Predicting Children's Myopia Risk: A Monte Carlo Approach to Compare the Performance of Machine Learning Models

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Abstract: This study presents the initial results of the Myopia Risk Calculator (MRC) Consortium, introducing an innovative approach to predict myopia risk by using trustworthy machine-learning models. The dataset included approximately 7,945 records (eyes) from 3,989 children. We developed a myopia risk calculator and an accompanying web interface. Central to our research is the challenge of model trustworthiness, specifically evaluating the effectiveness and robustness of AI (Artificial Intelligence)/ML (Machine Learning)/NLP (Natural Language Processing) models. We adopted a robust methodology combining Monte Carlo simulations with cross-validation techniques to assess model performance. Our experiments revealed that an ensemble of classifiers and regression models with Lasso regression techniques provided the best outcomes for predicting myopia risk. Future research aims to enhance model accuracy by integrating image and synthetic data, including advanced Monte Carlo simulations.

1 INTRODUCTION

1.1 The Role of AI/ML/NLP in Diagnosing the Risk of Myopia in Children

Global Perspective: The increasing prevalence of myopia, particularly among children, represents a significant public health challenge (World Health Organization, 2015). Characterized by the eye's inability to focus on distant objects, myopia not only compromises the quality of life but also predisposes individu-

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als to serious ocular conditions and visual impairment later in life (Haarman et al., 2020). Over the past few decades, the prevalence of myopia has increased on a large scale, especially in East and Southeast Asian countries, where the prevalence of myopia in young adults is 80-90%, and an accompanying high prevalence of high myopia in young adults (10-20%) (Morgan et al., 2012; Morgan et al., 2018). Several studies have shown connections of myopia with parental myopia, longer education, more near work time , and less time spent outdoors (Huang et al., 2015; Pärssinen and Kauppinen, 2022). In addition to the above factors, numerous other factors can influence the onset and progression of myopia. Due to those factors, there is great individual variation in the development of myopia and its progression. For the prevention of myopia and slowing its progression, it is of great interest to have prediction tools to know in advance which children are at risk of developing myopia. The methods developed in this manuscript aim to improve the predictability of the development of myopia.

Application to Myopia Diagnosis: In myopia management, these technologies may have a crucial role in the development of screening tools that accurately predict the onset and progression of myopia in children. AI algorithms can analyze vast datasets, identifying patterns that precede myopia development. For instance, machine learning models have been trained to predict myopia based on biometric data, environmental factors, and genetic data. These models are increasingly being utilized to alert healthcare providers and parents for early signs of myopia, enabling timely intervention.

Challenges in Implementation: Despite their potential, the deployment of AI/ML/NLP in myopia diagnosis is not without challenges. Issues such as data privacy, the need for large and diverse datasets for model training, and the integration of these technologies into existing healthcare infrastructures are ongoing concerns. Moreover, ensuring these advanced tools are accessible across various socioeconomic backgrounds remains a hurdle to achieving widespread benefit.

1.2 Selected Initiatives

United States. In response to the myopia surge among children, the United States has launched AI-powered initiatives that intertwine research with practical applications. The National Eye Institute (NEI) has catalyzed this movement by funding research into AI models capable of predicting myopia progression, with recent studies demonstrating a 30% improvement in early detection accuracy. School-based programs have seen an infusion of AI, particularly during the COVID-19 pandemic, where increased screen time has been linked to a marked rise in myopia cases (Kuehn, 2021; Ma et al., 2022). These programs benefit from collaborations such as the one between the American Ophthalmological Society and tech giants, aiming to create standardized screening protocols across various states.

China, Singapore, Japan, and South Korea. The Far Eastern countries have established a collaborative network, the East Asian Ophthalmology Alliance (EAOA), to facilitate the exchange of AI research and technologies. Groundbreaking studies, like China's AI-based analysis of retinal images, have reported an 80% accuracy in predicting myopia, showcasing the power of collaborative data sharing and algorithm development. For example the (Foo et al., 2023). Singapore's national program, integrating genetic data, has seen a 20% increase in predictive precision post-COVID-19, addressing the lifestyle changes that have potentially accelerated myopia rates in children. This collective effort underscores the potential for an international standard in myopia risk assessment.

