an independent variable, we divided the sample into two distinct groups: 35 years or older and younger than 35. The statistical analysis showed that patients younger than 35 years had higher AMH levels (mean 3.09 ng/mL) than those aged ≥35 years (mean 2.02 ng/mL). In addition, the one-way ANOVA demonstrated that the difference between the two age groups was statistically significant, $F(1,29) = 5.04$, $p = 0.033$(see Figure 1)

ANOVA for Euploid Embryo Number by Maternal Age Group

The same statistical approach was followed for the number of euploid embryos. Therefore, the results showed that patients younger than 35 years had a higher mean number of euploid embryos per IVF cycle (mean 2.23) compared with patients aged ≥35 years (mean 1.17). The one-way ANOVA indicated that the observed difference between the two groups was statistically significant, $F(1,29) = 5.08$, $p = 0.032$ (Figure 2).

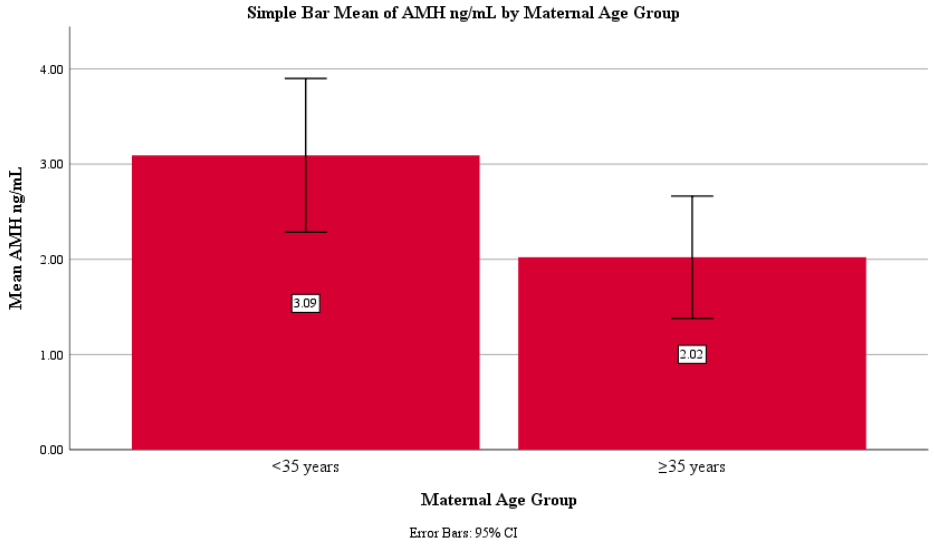

Figure 1. AMH levels by maternal age group. Patients in the <35 years group showed statistically significant higher values of AMH compared with those in the ≥35 years group.

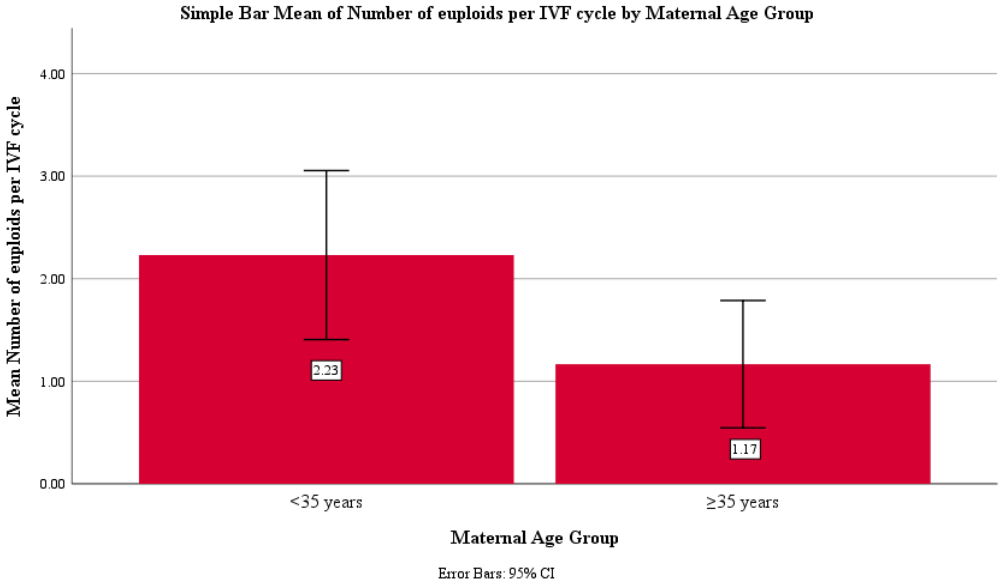

Figure 2. Euploid embryo number by maternal age group. Patients in the <35 years group showed statistically significant higher numbers of euploid embryos when compared with those in the ≥35 years group.

ANOVA – AMH values by Fertilisation Method

The next ANOVA tested whether AMH levels differed significantly among the three fertilisation method groups. The results of our statistical analysis demonstrated that AMH levels were not statistically significantly different across the three fertilisation methods. In the conventional IVF group, the mean AMH was 2.66 ng/mL, 2.07 ng/mL in the ICSI group, and 2.59 ng/mL in the IMSI group. Although some differences were observed between the groups, the one-way ANOVA demonstrated that these differences were not statistically significant, $F(2,28) = 0.52$, $p = 0.599$.

The subsequent post-hoc LSD comparisons confirmed that there were no significant differences between the three groups. The difference between IVF and ICSI was 0.59 ng/mL ($p = 0.329$), between IVF and IMSI was 0.07 ng/mL ($p = 0.910$), and between ICSI and IMSI was –0.52 ng/mL ($p = 0.474$). Furthermore, all confidence intervals for the post hoc analysis crossed zero, indicating no significant variation in AMH levels across the three method groups,given the exploratory nature of the study (Figure 3).

