

# Evaluating Machine Learning Models for Predicting Prostate Cancer Progression Using Lifestyle Factors: A Systematic Review and Meta-Analysis

Ernest E. Onuiri and Oluwabamise J. Adeniyi

Department of Computer Science, School of Computing, Babcock University, Nigeria

E-mail: [onuiri@babcock.edu.ng](mailto:onuiri@babcock.edu.ng), [adeniyi0416@pg.babcock.edu.ng](mailto:adeniyi0416@pg.babcock.edu.ng)

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**Abstract** - This systematic review and meta-analysis evaluated the performance of machine learning models in predicting prostate cancer progression using lifestyle factors as predictive biomarkers to improve prognostic accuracy. Various models were analyzed, including Support Vector Machine (SVM), Logistic Regression (LR), Random Forest (RF), Multi-Layer Perceptron (MLP), and Convolutional Neural Networks (CNN). These models were applied to identify diagnostic and prognostic biomarkers and to enhance the forecasting of prostate cancer progression. The meta-analysis demonstrated high predictive effectiveness across models, with mean performance metrics of 0.901 AUC (Area Under the Curve), 0.914 F1 Score, 0.889 accuracy, and 0.914 sensitivity. Among the models, the Multi-Layer Perceptron (MLP) emerged as the most effective, achieving 97% accuracy and an AUC of 95.8%. These findings underscore the potential of machine learning to integrate lifestyle factors as predictive biomarkers, advancing precision oncology in prostate cancer care.

**Keywords:** AUC (Area Under the Curve), Lifestyle Factors, Logistic Regression, Machine Learning, Multi-Layer Perceptron, Precision Oncology, Prostate Cancer, Support Vector Machine

## I. INTRODUCTION

Prostate cancer (PCa) is a major threat to global health, ranking as one of the most common cancers in men and significantly contributing to cancer-related deaths [1], [2]. PCa is responsible for a substantial number of new cancer cases and cancer-related deaths, according to recent statistics from the Cancer Journal for Clinicians. The incidence rate of PCa increased by 3% annually between 2014 and 2019, indicating 99,000 more cases - half of which were advanced - than if rates had remained stable. Since 2011, there have been 4.5% yearly increases in diagnoses at the regional and distant stages, contributing to this rise [2]. This highlights the urgent need to improve our knowledge and approaches to treating this disease. PCa's clinical development can vary greatly among individuals, regardless of advancements in diagnosis, treatment, and screening. Some PCa patients may face aggressive metastasis and therapy resistance, while others experience gradual and indolent progression [3].

In recent years, there has been an increased understanding of the impact of lifestyle factors on PCa risk and progression. These factors encompass a wide range of behaviors and habits, including dietary patterns, physical activity levels,

smoking habits, and alcohol consumption, which have been shown to affect various aspects of PCa biology and clinical outcomes [4]-[7]. Epidemiological studies indicate that factors such as obesity, sedentary behavior, and poor dietary habits are consistently associated with a higher risk of developing aggressive PCa [8]. Moreover, evolving evidence suggests that lifestyle modifications, such as eating a balanced diet and engaging in regular exercise, may positively influence PCa outcomes by reducing tumor aggression and improving treatment response [9]. Despite the growing understanding of lifestyle factors in the context of PCa, there remains a considerable gap in knowledge regarding their role as predictive biomarkers in disease progression.

Conventional prognostic tools often rely on clinical and pathological variables, which may not adequately represent the complex nature of PCa development [10]. In contrast, machine learning (ML) approaches have shown great potential for analyzing large and complex datasets and detecting predictive patterns that can guide clinical decision-making [11]. Studies also demonstrate that healthcare is being revolutionized by artificial intelligence (AI) due to its impact on analyzing massive datasets and enabling quicker and more precise prostate cancer lesion diagnosis. AI has exhibited exceptional precision in identifying prostate lesions and predicting patient survival and treatment response. Machine learning algorithms are effective methods for processing the vast amounts of data derived from the prostate tumor genome quickly and reliably [12], [13]. The application of machine learning in PCa aligns with precision oncology efforts aimed at tailoring treatment strategies to individual patient characteristics and tumor biology [14]. By integrating ML techniques with comprehensive lifestyle assessments, researchers may uncover innovative biomarkers and predictive models that enhance risk stratification, optimize treatment selection, and improve patient outcomes in PCa care.

### A. Rationale

This research is required due to the continuous challenges in accurately predicting prostate cancer progression and tailoring effective treatment methods to each patient [3], [11].

The traditional prognostic tools, like clinical and pathological factors, often fail to capture the heterogeneous nature of the disease despite their advancement [15]. Additionally, although lifestyle factors have demonstrated a significant effect on prostate cancer risk and progression, their usage in predictive models is still limited, therefore, machine learning techniques serve as a potential answer to these problems, because they utilize complex datasets to create predictive models that improve risk assessment and help in the selection of personalized treatments for each patients [16].

### B. Objectives

This systematic review, incorporating meta-analysis, aims to evaluate the performance of machine learning models in assessing lifestyle factors as predictive biomarkers for prostate cancer progression. To enhance knowledge and inform future research in machine learning and prostate cancer prognosis, this review synthesizes previous research and examines the approaches, algorithms, and results of the machine learning models employed [17]. Additionally, the meta-analysis seeks to combine data from multiple studies by aggregating summary statistics and analyzing the performance metrics of the machine learning models utilized. Appropriate statistical methods were applied for this purpose.

1. *Population:* What machine learning techniques have been employed to analyze lifestyle factors and predict prostate cancer progression among male patients diagnosed with the disease?
2. *Intervention:* How have lifestyle factors, such as physical activity, smoking habits, and diet, been incorporated as features in machine learning models for predicting prostate cancer progression?
3. *Comparison:* How effective are various machine learning algorithms in predicting the progression of prostate cancer based on lifestyle factors?
4. *Outcome:* What predictive biomarkers or indicators of prostate cancer progression identified by machine learning models trained on lifestyle factors contribute to personalized risk assessment and clinical decision-making?
5. *Study Design:* What observational studies (e.g., cohort, case-control) have investigated the correlation between lifestyle factors and the progression of prostate cancer? What predictive modeling studies employing machine learning approaches have been conducted to identify predictive biomarkers for prostate cancer progression?

## II. METHODOLOGY

The methodology employed in this systematic review involved a comprehensive search across four major databases - Scopus, PubMed, Google Scholar, and ResearchGate - to gather relevant studies published between January 2010 and February 2024. The chosen time frame was selected to enhance the comprehensiveness, relevance, and methodological rigor of the literature review. The search strategy incorporated key terms related to prostate cancer,

artificial intelligence, machine learning, predictive modeling, lifestyle factors, and predictive biomarkers. A total of 398 documents were retrieved from the databases, and rigorous eligibility criteria were applied to select the articles included in the review.