Europe. Europe's integration of AI in myopia detection is evolving, with the European Vision Institute leading multi-country studies that emphasize early biomarker identification. Despite challenges with data fragmentation, recent EU directives have sought to unify health data standards, promoting research like the Pan-European Myopia Study (PEMS), which reported a 15% increase in myopia detection since the pandemic began. The GDPR (General Data Protection Regulation), while stringent, is adapting to foster secure data sharing for AI applications, with the recent establishment of the European Health Data Space aiming to facilitate this shift.

1.3 Machine Learning Models Trustworthiness as an Imperative in Healthcare Applications

Trustworthiness in machine learning models transcends a mere desirable quality, becoming imperative in sensitive applications like healthcare. Users, particularly medical professionals, must be confident in the models' predictive capabilities to make crucial clinical decisions. Trustworthiness is a composite measure, including but not limited to, effectiveness, robustness, fairness, interpretability, reliability, transparency, security, replicability, scalability, and compliance with regulatory, environmental, and social standards. In medical contexts, effectiveness equates to predictive accuracy and clinical relevance, while robustness reflects the model's consistency across diverse patient demographics and datasets. These are the bedrock of operational reliability for clinical AI/ML applications. Under this directive, the ML models should aim to eliminate bias, ensuring equitable health outcomes. We implemented privacy safeguards, including advanced encryption and data management protocols, aligning with the HIPAA (Health Insurance Portability and Accountability Act) standards. This comprehensive approach to trustworthiness, grounded in the highest government guidelines, aims to redefine the application of AI in healthcare, ensuring machine learning models fulfill public service while adhering to safety and ethical norms. Recognized authorities such as the American Medical Informatics Association AMIA and Institute of Electrical and Electronics Engineers (IEEE) have long stressed the significance of trustworthiness in clinical AI/ML implementations. The FDA is delineating regulations for AI in diagnostics, emphasizing the importance of model validation and continuous monitoring. The NIH promotes open science for model replicability and independent verification, highlighting the necessity for transparency and security in protecting patient data and preventing system misuse.

2 METHODOLOGY

2.1 MRC Approach to Trustworthiness of Machine Learning Models

The Myopia Risk Calculator Consortium (MRC) recognizes the complex imperative of trustworthiness in machine learning models, especially within the delicate context of pediatric ophthalmology. Our systematic, phased approach harnesses the collective expertise of international ophthalmology experts, ensuring that the project embodies a truly interdisciplinary collaboration. Data scientists, clinicians, and ophthalmologists contribute uniquely, combining clinical insights with advanced computational methods to shape our methodology. The main assessment ML model methods proposed in the MRC methodology are the following:

2.1.1 Applications of Monte Carlo Methods

Our use of Monte Carlo (Robert and Casella, 2013) simulations extends beyond data augmentation; it encompasses the creation of synthetic datasets that mirror complex real-world variations, thus supporting robust model training and validation. The application of Monte Carlo Cross-Validation (MCCV) and bootstrapping techniques (Kohavi, 1995) underpins our models' reliability, providing transparent and statistically significant measures of performance.

2.1.2 Confidence Interval Evaluation

Performance evaluation of our models transcends point estimates, with confidence intervals drawn from MCCV-derived statistics, ensuring a replicable and trustworthy assessment of model reliability. It is worth to emphasize that:

- The application of Monte Carlo methods coupled with confidence interval evaluations spearheaded by MRC sets a proposal of new standards in the evaluation of ML models' effectiveness and robustness for medical applications, championing their reliability and transparency.
- The techniques based on MCCV showcased herein have affirmatively passed the initial litmus test in the ongoing pursuit of a comprehensive trustworthiness assessment framework for medical ML applications.

As we have navigated the initial phase, our traditional ML models, applied to alphanumeric data, have been meticulously crafted to predict myopia risk in children. This groundwork paves the way for incorporating more intricate data types, such as image data, and sophisticated methods. In particular, the WisTech approach to Interactive Granular Computing (IGrC) (Jankowski, 2017; Polkowski and Artiemjew, 2015; Lin et al., 2023) will be explored for its potential to dissect and utilize causal relationships, enhancing our model's predictive precision through nuanced 'what-if' scenario analyses. In the critical domain of data privacy, the consortium adheres to stringent protocols aligned with global standards such as GDPR and HIPAA, ensuring that our synthetic data generation process upholds the utmost patient confidentiality and security. Our methodology's integrity is underpinned by an ethical framework that guides synthetic data application, with oversight from an institutional review board dedicated to maintaining medical ethics at the forefront of our efforts. While the current focus is on effectiveness and robustness, we are laying a comprehensive foundation for a multi-dimensional trustworthiness framework. This framework, adaptable across the trust spectrum, is crafted to meet the apex of medical practice standards. Anticipating future clinical validation trials, we are preparing for the critical phase of practical application, aiming to integrate our models seamlessly into the medical community for the benefit of pediatric patient care.