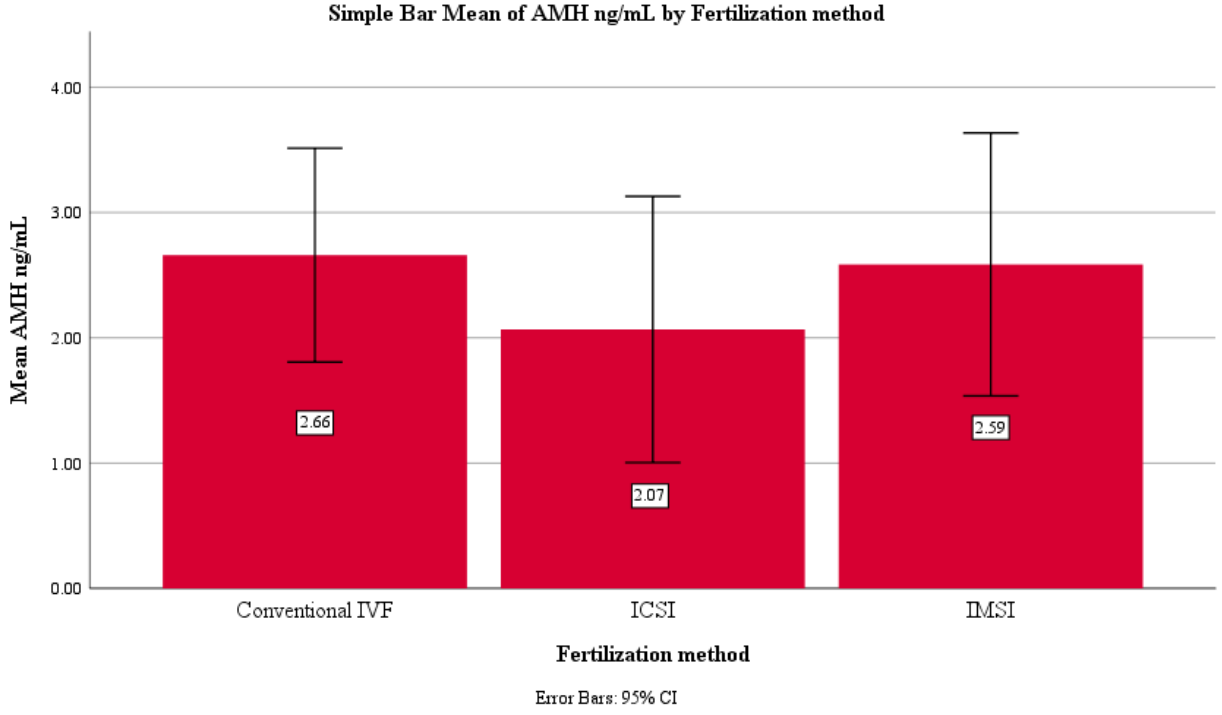

Figure 3. AMH levels by fertilisation method. Mean AMH values were not significantly different between the three fertilisation method groups.

ANOVA – Number of Euploid Embryos by Fertilization Method

Our final ANOVA tested whether the number of euploid embryos per IVF cycle differed significantly among the three fertilisation methods. The output showed that the mean values were 1.60 for conventional IVF, 1.67 for ICSI, and 1.57 for IMSI. In addition, the ANOVA demonstrated no significant differences among the three fertilisation method groups in the number of euploid embryos, $F(2,28) = 0.01$, $p = 0.990$.

The post-hoc LSD analysis confirmed that the methods were not statistically different. The difference between IVF and ICSI was –0.07 ($p = 0.913$), between IVF and IMSI was 0.03 ($p = 0.966$), and between ICSI and IMSI was 0.10 ($p = 0.896$). All post hoc comparisons had wide confidence intervals, included zero (Figure 4).

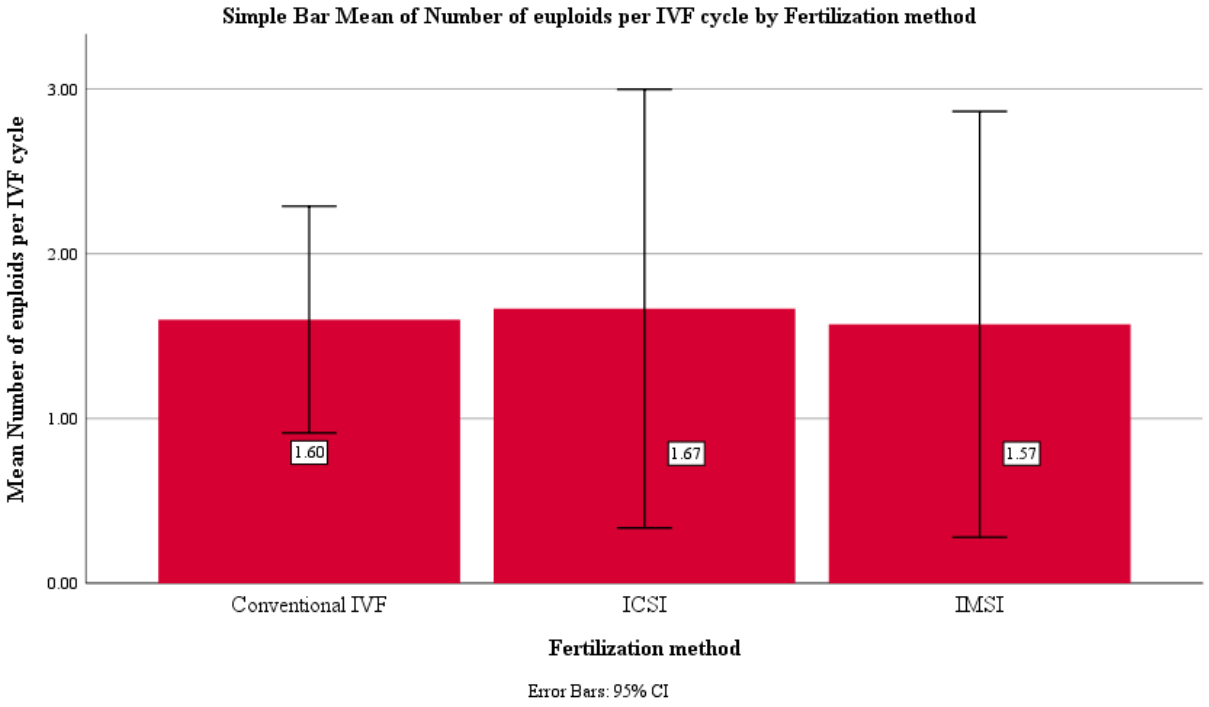

Figure 4. Number of Euploid Embryos by fertilization method. The mean number of Euploid Embryos was not significantly different between the three fertilization method groups.