### A. Eligibility Criteria

The PICOS [18] framework selection criteria were applied to articles for review inclusion:

1. *Population:* Men with prostate cancer diagnoses.
2. *Intervention:* Studies utilizing machine learning techniques to analyze lifestyle factors as predictive biomarkers for prostate cancer progression.
3. *Comparison:* Studies comparing different machine learning algorithms or approaches in predicting prostate cancer progression based on lifestyle factors.
4. *Outcome:* Studies employing machine learning models trained on lifestyle factors to identify predictive biomarkers or indicators of prostate cancer progression.
5. *Study Design:* Observational studies (e.g., cohort, case-control) investigating the correlation between lifestyle factors and the progression of prostate cancer.

### B. Inclusive Criteria

1. Studies involving male patients diagnosed with prostate cancer.
2. Studies utilizing machine learning techniques to analyze lifestyle factors as predictive biomarkers for prostate cancer progression.
3. Studies employing machine learning models trained on lifestyle factors to identify predictive biomarkers or indicators of prostate cancer progression.
4. Articles available in the English language.
5. Articles published between January 2010 and March 2024.

### C. Exclusive Criteria

1. Studies focusing exclusively on female patients, non-human subjects, or other cancer types.
2. Studies not employing machine learning techniques or not assessing lifestyle factors as predictive biomarkers for prostate cancer progression.
3. Studies that do not identify predictive biomarkers or indicators of prostate cancer progression or do not use machine learning models trained on lifestyle factors.
4. Articles not available in the English language.
5. Articles for which full texts are not accessible.
6. Case reports, reviews, editorials, letters, conference abstracts, and meta-analyses.

### D. Source of Information

An extensive search was conducted on Google Scholar, Scopus, ResearchGate, and PubMed to enhance the breadth, reliability, and validity of the systematic review, ultimately contributing to a more rigorous and impactful research

endeavor. The search strategy employed keywords relevant to the subject of the systematic review: prostate cancer, artificial intelligence, machine learning, predictive modeling, lifestyle factors, and predictive biomarkers.

### E. Search Strategy

To retrieve relevant articles, the search strategy utilized a combination of keywords and Boolean operators. Key terms included “prostate cancer,” “artificial intelligence,” “machine learning,” “predictive modeling,” “lifestyle factors,” and “predictive biomarkers.” Filters were applied to limit the search to articles published between January 2010 and February 2024, available in the English language, and classified as original research articles [19].

The search strategy used for the systematic review titled “Lifestyle Factors as Predictive Biomarkers in Prostate Cancer Progression: A Machine Learning Approach” on the aforementioned databases is as follows:

#### 1. Scopus Database

The following query string resulted in 147 documents on the Scopus database:

```
TITLE-ABS-KEY ( ( lifestyle OR behav* OR habit OR
“physical activity” OR diet* ) AND ( prostat* AND ( cancer
OR carcinoma OR tumor OR neoplasm OR adenocarcinoma
OR malignancy ) ) AND ( ( predictive OR prognostic ) AND
( biomarkers OR model* OR indicators ) ) AND ( ( “machine
learning” OR “artificial intelligence” OR “predictive” ) AND
( model* OR approach OR method ) ) ) AND PUBYEAR >
2009 AND PUBYEAR < 2025 AND ( LIMIT-TO
( SUBJAREA , “MEDI” ) OR LIMIT-TO ( SUBJAREA ,
“BIOC” ) OR LIMIT-TO ( SUBJAREA , “IMMU” ) OR
LIMIT-TO ( SUBJAREA , “NURS” ) OR LIMIT-TO
( SUBJAREA , “COMP” ) OR LIMIT-TO ( SUBJAREA ,
“NEUR” ) OR LIMIT-TO ( SUBJAREA , “PHAR” ) ) AND
( LIMIT-TO ( DOCTYPE , “ar” ) ) AND ( LIMIT-TO
( PUBSTAGE , “final” ) ) AND ( LIMIT-TO ( SRCTYPE ,
“j” ) ) AND ( LIMIT-TO ( LANGUAGE , “English” ) )
```

#### 2. PubMed Database

The following query string resulted in 121 documents in the PubMed database:

```
((“prostat*”[All Fields] AND (“carcinoma”[All Fields] OR
“neoplasm”[All Fields] OR “tumor”[All Fields])) AND
(“progression”[All Fields] OR “aggression”[All Fields]))
AND (“lifestyle factor”[All Fields] OR “habit”[All Fields])
OR ((“predictive”[All Fields] OR “prognostic”[All Fields])
AND (“biomark*”[All Fields] OR “indicator”[All Fields]
OR “model*”[All Fields])) AND ((“machine learning”[All
Fields] OR “deep learning”[All Fields] OR “artificial
intelligence”[All Fields] AND (“modeling”[All Fields]))
AND (medline[Filter] AND fha[Filter] AND fft[Filter] AND
humans[Filter] AND male[Filter] AND data[Filter] AND
english[Filter])
```

### 3. Google Scholar and Research Gate

A manual search for articles relevant to the subject of the systematic review was conducted using the search bars available on Google Scholar and ResearchGate. These articles were organized into separate folders using the Mendeley Web Importer. The following number of documents were extracted:

*Google Scholar*: 113 documents; *Research Gate*: 17 documents.

### F. Data Management

The articles resulting from the various database searches were exported in RIS (Research Information Systems) file format and further imported into Hubmeta, a cloud-based platform for meta-analysis and systematic reviews [20], for screening. The Hubmeta software includes an artificial intelligence feature that facilitates the efficient screening of articles. February 23, 2024, was the date of the most recent search.

### G. Study Selection

The study selection process was meticulously conducted by the sole reviewer for this research work, using Hubmeta, a systematic review management tool, to ensure that relevant articles met predefined criteria. The titles and abstracts of the articles were assessed to determine their relevance to the research question and compliance with the inclusion criteria during the screening process. Following this, a full-text review was performed on potentially relevant articles to ensure compliance with the inclusion criteria, and important information was extracted for analysis. Articles that satisfied the inclusion criteria were retained for further evaluation, while those that did not were excluded from the research.

### H. Data Extraction

Data extraction was conducted to gather relevant information from the selected articles. An organized protocol was followed to ensure accuracy and consistency in collecting key data points, including study characteristics, participant demographics, interventions/exposure, outcomes, and key findings from each article. Inconsistencies or uncertainties encountered during the extraction process were addressed through careful review.

A PRISMA flowchart, as shown in Fig. 1 [21], was used to document the screening and data extraction processes, providing a visual representation of the article selection process and ensuring that the reporting of results is reliable and transparent. The flowchart, which conforms to the PRISMA guidelines [22], depicts how many articles were collected, screened, evaluated for eligibility, and included in the systematic review. This method ensures the systematic review’s reliability [23].