3 EXPERIMENTAL PART

3.1 Performance of the MRC (Version 1.0)

Data and Variables. Data for 3989 children (7945 eyes) were used for the analysis of this study. Children from the Shahroud Schoolchildren Eye Cohort Study were included in this study. It is a prospective cohort study, conducted in Shahroud, northeast Iran, that recruited 5620 children aged 6 to 12 in 2015 (baseline), with a follow-up in 2018 (Emamian et al., 2019). Cycloplegic refractions were conducted to detect myopia at baseline and its progression after three years. A questionnaire was administered to collect data such as age, gender, near work time, outdoor time, living place, parental myopia, and mother's education. Ocular biometrics were measured using the Allegro Biograph. These are crucial risk factors to understand and predict myopia.

In our study, we categorized variables for ML models into four attribute classes:

1. **Effortless Attributes:** These are attributes that can be calculated without advanced medical knowledge or medical instruments. Intuitively, the values of these attributes should be readily available.
2. **Advanced Attributes:** These are attributes that are not considered effortless, requiring more specialized knowledge or equipment.
3. **Non-Cycloplegic Attributes:** These are attributes that do not require cycloplegic refraction.
4. **Cycloplegic Attributes:** These attributes require cycloplegic refraction, indicating that they relate to an eye examination procedure where the eye's ciliary muscle is temporarily paralyzed to determine refractive error.

Dependent Variables and Decision Classes. The main outcome variable of this study was the three-year spherical equivalent (SE2). The value of SE2 is equal to the final SE (after 3 years). Machine learning techniques were employed to create binary classifiers for myopia risk prediction and regression models for SE2 prediction. We focus on the following decision classes for binary classifiers:

- M01: The SE2 value will be $\leq$ -0.5 D.
- M02: The SE2 value will be $\leq$ -4.0 D.
- M05: The SE2 value will be $\leq$ -1.0 D.

In these variants, the values -0.5, -1 and -4 are the thresholds for creating a binary decision. In this way, binary decision systems are formed to model the disease prediction process.

For the regression models, we use SE2 as the dependent variable. In the considered cases, the variable SE2 depends on the independent variables derived from the initial examination (baseline).

Model Evaluation Methodology. We used an aggregation of Monte Carlo cross-validation and bootstrap methods for assessing models' effectiveness and robustness. We calculated bootstrap confidence intervals for the following standard statistics: classifier quality measures such as Sensitivity, Specificity, Precision, F1, Gm, AUC (Tharwat, 2021), and weighted averages and regression quality measures like MSA, MAE, and R^2 (Hastie et al., 2009).

Let us denote by S one of the above statistics. In our project, we use the following calculation methodology for the value of the statistic S measuring the model performance (e.g., Sensitivity, Specificity, Precision, AUC, F1, Gm, MSA, MAE, and R^2 (Hastie et al., 2009), etc.):

1. Generate 20 Monte Carlo-simulated cross-validations using 10 folds for model evaluation. In other words, we obtain 200 evaluation folds for model evaluation (i.e., ten times twenty). This leads to 200 values of the statistic S measuring the model performance (i.e., for any evaluation model from 200).
2. As a result of the above first step, we have 200 values of S. If it is necessary, then you may use more iterations for Monte Carlo-generated cross-validations and employ Markov Chain Monte Carlo (MCMC) methods for better approximating the empirical distribution of S (Robert and Casella, 2000).
3. Calculate the percentiles (Eubank, 2006) for the generated empirical distribution for S.
4. For each percentile p, report the Qp(S) value (e.g., Q02(Sensitivity)). For example, if S is the measure of AUC (i.e., Area Under the Curve), then Q25(AUC) is the first quartile of AUC, Q50(AUC) is the median, and Q75(AUC) is the third quartile.
5. Primarily, focus on Q05(S), Q50(S), and Q95(S).
6. Apply percentiles from the empirical distribution to determine confidence intervals for the statistic S for the required significance level.