Multiple Linear Regression

A multiple linear regression was performed to examine whether AMH values and maternal age could predict the number of euploid embryos per IVF cycle. The regression analysis showed that the overall model was statistically significant, $F(2,28) = 3.97$, $p = 0.030$, explaining 22.1% of the variance in the number of euploid embryos ($R^2 = 0.221$, adjusted $R^2 = 0.165$). The standard error of the estimate was 1.26.

Regarding the individual factors, AMH values showed a positive but non-significant association with the number of euploid embryos ($B = 0.27$, $SE = 0.18$, $p = 0.139$, 95% CI: –0.09 to 0.64). Furthermore, maternal age showed a negative, and non-significant association ($B = –0.11$, $SE = 0.07$, $p = 0.113$, 95% CI: –0.25 to 0.03). Therefore, none of the predictors included in the model reached statistical significance.

Although the overall model was statistically significant, the individual predictors did not reach significance in explaining the variation in the number of euploid embryos. However, the direction of the coefficients was clinically relevant: elevated AMH levels were associated with a higher number of euploid embryos. Furthermore, increased maternal age tended to be associated with fewer euploid embryos (Figure 5).

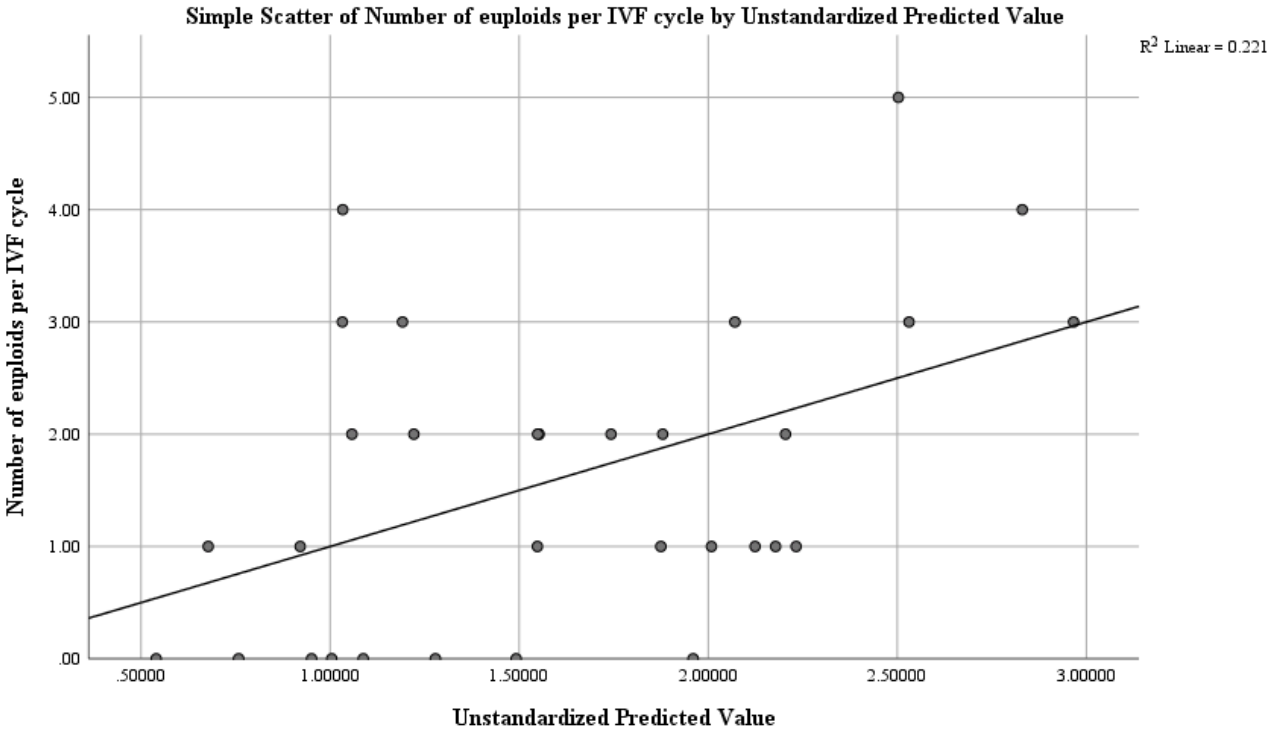

Figure 5. Scatterplot of observed and predicted euploid embryo counts. Predicted values were generated from the multiple regression model, which included AMH values and maternal age.

The following section presents a brief general introduction to contextualise DSS development**.**

4. Artificial Intelligence–Driven Euploidy Prediction in IVF: From Imaging to Embryo Selection

4.1. Applying Machine Learning to Predict Euploidy in Human Embryos: A Research for Optimal Models and Key Features

In recent years, artificial intelligence (AI) models have become an increasingly important component in the field of assisted reproductive technologies (ART), and are considered a modern and promising approach. They offer objective, rapid, non-invasive methods for the evaluation of human embryos. However, the use of computer-assisted analyses to predict the results of preimplantation genetic testing (PGT) is not a new idea. Over time, several attempts have been made to combine the analysis of embryonic morphokinetics with classical statistical methods to estimate the results of PGT.

In this context, machine learning (ML), as a branch of artificial intelligence, is emerging as a particularly useful alternative. It is based on algorithms capable of processing large volumes of data, learning from previous experiences and improving their performance over time, thus facilitating the achievement of more accurate classifications or predictions.

In the following study, a total of 539 embryos from 150 cycles of intracytoplasmic sperm injection (ICSI) fertilisation were analysed. Their morphokinetic parameters were evaluated using EmbryoViewer software (Vitrolife), integrated into the *EmbryoScope Plus* system, by manually marking the stages of cell division. Embryos were removed from the incubator on day four or in the morning of day five, for a fine laser incision in the zona pellucida. The blastocysts subjected to biopsy (n = 539) were subsequently classified into two categories: euploid (n=244) and aneuploid (n=295). The proportion of euploid embryos reported for each cycle was 0.47 (with a SD of 0.37).