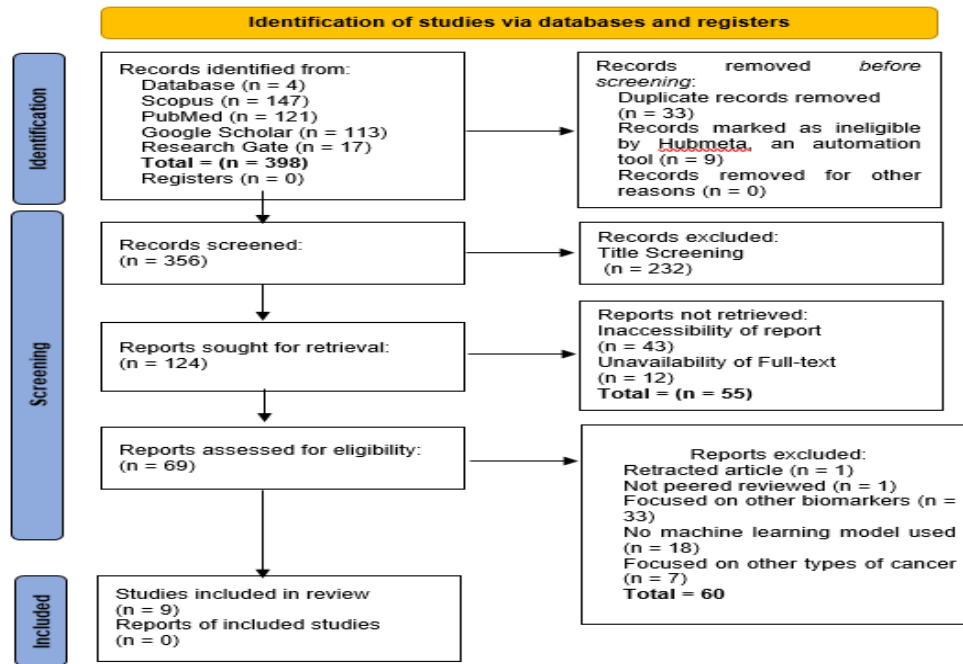


Fig. 1 The screened studies documented using PRISMA flowchart

*I. Risk of Bias*

To ensure the credibility and reliability of the systematic review, an assessment of bias risk within the included studies was conducted. As the sole reviewer, this evaluation was carefully performed in accordance with established guidelines for assessing various study designs. Articles that did not sufficiently address the research question or failed to meet the eligibility criteria were excluded during the screening process. A comprehensive search of multiple databases and sources further minimized the possibility of selection bias, and any inconsistencies were addressed through careful inspection and reference to relevant literature.

**III. RESULTS**

An evaluation of the performance of machine learning models in predicting prostate cancer progression based on lifestyle factors was conducted in this systematic review. The study focused on using biomarkers to identify predictive

patterns and improve prognostic accuracy. Key performance metrics were used to assess the predictive capabilities of the models, including AUC, sensitivity, F1 score, and specificity [24]-[26].

Initially, 398 articles were identified through a thorough database search. After applying a strict screening procedure based on the inclusion and exclusion criteria, nine articles were ultimately included in the review. The selection process followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [23], and the PRISMA flowchart shown in Fig. 1 [21] illustrates how the articles were selected. Only the most relevant studies were included in the final analysis due to this methodical approach.

Table I summarizes the nine studies published between January 2010 and March 2024. The table highlights their authors, publication year, title, study design, and key findings, showcasing recent advancements and growing interest in prostate cancer research.

TABLE I THE SELECTED STUDIES

Sl. No.	Author(s) (Year)	Title	Machine Learning Methodology	Result and Findings
1	Shin <i>et al.</i> , (2023) [27]	A Boolean-based machine learning framework identifies predictive biomarkers for HSP90-targeted therapy response in prostate cancer.	To identify biomarkers, the study employs a range of machine learning techniques, including OMC, KNN, Naïve Bayes, Random Forest, AdaBoost, and Deep Forest. The multiclass Support Vector Machine (mSVM), which achieves over 71% accuracy on an independent dataset, is identified as the best-performing algorithm.	The study produced a 16-protein biomarker panel with a 92% accuracy rate in predicting the response to the Hsp90 inhibitor 17-AAG. When reduced to a smaller 5-protein panel, it maintained an 80% prediction accuracy, illustrating its potential for clinical translation. This biomarker panel and the associated expression signatures could contribute to precision oncology and personalized treatment regimens by enabling better patient selection and more effective prostate cancer treatment plans.

2	Tong <i>et al.</i> , (2023) [24]	A Machine Learning Method for Predicting Biomarkers Associated with Prostate Cancer	The study evaluated prostate cancer (PCa) prognostic and diagnostic biomarkers using machine learning and protein-protein interaction (PPI) networks. It employed a graph autoencoder (GAE) framework to encode and decode graph features and construction, allowing for the understanding of graph generative distributions and network embedding from PPI nodes. This method proved effective for assessing PCa biomarkers.	Hub genes for prostate cancer (PCa), including UBE2C, CCNB1, TOP2A, TPX2, CENPM, F5, APOE, NPY, and TRIM36, were identified in the study as promising diagnostic and prognostic markers. Additionally, a four-gene prognostic factor was developed, with the model demonstrating high sensitivity and specificity in predicting patient survival, achieving an AUC value of 0.973 at one year. The study suggests that the combination of PPI networks and machine learning algorithms is highly effective in identifying biomarkers for PCa diagnosis and prognosis.
3	Lee <i>et al.</i> , (2022) [28]	Developing Machine Learning Algorithms for Dynamic Estimation of Progression During Active Surveillance for Prostate Cancer	For temporal predictive clustering, the study utilized the Actor-Critic reinforcement learning technique and the Dynamic-DeepHit-Lite (DDHL) model. With three years of data collection and three years of follow-up, the DDHL model demonstrated a C-index of 0.79 ( $\pm 0.11$ ), indicating superior predictive power and effectiveness in providing dynamic risk estimations during active surveillance.	To enable real-time risk predictions based on new observations, the study demonstrated the application of machine learning algorithms for dynamic progression estimation in patients with prostate cancer. The models also enhanced personalized prediction of progression risk by identifying temporal clusters of patients with similar future outcomes. The results underscore the potential of machine learning for managing prostate cancer.
4	Yeh <i>et al.</i> , (2022) [25]	Investigating the Role of Obesity in Prostate Cancer and Identifying Biomarkers for Drug Discovery: Systems Biology and Deep Learning Approaches	To predict drug candidates based on biomarkers, the study employed a drug-target interaction model utilizing Deep Neural Networks (DNNs). To reduce overfitting, the model incorporated dropout layers, multiple hidden layers, ReLU activation functions, and early stopping. With an AUC of 0.99, a standard deviation of 0.131, and an average accuracy of 94.89%, the model demonstrated strong predictive performance.	Researchers used a systems biology approach to identify prostate cancer and obesity-specific biomarkers for PCa. A DNN-based drug-target interaction (DTI) model accurately predicted drug candidates targeting these biomarkers, achieving an AUC value of 0.99. Two promising multi-molecule medications were suggested for preventing prostate cancer and obesity-specific PCa. This work highlights how combining systems biology with computational drug discovery can accelerate target identification and improve drug development processes.
5	Chen <i>et al.</i> , (2022) [29]	Machine Learning-Based Models Enhance Prostate Cancer Prediction	The study developed predictive models for prostate cancer using four supervised machine learning algorithms: logistic regression, decision trees, random forests, and support vector machines. The multivariate logistic regression (LR) model was found to be the most effective, demonstrating the best discrimination and generalizability, with minimal performance variation between training and test datasets.	According to the research, machine learning methods are more accurate and efficient for predicting prostate cancer than PSA screening. With an AUC of 0.918, the multivariate logistic regression (LR) model demonstrated the best discrimination. This suggests that machine learning models can enhance clinical decision-making in prostate cancer diagnosis, reduce unnecessary biopsies, and improve prostate cancer detection.
6	Ebru Erdem and Ferhat Bozkurt (2021) [30]	A Comparison of Various Supervised Machine Learning Techniques for Prostate Cancer Prediction	Deep Neural Networks, Multi-Layer Perceptrons, Naive Bayes, Support Vector Machines, K-Nearest Neighbors, Logistic Regression, Linear Regression, and Linear Discriminant Analysis were among the nine supervised machine learning algorithms compared in the study. The Multi-Layer Perceptron (MLP) classifier was identified as the most effective in predicting prostate cancer, achieving a 95.8% AUC and a 97% F1 Score, outperforming the other techniques.	The MLP classifier, trained using machine learning techniques, achieved the highest accuracy of 97% and an AUC value of 95.8% in predicting prostate cancer. Its F1 Score was also 97%, indicating high precision and recall. This makes it a clinically useful method for predicting prostate cancer, potentially preventing unnecessary biopsies and demonstrating its effectiveness in predicting cancer based on patient information.
7	J. Dai (2020) [31]	Analysis of Lifestyle and	The study employed various machine learning techniques, including deep neural	The research identified 84 important features related to environmental factors using