The quality of classifiers planned for deployment in a specific world region should reflect the level of medical care in a particular area. Generally, the most important feature is always the sensitivity, which is as high as possible on an acceptable level of precision (and sometimes other parameters). Conditions may be imposed on Precision based on physician availability. For example, we may prefer classifiers with very high Precision if doctors are unavailable. After the discussion, we concluded that the primary assessment of the classifiers should be using a weighted average, which we will symbolically denote as *SimWAvr*, preferably according to the formula below.

$$SimWAvr = \frac{1}{2} Q05(Sensitivity) + \frac{1}{4} Q05(Specificity) + \frac{1}{4} Q05(Precision). \tag{1}$$

Below, we present the classification results of classifiers sorted by *SimWAvr* values.

Results. The effectiveness of traditional ML methods, such as Logistic Regression (LR), k-Nearest Neighbor (kNN), Support Vector Machines (SVM), Random Forest (RF), Gradient Boosting (GB), and Artificial Neural Network (ANN), was verified. In addition, the models were constructed as an aggregation of traditional models, i.e., ensemble models.

The best results for the binary classifiers of the defined decision classes M01, M02, and M05 are as follows.

Table 1: Selected best results - a **classification** problem. Using **Cycloplegic** Attributes; BestMet = Best ML model method, RF = Random Forest, SVM = Support Vector Machine, LR+RF=Ensemble model of Lasso Regression and Random Forest. See visualisation in Fig. 1.

Statistic	M01	M02	M05
BestMet	**RF**	**SVM**	**LR+RF**
SimWAvr	73%	64%	74%
Q05 (AUC)	86%	86%	87%
Q50 (AUC)	90%	94%	92%
Q05 (Sens)	79%	72%	79%
Q50 (Sens)	87%	91%	89%
Q05 (Spec)	91%	97%	94%
Q50 (Spec)	93%	98%	96%
Q05 (Prec)	44%	16%	44%
Q50 (Prec)	51%	22%	53%

In addition to binary classifiers, we have examined regression models. We used SE2 as the dependent variable for regression models in this case. The variable SE2 depends on the independent variables derived from the initial examination. Analogously to binary classifiers, we analysed two types of models:

1. Type 1: Using cycloplegic independent variables.
2. Type 2: Using only non-cycloplegic independent variables.

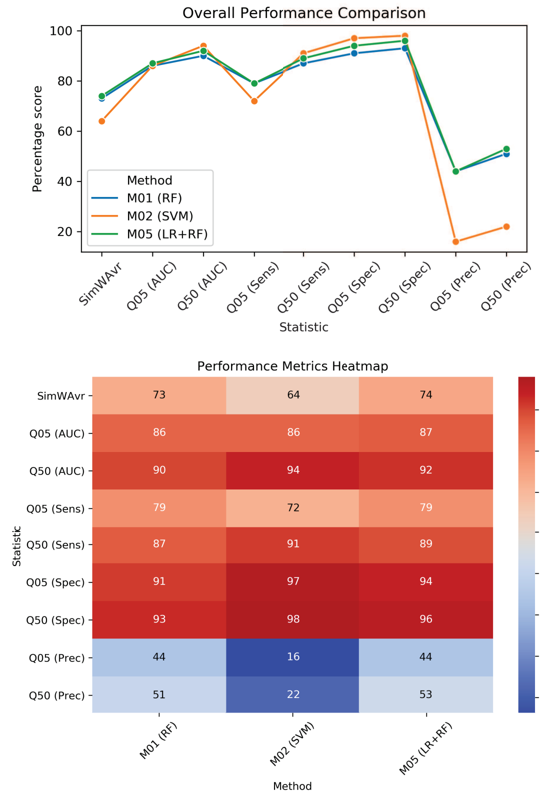

Figure 1: Visualisation of the results for Table 1: Using **Cycloplegic** Attributes; BestMet = Best ML model method, RF = Random Forest, SVM = Support Vector Machine, LR+RF=Ensemble model of Lasso Regression and Random Forest.

Table 2: Selected best results - a **classification** problem. Using **Non-Cycloplegic** Attributes; BestMet = Best ML model method, LR+RF=Ensemble model of Lasso Regression and Random Forest, SVM = Support Vector Machine, RF = Random Forest. See visualisation in Fig. 2.