Depending on the purpose of the analysis and the type of variables investigated, five classification models based on machine learning techniques were applied: random forest (RFC), an ensemble algorithm that combines several simple models, such as decision trees,which is suitable for both numerical and categorical data; gradient boosting from the scikit-learn library (GB, Python), another ensemble algorithm based on trees optimised by boosting; support vector machine (SVM), which projects the data into a space where they become separable; multivariate logistic regression; and the naïve Bayes (Gaussian) model, based on Bayes' theorem and the assumption of independence between variables.

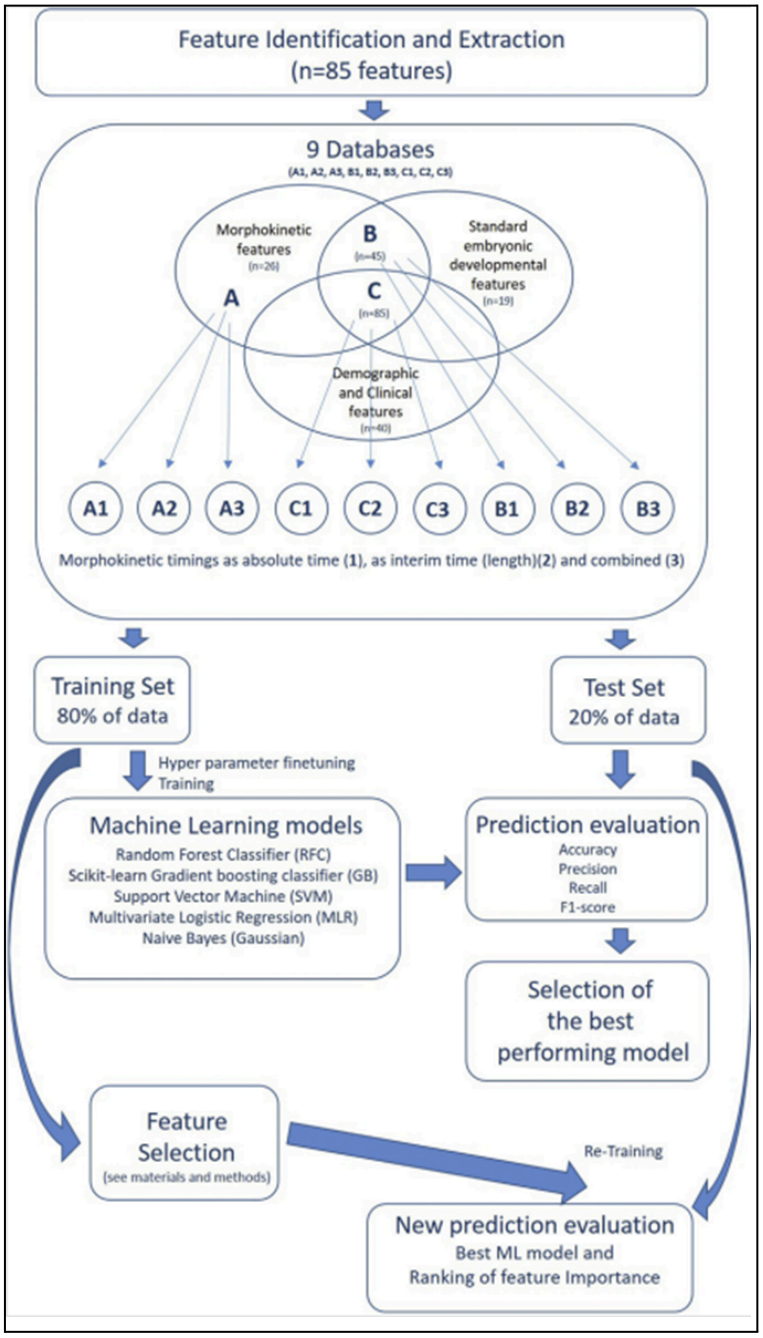

Figure 6. Machine learning- study design to predict embryo euploidy adapted by De Gheselle, S., Jacques, C., Chambost, J., Blank, C., Declerck, K., De Croo, I., Hickman, C., & Tilleman, K. (2022). Machine learning for prediction of euploidy in human embryos: In search of the best-performing model and predictive features. Fertility and Sterility, 117(4), 738–746. https://doi.org/10.1016/j.fertnstert.2021.11.029

Three distinct datasets were created: set A, consisting exclusively of morphokinetic parameters (26 in total); set B, which included both morphokinetic parameters and standard indicators of embryonic development (45 in total); and set C, which includes all these variables,with the addition of demographic, clinical and cycle-related information of the subjects (85 in total). Also, the morphokinetic parameters were represented in three ways: as absolute values, as intermediate values and as a combination of these (corresponding to subclasses 1, 2 and 3). Consequently, nine distinct datasets resulted: A1, A2, A3, B1, B2, B3, C1, C2 and C3, as shown in Figure 6.

For the training process, each dataset was randomly divided into two subsets: one for training (80% of the total) and one for testing (20%). Subsequently, several random splits were performed, with each model trained separately on 9 training subsets. To assess the stability and robustness of the model, the standard deviation of the accuracy obtained from the 10 random splits generated by 10-fold cross-validation was monitored.

The evaluation considered the overall accuracy, precision, correct identification rate (recall/sensitivity), F1 score (weighted average of precision and recall), and area under the ROC curve (AUC) for the machine learning models, analysed on each dataset. As a secondary measure, the ranking of variable importance for the best-performing model–dataset combination was analysed.

The RFC model achieved the best results in terms of accuracy (71%) and AUC (0.75) when trained and applied to the C1 dataset. The values for precision, sensitivity (recall), F1 score, and AUC were 66%, 86%, 75%, and 0.75, respectively. After the variable selection process and model retraining, the accuracy, sensitivity, and F1 score increased to 72%, 88% and 76%. Morphokinetic characteristics had the highest contribution to the prediction.In conclusion, the RFC model can predict euploidy with a satisfactory level of accuracy (over 70%), using a dataset that includes embryo morphokinetic parameters and standard indicators of embryonic development. (De Gheselle et al., 2022)

4.2. An Artificial Intelligence Approach for Predicting Embryo Euploidy Using Blastocyst Images from Diverse IVF Imaging Systems

The objective of the referenced study was to design and validate a robust artificial intelligence (AI)-based method for non-invasive assessment of the genetic status of embryos (ploidy) using static two-dimensional images. The proposed method aims to analyse the embryo as a whole and uses its phenotypic or morphological characteristics as indicators of development, especially in the context of severe genetic disorders.