		Environmental Factors for Cancer Prevention Using Deep Learning and Conventional Machine Learning with UK Biobank Data	networks, convolutional neural networks (CNNs), support vector machines, random forests, and logistic regression. Among these techniques, CNNs demonstrated the most effective prediction performance, with a sensitivity of 0.933 and an F1 Score of 0.961. The use of deep learning processes with multi-layer neural networks significantly enhanced predictive power in analyzing environmental factors for cancer prevention.	machine learning techniques, which were further refined to 27 significant features through logistic regression with the lasso penalty model. These features were then applied to logistic regression, resulting in a sensitivity of 0.900, an F1 Score of 0.919, and an AUC of 0.974. Additionally, age and gender were found to be significantly associated with cancer risk, emphasizing the importance of considering lifestyle and environmental factors in cancer prevention strategies.
8	Lee <i>et al.</i> , (2019) [32]	Machine Learning Approaches for Predicting Prostate Cancer Based on Age and Prostate-Specific Antigen Level	The study employed five machine learning algorithms: Support Vector Machine (SVM), Random Forest (RF), Logistic Regression (LR), Light Gradient Boosting Machine (LGBM), and Extreme Gradient Boosting (XGB). The results indicated that, across most patient categories, the Random Forest (RF) algorithm was the most effective for predicting prostate cancer.	predicting prostate cancer at rates ranging from 65.6% to 74.6%. The highest-scored feature influencing prostate cancer prediction was prostate-specific antigen (PSA) density in patients under 75 years old with a PSA level below 20 ng/mL. Other significant features also impacted prediction rates across different patient groups, providing valuable insights into factors affecting prostate cancer detection.
9	Toth <i>et al.</i> , (2019) [26]	Random Forest-Based Modeling for Detecting Biomarkers of Prostate Cancer Progression	Using the Random Forest technique for ensemble learning, the study constructed multiple classification trees. The model was trained on a training set and validated on a test set. Variable selection was based on accuracy reduction and Gini scores. The Random Forest model achieved a high performance, with an area under the ROC curve (AUC) of 95%.	According to Kaplan-Meier survival analyses, a methylation-based classifier effectively distinguishes between prognosis subgroups in prostate cancer, with a log-rank p-value of less than 0.0001. External validation using separate prostate cancer cohorts yielded AUCs of 77.1% and 68.7% for sensitivity analyses. The model demonstrated a shorter time to biochemical recurrence associated with ZIC2 protein expression loss and identified candidate genes not previously linked to prostate cancer progression.

### A. Summary of Findings

The findings from the nine studies included in the review, involving a total of 42,949 male patients with prostate cancer, are discussed below. J. Dai’s study (2020) [31] is notable for employing both traditional machine learning and deep learning techniques to explore the relationship between environmental factors, lifestyle choices, and cancer incidence. In this study, convolutional neural networks (CNNs) exhibited strong predictive performance, with a sensitivity of 0.933 and an F-1 Score of 0.961. Among the machine learning techniques employed, CNNs demonstrated the best prediction performance, highlighting their effectiveness in this context.

In another study by Ebru Erdem and Ferhat Bozkurt (2021) [30], the multi-layer perceptron (MLP) classifier achieved 97% accuracy and a 95.8% AUC, making it the top-performing machine learning model across all studies. The performance metrics analysis indicated that the MLP is highly effective in predicting cancer, and it offers significant potential for

improving diagnostic methods and treatment strategies for prostate cancer.

The findings underscore the potential of machine learning techniques to enhance risk stratification and treatment selection for prostate cancer. While several algorithms show promise for detecting biomarkers and predictive patterns, the MLP classifier demonstrated superior predictive performance. Its high precision and accuracy have the potential to improve clinical judgment and patient care, providing hope for future advancements in prostate cancer treatment.

These findings are expected to significantly impact future practices, research, and policies, as machine learning techniques have proven capable of guiding clinical decision-making, including personalized treatment, and informing policy decisions related to cancer care [33]. Future research should focus on addressing limitations, refining machine learning frameworks, validating prognostic biomarkers, and exploring the implementation of these models in healthcare settings.