Statistic	M01	M02	M05
BestMet	**LR+RF**	**SVM**	**RF**
SimWAvr	66%	72%	68%
Q05 (AUC)	80%	91%	85%
Q50 (AUC)	85%	99%	90%
Q05 (Sens)	71%	84%	81%
Q50 (Sens)	82%	99%	90%
Q05 (Spec)	87%	98%	86%
Q50 (Spec)	89%	99%	88%
Q05 (Prec)	33%	20%	24%
Q50 (Prec)	38%	28%	29%

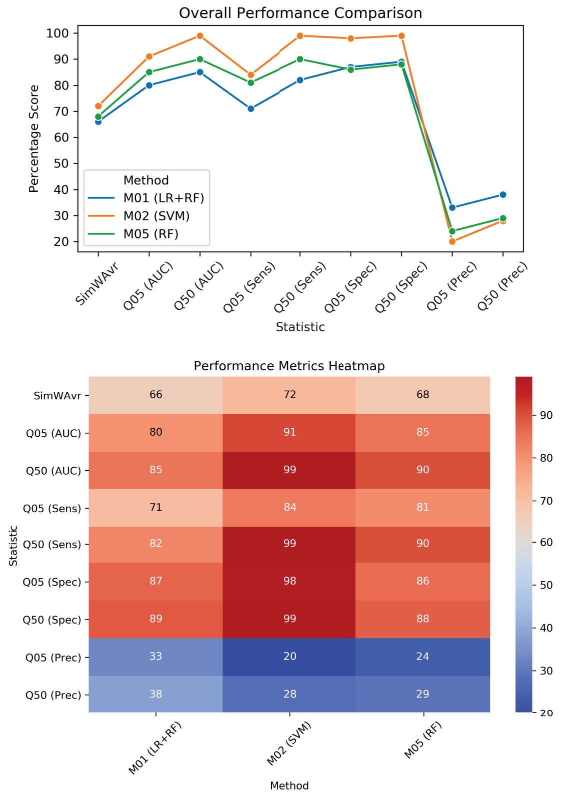

Figure 2: Visualisation of the results for Table 2: Using **Non-Cycloplegic** Attributes; BestMet = Best ML model method, LR+RF=Ensemble model of Lasso Regression and Random Forest, SVM = Support Vector Machine, RF = Random Forest.

We used typical regression model performance indicators: Q05(R2_score), Q50(R2_score) and measured diopters: Q95(MSE), Q50(MSE), Q95(RMSE), Q50(RMSE), Q95(MAE) and Q50(MAE). The most interesting results are present in the following tables:

Table 3: Selected best results - a **regression** problem. **Cycloplegic Attributes**; BestMet = Best ML model method, GB = Gradient boosting, RF = Random Forest. See visualisation in Fig. 3.

Statistic	**Model 1**	**Model 2**
BestMet	GB	RF
Q95 (MSE)	0.28	0.29
Q50 (MSE)	0.18	0.19
Q95 (RMSE)	0.52	0.54
Q50 (RMSE)	0.42	0.44
Q95 (MAE)	0.33	0.36
Q50 (MAE)	0.30	0.32
Q05 (R2_score)	0.69	0.68
Q50 (R2_score)	0.79	0.78

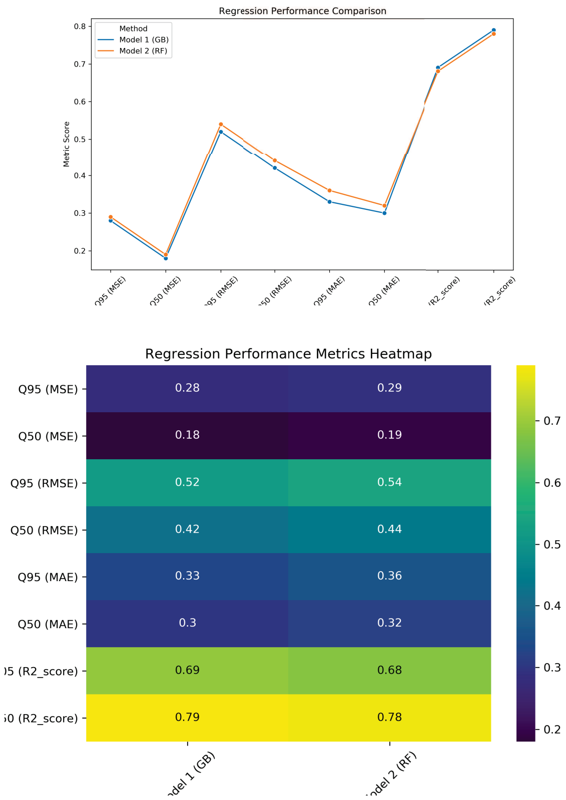

Figure 3: Visualisation of the results for Table 3: **Cycloplegic Attributes**; BestMet = Best ML model method, GB = Gradient Boosting, RF = Random Forest.