The following study aimed to collect and analyse datasets necessary for the development of an artificial intelligence model capable of assessing the genetic status (ploidy) of embryos during in vitro fertilisation (IVF) procedures. The study included women patients aged 18 years or older who underwent IVF treatments between 2011 and 2021. Most of the data was obtained retrospectively, and an additional set was collected prospectively to validate, under double-blind conditions, the final AI model. The main dataset analysed consisted of embryo images, obtained by light optical microscopy, correlated with the results of the PGT-A genetic testing, considered the reference standard. Images from days 5, 6, and 7 of embryo culture were included, but only those from day 5 were used for training and model development of the artificial intelligence.

To be eligible, images had to be from in vitro-cultured embryos and taken with standard optical microscopy systems before biopsy or cryopreservation. A minimum resolution of 480 × 480 pixels was also required, so that the embryo was fully visible in the frame and the focus was on the inner cell mass (ICM). Before the analysis stage, the images underwent an extensive preprocessing procedure , inspired by VerMilyea et al. (2020), but improved by integrating modern computer vision techniques, as follows:

- Step 1: The alpha channel was removed from the images, and they were converted to a standard three-channel format.

- Step 2: Each image was converted to a tensor, a format required for use as input in deep learning-based artificial intelligence models.
- Step 3: To ensure the uniformity of the input data, the images were expanded to square dimensions. The classic padding method previously used in VerMilyea et al. (2020) was replaced by a deep learning model from the Region-Based Convolutional Neural Networks family, namely Faster R-CNN, recognised for its ability to efficiently handle background noise (Ren et al. (2015)).
- Step 4: The images were cropped according to the final bounding box identified, thus removing unnecessary background and positioning the embryo in the centre of the frame. The previous method based on the elliptical Hough transform was replaced by the Faster R-CNN approach described previously.
- Step 5: For some models, image segmentation was optionally applied. This allows the separation of different regions of the embryo, highlighting either the zona pellucida or the intra-zonal cavity (IZC) — i.e. the interior of the blastocyst, including both the inner cell mass (ICM) and the trophectoderm. The classic "snake" segmentation method (active contour models), used in VerMilyea et al. (2020), was replaced by a more efficient and robust semantic segmentation technique called U-Net.

During the training and selection process, the CNN architectures that performed best for determining the ploidy status of embryos were ResNet and DenseNet. Two main techniques were integrated into the development of the AI model for genetic analysis that go beyond the approaches used in the study by VerMilyea et al. (2020): untrainable data cleaning (UDC) and distillation. UDC is an AI method used to detect mislabelled data by eliminating images that many AI models fail to classify correctly during training. This happens either because the images are of very poor quality and do not contain features relevant for classification (noisy data), or because they present features that indicate the opposite of the assigned label, contrary to the trend of most of the data in the set (mislabelled data).

The final ensemble model proposed in this study was composed of three deep learning models, selected through a voting strategy that combines majority rule with averaging of results. Each component model in the ensemble performed binary classification and used cosine annealing to adjust the learning rate, a stochastic gradient descent optimiser, and a uniform normalisation scheme applied to each input image.

The final structure of the ensemble was as follows:

- Model 1: A DenseNet-161 was used in its full version (without segmentation), trained on a set of images processed with UDC.
- Model 2: A full ResNet-50 (without segmentation) was trained on images with UDC applied in the same way. Two teacher models were involved in the training process: a DenseNet-161 and a ResNet-50
- Model 3: A DenseNet-121 of IZC type was trained on a dataset containing images processed with UDC using the IZC method.

The overall accuracy of euploidy prediction, assessed on a "blind" test set, was 65.3%, and the sensitivity reached 74.6%. After removing low-quality and incorrectly labelled images from this set, the overall accuracy increased to 77.4%. This performance may be relevant in clinical settings where confounding factors, such as variability in PGT-A testing, are controlled.

A significant positive correlation was observed between the AI-generated score and the proportion of euploid embryos. Thus, embryos with very high scores (9.0 - 10.0) were twice as likely to be euploid compared with those with low scores (0.0 - 2.4).

When the genetic AI model was applied to rank embryos in a batch, the chance that the top-ranked embryo was euploid was 82.4%. This represented a 26.4% improvement over random classification and a 13–19% improvement over the Gardner score-based method. The probability increased to 97.0% when considering the possibility that one of the first two embryos was euploid, while the probability that both were euploid was 66.4%.

Further analyses indicated that the AI model scaled well across patient demographics and could be used to assess both day 6 embryos and images from different time-lapse systems. The results also suggest that the model may differentiate mosaic embryos based on the degree of mosaicism (Diakiw et al., 2022).

4.3. Prediction of embryo ploidy status from time-lapse data using an AI-based euploid prediction algorithm

In the field of assisted reproductive technologies (ART), the identification of embryos with the highest developmental potential has remained the central focus of research and is also the main objective of embryologists. Over time, numerous methods of embryo selection have been proposed, which can be broadly classified into two categories: invasive and non-invasive. Non-invasive methods include, among others, proteomic and metabolomic studies, as well as the analysis of embryonic development dynamics. Compared to invasive techniques, non-invasive approaches are generally considered to be closer to natural processes and to have a higher level of safety.

Among non-invasive methods, time-lapse technology (TLT) provides extensive information on how embryonic development evolves over time. This allows embryologists to move beyond the traditional static assessment and adopt a dynamic analysis, significantly contributing to the selection of the most suitable embryos.

The objective of this study was to develop a model called euploidy prediction algorithm (EPA), capable of estimating embryonic ploidy based on TLT data, thus contributing to the improvement of the embryo selection and classification process within standard IVF-ET cycles.

In this single-centre cohort study, a total of 469 PGT cycles and 1803 blastocysts were analysed. Embryo images were obtained on days 5 or 6 after fertilisation, prior to biopsy or cryopreservation. All embryos were evaluated on the morning of the third day after oocyte collection. They were then transferred to a specific medium for blastocyst development, where they remained in culture until day 5/6. The blastocyst biopsy procedure was performed on these days (5 or 6), preceded by the creation of a small opening in the zona pellucida using a laser. A mechanical sectioning technique was then applied to harvest 3 to 6 cells from the trophectoderm.