TABLE II SUMMARY OF FINDINGS FROM SELECTED STUDIES

Sl. No.	Author(s) (Year)	Model	Biomarkers	Datasets	F-1 Score	AUC	Accuracy	Sensitivity
1	Chen <i>et al.</i> , (2022) [29]	tPSA LR	tPSA, Age, fPSA, PV, NLR, peripheral blood neutrophil count, lymphocyte count, PSAD, f/tPSA, biopsy results	Data from 551 patients.	N/A	0.846	0.771	0.639
		Multivariate LR				0.918	0.876	0.880
		Decision Tree (DT)				0.886	0.788	0.867
		Random Forest (RF)				0.898	0.818	0.840
		Support Vector Machine (SVM)				0.895	0.861	0.867
2	Yeh <i>et al.</i> , (2022) [25]	Deep Neural Network (DNN)	Essential biomarkers for prostate cancer (PCa) and obesity-specific PCa	Microarray data for normal prostate cells (lean and obese groups), and lean and obese PCa	N/A	0.990	0.949	N/A
3	E. Erdem and F. Bozkurt (2021) [30]	K-Nearest Neighbor (KNN)	Patient age, cancer volume, Gleason score, prostate weight, antigen, MRI images	100 patients from DBCR dataset, Kaggle prostate cancer dataset, and PROSTATEx database	0.860	0.833	0.830	0.830
		Support Vector Machines (SVM)			0.910	0.903	0.900	0.920
		Logistic Regression			0.810	0.847	0.830	0.920
		Naive Bayes (NB)			0.880	0.862	0.870	0.760
		Neural Networks,			0.930	0.885	0.900	0.860
		Random Forest (RF)			0.860	0.876	0.830	0.860
		Linear Regression			0.890	0.905	0.870	0.100
		Linear Discrimination Analysis (LDA)			0.970	0.958	0.970	0.920
		Multi-Layer Perceptron (MLP)			0.900	0.903	0.900	0.920
		Multi-Layer Perceptron (MLP)-Regressor			0.920	0.889	0.900	0.830
4	J. Dai (2020) [31]	Deep Neural Networks (DNNs)	1. Age 2. Number of self-reported non-cancer illnesses 3. Number of operations, self-reported 4. Other serious medical conditions/disability diagnosed by a doctor 5. Gender 6. Long-standing illness, disability or infirmity 7. Sleeplessness/insomnia 8. Water intake 9. Sleep duration 10. Illness, injury, bereavement, stress in last 2 years 11. Overall health rating 12. Frequency of stair climbing in last 4 weeks 13. Time spent watching television (TV) 14. Snoring	50,000 participants extracted from UK Biobank	0.956	N/A	0.957	0.933
		Convolutional Neural Networks (CNNs)			0.961		0.962	0.933
		Support Vector Machine (SVM)			0.957		0.959	0.918
		Random Forest (RF)			0.945		0.948	0.896
		Extra Trees			0.948		0.951	0.902
		Logistic Regression			0.919		0.920	0.920
						0.974		

			<p>15. Salad / raw vegetable intake</p> <p>16. Dried fruit intake</p> <p>17. Oily fish intake</p> <p>18. Non-oily fish intake</p> <p>19. Alcohol usually taken with meals</p> <p>20. Breastfed as a baby</p> <p>21. Comparative body size at age 10</p> <p>22. Comparative height size at age 10</p> <p>23. Maternal smoking around birth</p> <p>24. Mood swings</p> <p>25. Irritability</p> <p>26. Blood clot, DVT, bronchitis, emphysema, asthma, rhinitis, eczema, allergy diagnosed by doctor</p> <p>27. Types of transport used (excluding work)</p> <p>28. Duration of walks</p> <p>29. Duration of moderate activity</p> <p>30. Waist circumference</p> <p>31. Hip circumference</p> <p>32. Standing height</p> <p>33. Seated height</p> <p>34. Pulse rate, automated reading</p> <p>35. Townsend deprivation index at recruitment</p> <p>36. Diastolic blood pressure, automated reading</p> <p>37. Systolic blood pressure, automated reading</p> <p>38. Nitrogen dioxide air pollution</p> <p>39. Nitrogen oxide air pollution</p> <p>40. Particulate matter air pollution (pm10)</p> <p>41. Particulate matter air pollution (pm2.5)</p> <p>42. Particulate matter air pollution (pm2.5) absorbance</p> <p>43. Particulate matter air pollution 2.5-10um</p>					
5	Toth <i>et al.</i> , (2019) [26]	Random forest,-based classifier	DNA methylation changes, ZIC2 protein expression	<p>Discovery cohort (n = 70)</p> <p>ICGC cohort (n = 222)</p> <p>TCGA PRAD cohort (n = 477)</p>	N/A	<p>0.950</p> <p>0.771</p> <p>0.637</p>	N/A	N/A



TABLE I MACHINE LEARNING MODELS AND THEIR PERFORMANCE METRICS

Sl. No.	Year	Model	F-1 Score (%)	AUC (%)	Accuracy (%)	Sensitivity (%)
1	2022	tPSA LR	N/A	0.846	0.771	0.639
		MLR		0.918	0.876	0.880
		DT		0.886	0.788	0.867
		RF		0.898	0.818	0.840
		SVM		0.895	0.861	0.867
2	2022	DNN	N/A	0.990	0.949	N/A
3	2021	KNN	0.860	0.833	0.830	0.830
		SVM	0.910	0.903	0.900	0.920
		LR	0.810	0.847	0.830	0.920
		NBNN	0.880	0.862	0.870	0.760
		RF	0.930	0.885	0.900	0.860
		LinReg	0.860	0.876	0.830	0.860
		LDA	0.890	0.905	0.870	0.100
		MLP	0.970	0.958	0.970	0.920
		MLP-R	0.900	0.903	0.900	0.920
		DNN	0.920	0.889	0.900	0.830
4	2020	DNN	0.956	N/A	0.957	0.933
		CNN	0.961		0.962	0.933
		SVM	0.957		0.959	0.918
		RF	0.945		0.948	0.896
		ET	0.948		0.951	0.902
		LR	0.919		0.974	0.920
5	2019	RF	N/A	0.950	N/A	N/A

Note: tPSA LR= Total Prostate-Specific Antigen Logistic Regression, MLP= Multi-Layer Perceptron, DT= Decision Tree, SVM= Support Vector Machine, KNN= K-Nearest Neighbor, RT= Random Forest, NBNN= Naive Bayes Neural Networks, LinReg= Linear Regression, LDA= Linear Discrimination Analysis, LR=Logistic Regression, MLP-R=Multi-Layer Perceptron-Regressor, Convolutional Neural Networks (CNNs), ET= Extra Trees, Multivariate LR= Multivariate Logistic Regression, DNN= Deep Neural Network.

Note: Models labeled with the same name (e.g., DNN) but different publication years (e.g., DNN (2020)) represent duplicate instances from separate studies.

TABLE II F-1 SCORE DATA

Model	F-1 Score
KNN	0.860
SVM (2021)	0.910
LR (2021)	0.810
NBNN	0.880
RF (2021)	0.930
LinReg	0.860
LDA	0.890
MLP	0.970
MLP-R	0.900
DNN (2021)	0.920
DNN (2020)	0.956
CNN	0.961
SVM (2020)	0.957
RF (2020)	0.945
ET	0.948
LR (2020)	0.919

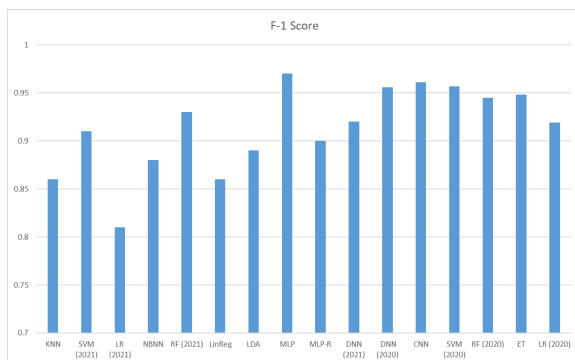


Fig. 2 Bar chart representing the F-1 Score of the models

Min = LR (0.810), Max = MLP (0.970), Mean F-1 Score = 0.914

TABLE III AUC DATA

Model	AUC
tPSA LR	0.846
MLR	0.918
DT	0.886
RF (2022)	0.898
SVM (2022)	0.895
DNN (2022)	0.990
KNN	0.833
SVM (2021)	0.903
LR (2021)	0.847
NBNN	0.862
RF (2021)	0.885
LinReg	0.876
LDA	0.905
MLP	0.958
MLP-R	0.903
DNN (2021)	0.889
LR (2020)	0.974
RF (2019)	0.950