Table 4: Selected best results - a **regression** problem. **Non-Cycloplegic Attributes**; BestMet = Best ML model method, GB = Gradient Boosting, ANN = Artificial Neural Network. See visualisation in Fig. 4.

Statistic	**Model 1**	**Model 2**
BestMet	**GB**	**ANN**
Q95 (MSE)	0.50	0.63
Q50 (MSE)	0.40	0.48
Q95 (RMSE)	0.71	0.79
Q50 (RMSE)	0.63	0.69
Q95 (MAE)	0.53	0.59
Q50 (MAE)	0.46	0.52
Q05 (R2_score)	0.39	0.29
Q50 (R2_score)	0.53	0.45

4 CONCLUSIONS

This study represents a key advancement in using machine learning to predict the risk of myopia among children. The Myopia Risk Calculator (MRC) Consortium has successfully fused classical machine learning methodologies with cutting-edge AI innovations, forging a trailblazing path in ophthalmic health

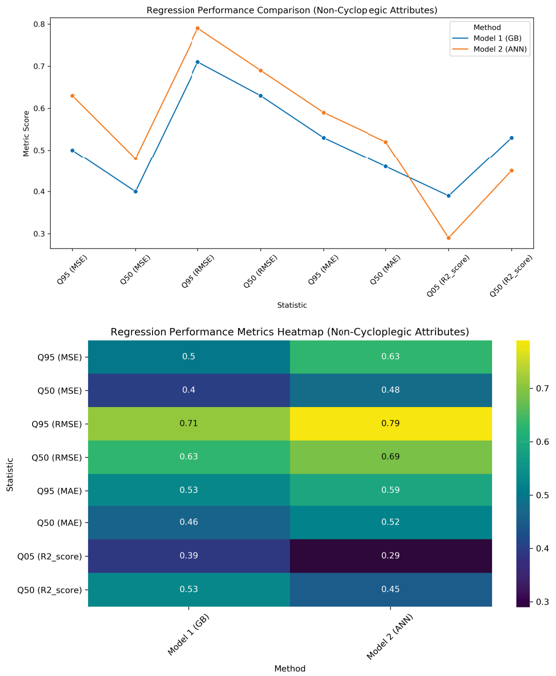

Figure 4: Visualisation of the results for Table 4: **Non-Cycloplegic Attributes**; BestMet = Best ML model method, GB = Gradient Boosting, ANN = Artificial Neural Network.

solutions.

Key Findings:

- Validation of traditional ML methods for creating classifiers and regression models has been achieved, with promising outcomes within the Iranian pediatric cohort, hinting at the potential for cross-population applicability subject to further empirical investigation.
- The application of Monte Carlo methods coupled with confidence interval evaluations spearheaded by MRC sets a proposal of new standards in the evaluation of ML models' effectiveness and robustness for medical applications, championing their reliability and transparency.
- The techniques based on MCCV showcased herein have affirmatively passed the initial litmus test in the ongoing pursuit of a comprehensive trustworthiness assessment framework for medical ML applications.

Now lets present our future plans and final thoughts. The MRC Consortium is strategically expanding its investigative purview to include transfer learning methodologies, seeking to augment the precision and adaptability of our models to a variety of population datasets, which will entail the generation of specialized synthetic data. Exploring image data, the consortium anticipates unlocking advanced diagnostic potential, thereby enhancing the utility of the models. With a nod to the future, the application of the Wis-Tech methodology for Interactive Granular Computing (IGrC) is anticipated to unravel the complexities of causation, offering refined 'what-if' analytical scenarios that could revolutionize predictive accuracy. The MRC is at the vanguard of an evolving healthcare paradigm wherein AI and ML transcend their roles as mere computational tools to become integral allies in the delivery of advanced medical care. Central to this paradigm is the trustworthiness of ML models, a critical component that our research addresses with a pioneering assessment methodology. As we stand on the brink of a transformative era in medical technology, the consortium is propelling this movement with unwavering commitment and a vision for a future where healthcare is both innovative and reliable.

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