The algorithm was essentially structured in three distinct components. The first component was designed to extract relevant features from the images that constitute the embryonic sequence. The second component deals with the standardisation of features from both embryonic and clinical data. The third component is dedicated to integrating these features and making predictions using the model.

At the end of the study, 415 cycles and 1803 blastocysts were included. All 1803 blastocysts were biopsied and sequenced, and results were obtained for 1779 of them, corresponding to a detection rate of 99%. The analysis revealed that 617 blastocysts were euploid, 873 were aneuploid, and 289 showed mosaicism.

The development of the EPA model involved testing several types of datasets. In the first step, using a single image taken just before biopsy, at the blastocyst stage, an AUC of 0.57 was obtained. Subsequently,the use of a video from the blastocyst stage (corresponding to the interval from 70 hours to before biopsy) resulted in an AUC of 0.60. Extending the analysis to full videos, covering both cleavage and blastocyst stages, increased the AUC to 0.63.

Introducing additional variables, such as patient age and blastocyst age (day 5 or day 6), further improved the model performance, achieving an AUC of 0.72. Furthermore, including kinetic parameters allowed the achievement of an AUC of 0.77 for euploidy prediction on the test set. In the final step, to make the algorithm more efficient, the use of the video material was optimised by selecting only relevant time intervals, which increased the AUC to 0.80.

In conclusion, the artificial intelligence model called EPA was able to accurately estimate embryo ploidy based on information provided by the TLT. It is expected that in the future, this system may be widely used in patients undergoing in vitro fertilisation and embryo transfer

(IVF-ET) procedures, providing embryologists with additional, non-invasive tools to identify and select the optimal embryo for transfer (Huang et al., 2021).

The current study aims to extend this paradigm by developing a clinically oriented, explainable decision support system designed to translate statistical information into practical tools for fertility counseling, building on these advances in AI-based embryo evaluation.

5. Implementation, Clinical Utility, and Ethical Considerations of the EuploPredict Application

To bridge the gap between complex statistical modelling and patient-centred counselling, we developed EuploPredict, an explainable AI-driven decision-support system. The application was developed using *Google AI Studio* and built on a modern *React 19* and *TypeScript* architecture,and was designed to synthesise raw clinical biomarkers into clear, actionable probabilistic data. This enables clinicians to provide more nuanced, data-driven insights during patient consultations.

The platform is available for clinical and educational purposes at https://euplopredict.edusoft.ro.

Google AI Studio is an advanced prototyping environment that allows developers to leverage the Gemini generative models to handle complex data reasoning. For healthcare applications, it can facilitate the creation of "explainable AI" by allowing developers to fine-tune how models interpret and verbalise clinical data. This helps ensure that the output remains consistent, transparent, and aligned with the rigorous standards required for medical decision support.

5.1. User Interaction and Methodology

The interface is engineered to visualise a longitudinal success roadmap based on an attrition modelling engine. As illustrated in Figure 7, the user interaction follows a structured flow:

1. Input of clinical parameters: The user adjusts three primary sliders—Maternal Age, AMH Level, and Antral Follicle Count (AFC). These parameters serve as the independent variables that drive the stochastic model.

2. Mathematical Framework: The core "Euploid Chance" score is calculated using a binomial probability model. If r represents the age-adjusted euploidy rate (derived from the benchmark curve in Figure 8) and b represents the number of expected blastocysts (calculated via AFC/AMH attrition), the probability P of obtaining at least one (≥ 1) euploid embryo is defined by the formula:

$$P(\text{success}) = 1 - (1 - r)^b$$

This formula, detailed in the "The Math of Success" section of the interface, explains how even with a high embryo yield, the cumulative success remains tethered to the age-dependent quality factor r.

Yield Prediction and Navigation: The "Embryo Yield AI" module provides a probability distribution of retrieving 0 to 3+ euploid embryos. Furthermore, the IVF Outcome Navigator (Figure 7, centre) allows for a comparative scenario analysis, modelling the "Opportunity Cost" of delaying treatment by three years.