Min = KNN (0.833), Max = DNN (0.990), Mean Accuracy = 0.901

TABLE IV ACCURACY DATA

Model	Accuracy
tPSA LR	0.771
MLR	0.876
DT	0.788
RF (2022)	0.818
SVM (2022)	0.861
DNN (2022)	0.949
KNN	0.830
SVM (2021)	0.900
LR (2021)	0.830
NBNN	0.870
RF (2021)	0.900
LR (2020)	0.920
LinReg	0.830
LDA	0.870
MLP	0.970
MLP-R	0.900
DNN (2021)	0.900
DNN (2020)	0.957
CNN	0.962
SVM (2020)	0.959
RF (2020)	0.948
ET	0.951

Min = tPSA LR (0.771), Max = MLP (0.970), Mean Accuracy = 0.889

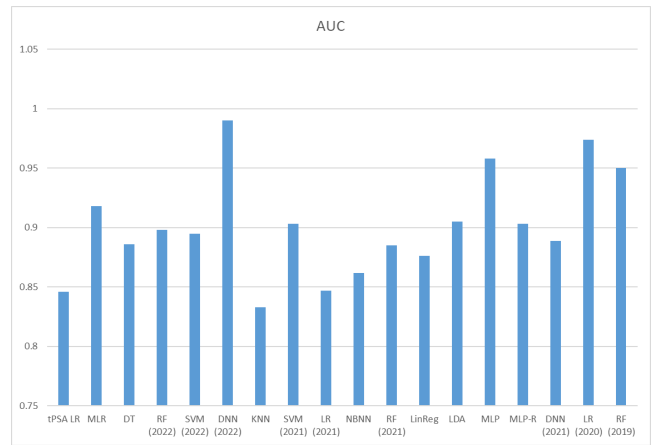


Fig. 3 Bar chart representing the AUC value of the models

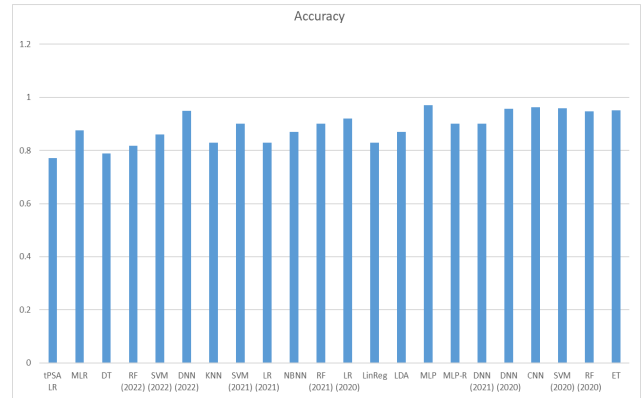


Fig. 4 Bar chart representing the Accuracy of the models

TABLE V SENSITIVITY DATA

Model	Sensitivity
tPSA LR	0.639
MLR	0.880
DT	0.867
RF (2022)	0.840
SVM (2022)	0.867
KNN	0.830
SVM (2021)	0.920
LR (2021)	0.920
NBNN	0.760
RF (2021)	0.860
LinReg	0.860
LDA	1.000
MLP	0.920
MLP-R	0.920
DNN (2021)	0.830
DNN (2020)	0.933
CNN	0.933
SVM (2020)	0.918
RF (2020)	0.896
ET	0.902
LR (2020)	0.920

Min = tPSA LR (0.639), Max = LDA (1.000), Mean Accuracy = 0.877

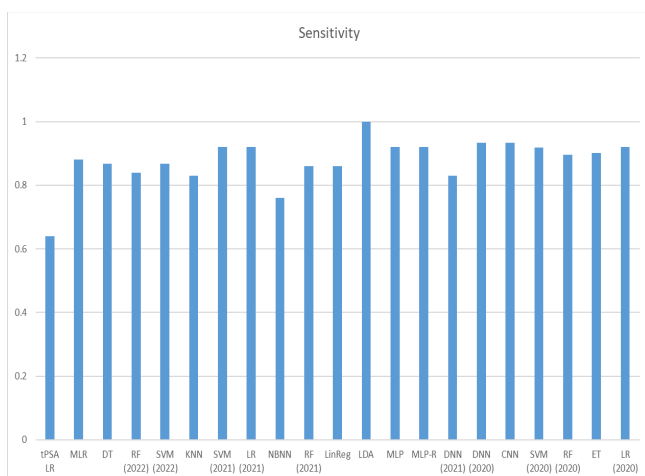


Fig. 5 Bar chart representing the Sensitivity of the mode

TABLE VI STATISTICAL REPRESENTATION OF THE PERFORMANCE METRICS

Performance Metrics	F-1 Score	AUC	Accuracy	Sensitivity
N Valid	16	18	22	21
Mean	0.914	0.901	0.889	0.877
Std. Error of Mean	0.011	0.010	0.013	0.016
Median	0.920	0.897	0.900	0.896
Std. Deviation	0.045	0.044	0.060	0.074
Variance	0.002	0.002	0.004	0.006
Minimum	0.810	0.833	0.771	0.639
Maximum	0.970	0.990	0.970	1.000

In TABLE VII presents the performance metrics extracted from the studies included in the review. These metrics are crucial indicators of the effectiveness of machine learning models in evaluating lifestyle factors as predictive biomarkers for prostate cancer progression.

1. *F-1 Score*: The F-1 Score is a metric that balances model recall and precision. A high F-1 Score indicates that recall - the ability to identify all positive - cases and precision - the accuracy of identifying positive cases - are well-balanced in the model [34]. The mean F-1 Score of 0.914 suggests that, on average, the machine learning models perform effectively in predicting prostate cancer progression based on lifestyle factors. The range of the F-1 Score, from 0.810 to 0.970, reflects the variation in performance across different models in the studies.

2. *AUC*: The Area Under the Curve (AUC) measures a model’s ability to distinguish between positive and negative cases. A higher AUC value indicates better discriminatory ability, with a perfect value of 1 and random chance represented by 0.5 [35]. The mean AUC of 0.901 indicates strong discriminatory power in predicting prostate cancer progression. The range of AUC values, from 0.830 to 0.990, demonstrates variations in the predictive accuracy of the models evaluated.

3. *Accuracy*: Accuracy measures the percentage of correct predictions made by the model out of all predictions. It reflects the overall performance of the model, regardless of class imbalance [36]. Higher accuracy values denote better overall predictive performance. On average, the models achieve an accuracy of 88.9%, with a mean accuracy of 0.889.

4. *Sensitivity*: Sensitivity measures the model’s ability to detect positive cases accurately. A sensitivity value of 1.000 indicates perfect detection of positive cases [37]. The mean sensitivity of 0.877 suggests that the models, on average, correctly identified 87.7% of positive cases. The sensitivity range, from 0.640 to 1.000, highlights differences in the models’ ability to detect prostate cancer progression across studies.

The performance metrics detailed in Table VII provide valuable insights into the effectiveness of the machine learning models in predicting prostate cancer progression based on lifestyle factors. These metrics demonstrate the promising performance of the models in forecasting prostate cancer progression.

#### IV. DISCUSSION

The performance of machine learning techniques in predicting prostate cancer progression based on lifestyle factors was evaluated through a systematic review and meta-analysis. The machine learning models exhibited high predictive capabilities, as illustrated by the mean values of their performance metrics: an accuracy of 0.889, sensitivity of 0.914, F-1 Score of 0.914, and AUC of 0.901. Among these models, the multi-layer perceptron (MLP) classifier was notably the most effective, with an accuracy of 97% and an AUC of 95.8%. These results demonstrate how machine learning methods can enhance risk assessment and treatment selection for prostate cancer.

Furthermore, the findings highlight that lifestyle factors - such as physical activity, diet, and smoking habits - significantly impact cancer progression and are crucial for predicting prostate cancer. The analysis of performance metrics, combined with the outstanding performance of the MLP classifier, underscores the importance of incorporating lifestyle factors into prostate cancer progression predictions. This integration of machine learning techniques into clinical decision-making processes, including personalized treatment, shows promise for improving risk assessment and contributing to policy decisions related to cancer care.

In conclusion, the results illustrate the efficacy of machine learning models in predicting prostate cancer progression based on lifestyle factors. They emphasize the importance of lifestyle factors in cancer prediction and highlight the potential for personalized risk assessment and clinical decision-making. These findings pave the way for further research into the practical application of these models in medical settings, as well as improvements in machine learning algorithms and predictive biomarkers.

## V. CONCLUSION

The results of the systematic study demonstrate how machine learning methods can enhance prostate cancer detection and treatment. The analysis of performance metrics underscores the significance of lifestyle factors in predicting prostate cancer progression, particularly highlighting the effectiveness of the multi-layer perceptron (MLP) classifier. The average performance metrics reveal that the machine learning models exhibit high predictive capabilities, emphasizing their potential to improve risk assessment and treatment selection for prostate cancer. The research findings are poised to significantly impact clinical decision-making, as machine learning techniques have shown the potential to influence personalized risk assessment and cancer care through their ability to analyze large datasets and predict patterns for cancer prognosis. Finally, the systematic review and meta-analysis have confirmed that lifestyle factors play a crucial role in the progression of prostate cancer, suggesting their importance as biomarkers for predicting cancer progression. The results also indicate that the machine learning models reviewed performed exceptionally well in predicting prostate cancer progression. Future research should focus on refining machine learning algorithms, validating predictive biomarkers, and exploring the practical implementation of these models in healthcare settings.