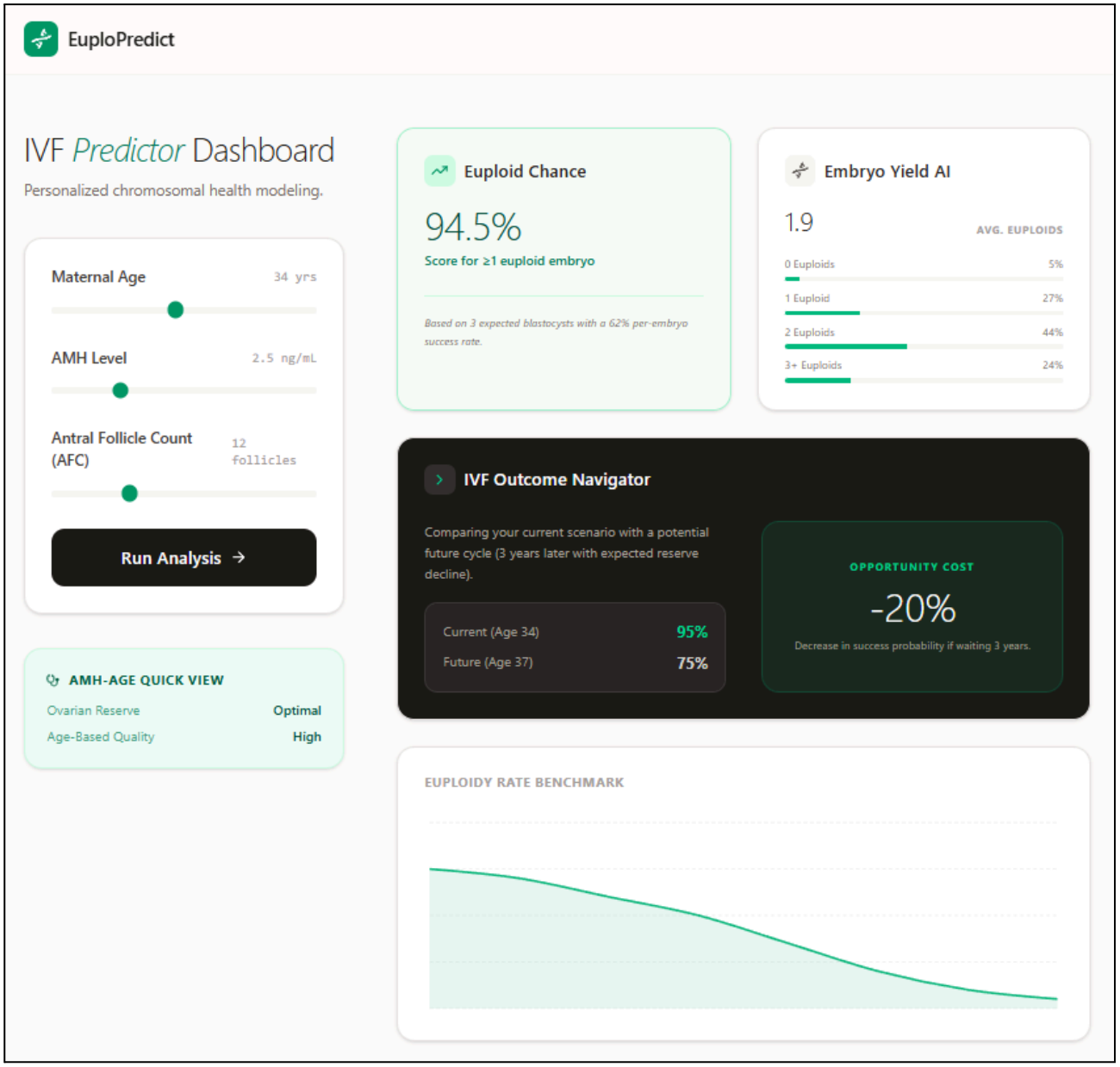

Figure 7 The EuploPredict Interactive Dashboard: Clinical Parameter Input and Predictive Analytics Interface

5.2. Ethical Framework and "explainable AI"

The deployment of predictive algorithms like EuploPredict necessitates a robust ethical framework centred on transparency and the mitigation of "algorithmic paternalism." A primary ethical risk in medical AI is the "black box" effect, in which patients receive a success rate without understanding the underlying biological drivers.

EuploPredict mitigates this through its "AMH-Age Quick View" (Figure 7, bottom left). By explicitly decoupling ovarian reserve (quantity) from age-based chromosomal health (quality), the tool prevents the common misconception that a high AMH level can "fix" the biological realities of advanced maternal age.

It is ethically imperative that such models are framed as probabilistic aids rather than deterministic guarantees. By presenting even a 5% chance of "0 Euploids" in high-prognosis cases, the interface promotes a grounded, transparent informed consent process. While the model utilises data derived from SART and CDC clinical registries, it is intended to augment, not replace, the

patient-specialist relationship, ensuring that technology empowers patient autonomy through clarity and data-driven empathy.

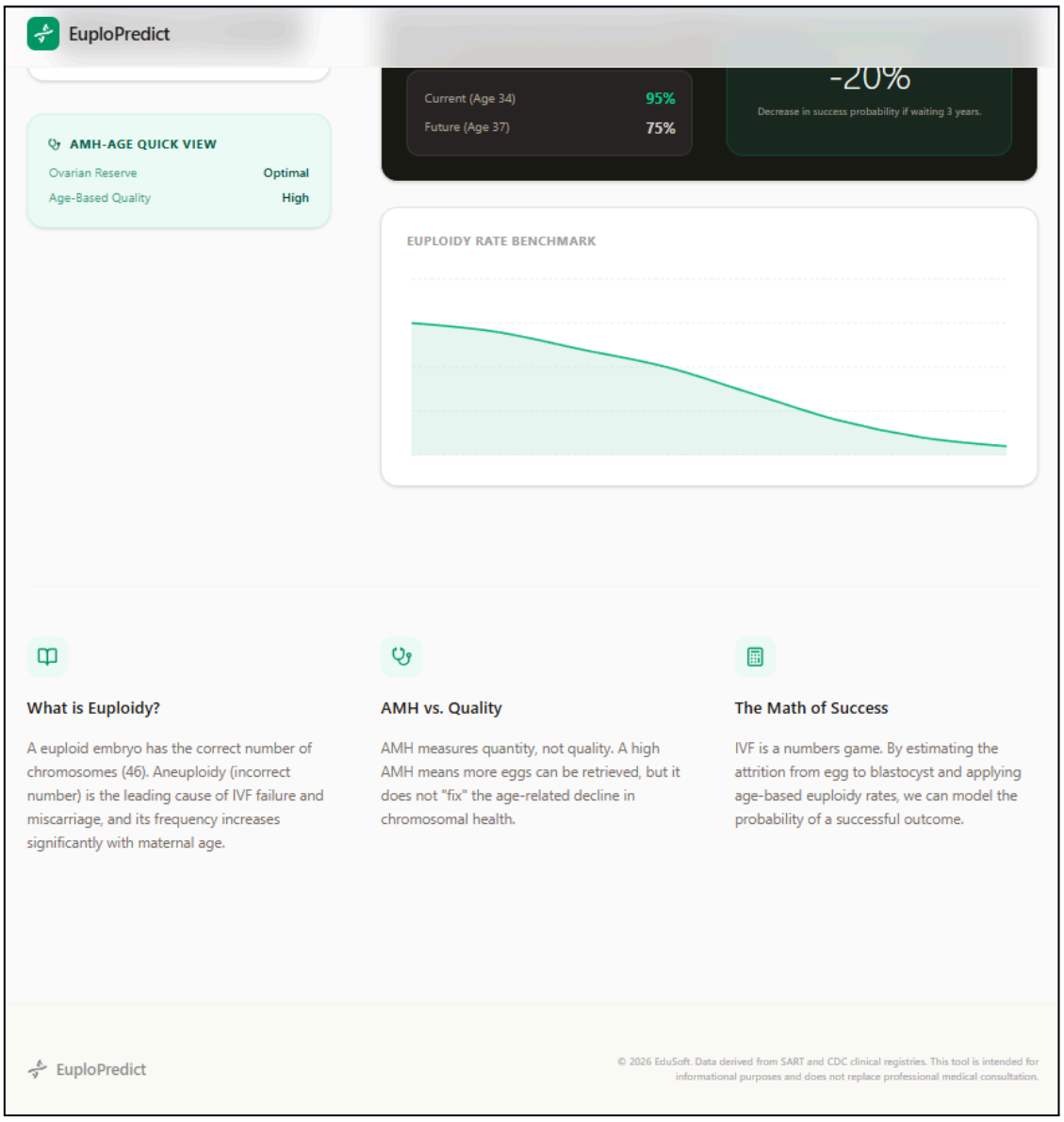

Figure 8. Analytical Benchmarking and Educational Framework: Age-Dependent Euploidy Rates and Attrition Mathematical Modeling

6. Discussion

This study examined how the number of euploid embryos is affected by various factors such as maternal age, AMH levels, and the fertilisation method. The results of our study showed that younger women present higher AMH levels and produce more euploid embryos. These findings are consistent with studies which report a significant decline in ovarian reserve and oocyte competence with increasing age (Broekmans, Soules, and Fauser, 2009). The molecular mechanisms that may explain these findings are linked to potential increases in meiotic errors, various mitochondrial dysfunctions, and meiotic spindle instability (Hassold & Hunt, 2001). Therefore, our findings may be explained by these biological patterns. In addition, the evidence obtained in this manuscript supports the idea that maternal age plays a central role in determining embryo chromosomal competence.

In contrast, the fertilisation method (IVF, ICSI, IMSI) did not influence AMH levels or the number of euploid embryos. More specifically, in our ANOVA model, when we analysed whether AMH values or the number of euploid embryos differed significantly across the three fertilisation method groups, the results were non-significant. However, these results are consistent with previous studies demonstrating that different laboratory techniques do not alter the intrinsic chromosomal quality of the oocyte or embryo (Lemseffer et al., 2022). The possible explanation might be connected to the fact that the ICSI and IMSI methods are indicated for specific sperm-related issues and, therefore, without severe male-factor infertility, these techniques cannot improve euploidy rates in women (Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology, 2020). Our results support the probable underlying mechanisms, suggesting that embryo chromosomal status is primarily driven by female factors rather than by the insemination technique (Nagaoka, Hassold, and Hunt, 2012).

The multiple regression model in our statistical analysis showed that AMH values and maternal age together explained 22.1% of the observed variance in the number of euploid embryos. Although neither predictor reached statistical significance, the direction of the measured associations was clinically coherent. The results reported in the literature were consistent with our findings. Various studies have demonstrated that both age and AMH values contribute to the probability of obtaining euploid blastocysts (Vijay et al., 2022). These conclusions may be explained by the mechanisms through which AMH reflects the size of the growing follicle pool. Furthermore, AMH values correlate with the number of oocytes retrieved. This association may increase the absolute chance of obtaining euploid embryos, even if the proportion of euploidy per oocyte remains relatively stable (Dewailly et al., 2014; Broer et al., 2013; Labarta et al., 2017). This biological rationale may explain the significance of our overall regression model and the positive trend observed for the two individual predictors, age and AMH values.

The lack of statistical significance of our individual predictors in our model may be due to the limited sample size and the inherent variability of ovarian response. This hypothesis is supported by larger cohort investigations that have demonstrated stronger independent effects of AMH values on the number of euploid embryos, particularly when controlling for age across different regression models (Tal and Seifer, 2017; Choi et al., 2011).

Therefore, AMH values may represent an important contributing factor in the observed variation in the number of euploid embryos. The available literature demonstrates that AMH may influence the number of euploid embryos through molecular mechanisms that maintain chromosomal stability during follicular development (Fraire-Zamora et al., 2023). In addition, AMH values have been shown to interact with intracellular signalling systems that control the timing of follicle activation (Durlinger et al., 2002). Therefore, through these two processes, higher levels of AMH may reduce the accumulation of age-related chromosomal errors.

Furthermore, studies suggest that AMH can also interact with various processes involving granulosa cells (Dilaver et al., 2019). Some of these processes involving granulosa cells are relevant to our study. The pathways of these associations include the expression of factors involved in spindle organisation and chromosome alignment. These molecular processes are important because, through these physiological mechanisms, higher AMH values may offer a more stable setting for maintaining chromosomal integrity during follicular growth. This stable environment can significantly increase the likelihood of producing euploid embryos.

These additional molecular mechanisms are consistent with our findings. In our statistical models, higher AMH values were positively associated with a greater number of euploid embryos. This observed relation aligns with the idea that higher AMH levels in the bloodstream support chromosomal stability during follicular development. At the same time, our results show that maternal age was negatively associated with the number of euploid embryos. These findings are also compatible with the demonstrated age-related decline in these protective mechanisms. Taken together, all these biomolecular processes may provide important explanations for the overall pattern observed in our regression analysis.

Overall, this study supports the idea that maternal age is the dominant influence on embryo chromosomal competence. Furthermore, our findings suggest that AMH might be useful, especially for estimating ovarian reserve. However, across different regression models, AMH values might have a modest, context-dependent predictive value for explaining the variance in the number of euploid embryos. Therefore, future investigations with larger sample sizes and additional biological markers are needed to help redefine these prediction models.

Artificial intelligence is being explored in the field of assisted reproduction as a non-invasive, data-driven approach to estimate embryo ploidy using imaging technologies and time-lapse sequences. In this context, by evaluating morphological and morphokinetic characteristics using advanced models, such as convolutional neural networks (CNN) and machine learning algorithms, AI may contribute to improving the accuracy and objectivity of embryo selection. Consequently, these methods have the potential to support clinical decision-making, facilitating the selection of euploid embryos and potentially improving in vitro fertilisation (IVF) outcomes. Building on these advances, by synergising retrospective data with explainable AI, the EuploPredict framework may offer a transparent, data-driven approach to fertility counseling, bridging the gap between statistical analysis and patient-centred clinical practice.

While the linear regression model provided a statistically significant foundation, the decision-support system extends this utility by offering an accessible visual interface. This may allow for the translation of complex correlations between maternal age and AMH into a tangible probability score, thereby facilitating the clinical counselling process and the effective management of patient expectations.

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