## REFERENCES

- [1] R. L. Siegel, K. D. Miller, H. E. Fuchs, and A. Jemal, "Cancer Statistics, 2021," *CA. Cancer J. Clin.*, vol. 71, no. 1, pp. 7-33, 2021, doi: 10.3322/caac.21654.
- [2] R. L. Siegel, K. D. Miller, N. S. Wagle, and A. Jemal, "Cancer Statistics, 2023," *CA. Cancer J. Clin.*, vol. 73, no. 1, pp. 17-48, 2023, doi: 10.3322/caac.21763.
- [3] M. Litwin, H. T.-Jama, and undefined, "The diagnosis and treatment of prostate cancer: a review," *JAMA*, vol. 317, no. 24, pp. 2532-2542, 2017. [Online]. Available: <https://jamanetwork.com/journals/jama/article-abstract/2633921>. [Accessed: Mar. 11, 2024].
- [4] S. Kenfield, M. Stampfer, and E. G.-J. of C., "Physical activity and survival after prostate cancer diagnosis in the health professionals follow-up study," *J. Clin. Oncol.*, vol. 29, no. 6, pp. 726-732, 2011. [Online]. Available: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3056656/>. [Accessed: Mar. 11, 2024].
- [5] S. F. Peisch, E. L. Van Blarigan, J. M. Chan, M. J. Stampfer, and S. A. Kenfield, "Prostate cancer progression and mortality: a review of diet and lifestyle factors," *World J. Urol.*, vol. 35, no. 6, pp. 867-874, Jun. 2017, doi: 10.1007/S00345-016-1914-3.
- [6] C. Leitão, B. Matos, F. Roque, M. T. Herdeiro, and M. Fardilha, "The Impact of Lifestyle on Prostate Cancer: A Road to the Discovery of New Biomarkers," *J. Clin. Med.*, vol. 11, no. 10, pp. 1-17, May 2022, doi: 10.3390/jcm11102925.
- [7] Z. Dovey, A. Horowitz, and N. Waingankar, "The influence of lifestyle changes (diet, exercise and stress reduction) on prostate cancer tumour biology and patient outcomes: A systematic review," *BJUI Compass*, vol. 4, no. 4, pp. 385-416, Jul. 2023, doi: 10.1002/bco2.237.
- [8] M. Rivera-Izquierdo et al., "Obesity as a risk factor for prostate cancer mortality: A systematic review and dose-response meta-analysis of 280,199 patients," *Cancers (Basel)*, vol. 13, no. 16, p. 4169, Aug. 2021, doi: 10.3390/cancers13164169.
- [9] J. P.-C. opinion in urology, "Lifestyle factors, benign prostatic hyperplasia, and lower urinary tract symptoms," *Current Opin. Urol.*, vol. 25, no. 1, pp. 1-6, 2011. [Online]. Available: [https://journals.lww.com/co-urology/fulltext/2011/01000/lifestyle\\_factors\\_benign\\_prostatic\\_hyperplasia\\_2.aspx](https://journals.lww.com/co-urology/fulltext/2011/01000/lifestyle_factors_benign_prostatic_hyperplasia_2.aspx). [Accessed: Mar. 11, 2024].
- [10] J. A. Schalken et al., "Molecular prostate cancer pathology: Current issues and achievements," *Scand. J. Urol. Nephrol.*, vol. 39, no. 216, pp. 82-93, May 2005, doi: 10.1080/03008880510030950.
- [11] A. Esteva, A. Robicquet, B. Ramsundar, V. Kuleshov, M. DePristo, K. Chou, C. Cui, G. Corrado, "A guide to deep learning in healthcare," *Nat. Med.*, vol. 25, no. 1, pp. 24-29, 2019, doi: 10.1038/s41591-018-0316-z.
- [12] O. S. Tătaru et al., "Artificial intelligence and machine learning in prostate cancer patient management-current trends and future perspectives," *Diagnostics*, vol. 11, no. 2, pp. 1-20, 2021, doi: 10.3390/diagnostics11020354.
- [13] S. L. Goldenberg, G. Nir, and S. E. Salcudean, "A new era: artificial intelligence and machine learning in prostate cancer," *Nat. Rev. Urol.*, vol. 16, no. 7, pp. 391-403, May 2019, doi: 10.1038/s41585-019-0193-3.
- [14] O. Ernest, O. Komolafe, S. O., and A. Oludele, "Ontology: A Case for Disease and Drug Knowledge Discovery," *Commun. Appl. Electron.*, vol. 5, no. 9, pp. 6-13, 2016, doi: 10.5120/cae2016652362.
- [15] M. A. Dall'era et al., "Active surveillance for early-stage prostate cancer: review of the current literature," *Cancer*, vol. 112, no. 8, pp. 1650-1659, Apr. 2008, doi: 10.1002/cncr.23373.
- [16] G. S. Collins, J. B. Reitsma, D. G. Altman, and K. G. M. Moons, "Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement," *Ann. Intern. Med.*, vol. 162, no. 1, pp. 55-63, Jan. 2015, doi: 10.7326/M14-0697.
- [17] A. A. Adegbenjo et al., "Design and Analysis of an Automated IoT System for Data Flow Optimization in Higher Education Institutions," *J. Eur. des Syst. Autom.*, vol. 56, no. 5, pp. 889-897, 2023, doi: 10.18280/jesa.560520.
- [18] M. Amir-Behghadami and A. Janati, "Population, Intervention, Comparison, Outcomes and Study (PICOS) design as a framework to formulate eligibility criteria in systematic reviews," *Emerg. Med. J.*, vol. 37, no. 6, pp. 387-387, Jun. 2020, doi: 10.1136/emered-2020-209567.
- [19] O. Akande et al., "A Systematic Review of Machine Learning Prediction Models for Colorectal Cancer Patient Survival Using Clinical Data and Gene Expression Profiles," *Revue d'Intelligence Artif.*, 2023, doi: 10.18280/ria.370520.
- [20] "HubMeta - Systematic Review and Meta Analysis Cloud Platform." [Online]. Available: <https://hubmeta.com/>. [Accessed: Mar. 11, 2024].
- [21] N. R. Haddaway, M. J. Page, C. C. Pritchard, and L. A. McGuinness, "PRISMA2020: An R package and Shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimised digital transparency and Open Synthesis," *Campbell Syst. Rev.*, vol. 18, no. 2, p. e1230, Jun. 2022, doi: 10.1002/cl2.1230.
- [22] D. Moher et al., "Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement," *Syst. Rev.*, vol. 4, no. 1, pp. 148-160, 2015, doi: 10.1186/2046-4053-4-1.
- [23] D. Moher et al., "Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement," *PLoS Med.*, vol. 6, no. 7, 2009, doi: 10.1371/journal.pmed.1000097.
- [24] Y. Tong, Z. Tan, P. Wang, and X. Gao, "A Machine Learning Method for Predicting Biomarkers Associated with Prostate Cancer," vol. 28, no. 12, 2023.
- [25] S. Yeh, Y. Chung, and B. C.-Molecules, "Investigating the Role of Obesity in Prostate Cancer and Identifying Biomarkers for Drug Discovery: Systems Biology and Deep Learning Approaches," *Molecules*, vol. 27, no. 3, p. 900, 2022. [Online]. Available: <https://www.mdpi.com/1420-3049/27/3/900>. [Accessed: Feb. 22, 2024].
- [26] R. Toth, H. Schiffmann, C. Hube-Magg, and F. B.-C., "Random forest-based modelling to detect biomarkers for prostate cancer progression," *Springer*, 2019. [Online]. Available: <https://link.springer.com/article/10.1186/s13148-019-0736-8>. [Accessed: Feb. 22, 2024].
- [27] S. Y. Shin et al., "A Boolean-based machine learning framework identifies predictive biomarkers of HSP90-targeted therapy response in prostate cancer," *Front. Mol. Biosci.*, vol. 10, pp. 1-16, Jan. 2023, doi: 10.3389/fmolb.2023.1094321.
- [28] C. Lee, A. Light, and E. S. Saveliev, "Developing machine learning algorithms for dynamic estimation of progression during active surveillance for prostate cancer," *Nat. Comput. Sci.*, 2022, doi: 10.1038/s41746-022-00659-w.

- [29] S. Chen *et al.*, "Machine Learning-Based Models Enhance the Prediction of Prostate Cancer," *Front. Oncol.*, vol. 12, Jul. 2022, doi: 10.3389/fonc.2022.941349.
- [30] E. Erdem, F. B.-A. B. ve T. Dergisi, "A comparison of various supervised machine learning techniques for prostate cancer prediction," *DergiPark*, 2021. [Online]. Available: <https://dergipark.org.tr/en/pub/ejosat/issue/59648/802810>. [Accessed: Feb. 23, 2024].
- [31] J. Dai, "Analyses of Lifestyle and Environmental Factors for Cancer Prevention using Deep Learning and Conventional Machine Learning from UK Biobank Data," 2020.
- [32] J. Lee *et al.*, "Machine learning approaches for the prediction of prostate cancer according to age and the prostate-specific antigen level," *KJUO*, 2024. [Online]. Available: <http://www.kjuo.or.kr/journal/view.php?number=427>. [Accessed: Feb. 16, 2024].
- [33] O. C. Ngige, F. Y. Ayankoya, J. A. Balogun, E. Onuiri, C. Agbonkhese, and F. A. Sanusi, "A dataset for predicting Supreme Court judgments in Nigeria," *Data Brief*, vol. 50, p. 109483, 2023, doi: 10.1016/j.dib.2023.109483.
- [34] D. M. W. Powers, "Evaluation: From Precision, Recall and F-Measure to ROC, Informedness, Markedness & Correlation," *J. Mach. Learn. Technol.*, vol. 2, no. 1, pp. 37-63, 2011. [Online]. Available: <https://www.researchgate.net/publication/228529307>.
- [35] K. S., "Receiver-operating characteristic curve analysis in diagnostic, prognostic and predictive biomarker research," *J. Clin. Pathol.*, vol. 62, no. 1, pp. 1-6, 2009. [Online]. Available: <https://jcp.bmj.com/content/62/1/1.short>.
- [36] P. Baldi, S. Brunak, Y. Chauvin, and C. A.-, "Assessing the accuracy of prediction algorithms for classification: an overview," *Bioinformatics*, vol. 16, no. 5, pp. 412-424, 2000. [Online]. Available: <https://academic.oup.com/bioinformatics/article-abstract/16/5/412/192336>.
- [37] R. Parikh, A. Mathai, S. Parikh, G. C. Sekhar, and R. Thomas, "Understanding and using sensitivity, specificity and predictive values," *Indian J. Ophthalmol.*, vol. 56, no. 1, pp. 45-50, 2008, doi: 10.4103/0301-4738.37595.