

# Mathematical and Computational Models in Prostate Cancer: From Early Detection to Precision Therapy

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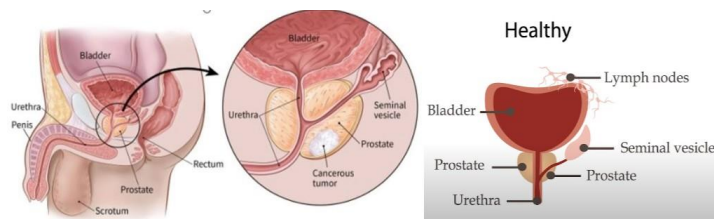
## ABSTRACT

This study critically analyses the biases impacting scientific credibility and equality while looking into the main data sources used in prostate cancer research. It examines important repositories and describes their function in epidemiological and clinical analysis, including The Cancer Genome Atlas (TCGA), Surveillance, Epidemiology, and End Results (SEER), and GLOBOCAN. In particular, the under-representation of minorities and low- and middle-income groups, as well as structural biases resulting from electronic health records and diagnostic access, are highlighted in the paper as limits in data completeness, representativeness, and annotation. These problems limit the generalisability of sophisticated analytical techniques like machine learning and spread algorithmic bias, as it is discussed. In order to improve scientific rigour and equity, the study investigates solutions such as external validation, synthetic data production, and standardised protocols. Results show that in order to facilitate thorough, equitable, and globally applicable prostate cancer research, inclusive data collecting and transparent annotation are essential.

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## INTRODUCTION

Among men, especially those over 65 years of age, prostate cancer is one of the most common cancers [1, 4, 23, 21]. It starts in the prostate gland and can range from mild tumors to severe, spread-related illnesses. One kind of cancer that arises in the prostate gland, a little, walnut-shaped gland situated just behind the bladder in males, is called prostate cancer. As a component of the male reproductive system, the prostate is essential for the production of seminal fluid, which feeds and carries sperm [11]. When cells in the prostate start to grow out of control and form a tumor, prostate cancer results. Prostate cancer frequently progresses slowly and may not be life-threatening [10, 20]. While some forms are more aggressive, grow more quickly, and spread to other regions of the body like the bones or lymph nodes, others are restricted to the prostate and are often benign [6, 5]. A malignant tumor inside the prostate gland is seen in the accompanying Fig. 1, which also shows the gland's anatomical location and how it might impact the urethra and nearby tissues including the bladder, seminal vesicles, and rectum. This illustration helps explain how a prostate tumor's growth might cause problems for the affected person's reproductive system and urine system.



**Figure 1: Prostate cancer development and the prostate gland's anatomical position [51]**

### 1.1 Stages

The TNM classification system, serum levels of prostate-specific antigen (PSA), and the Gleason grading system are used to clinically grade prostate cancer. These methods are used to create a four-stage framework (Stage I–IV) that directs treatment planning and prognosis. The seminal vesicle,

urethra, bladder, prostate gland, and lymph nodes are among the typical anatomical features seen in the Fig. 1. In order to compare the baseline anatomy with the clinical stages of prostate cancer, the prostate is depicted in its healthy form, free of any indications of tumor or aberrant growth.

## STAGES OF CANCER

Prostate cancer is classified into four distinct stages according to the extent of tumor involvement, histologic characteristics, and metastatic spread. In Stage I, the disease is typically asymptomatic and remains confined within the prostate gland. It is often detected incidentally following benign prostatic hyperplasia surgery or through prostate-specific antigen (PSA) screening and

histopathological examination. Tumors at this stage exhibit PSA levels below 10 ng/mL, a Gleason score of 6 (Grade Group 1), and are either clinically non-palpable (T1) or involve half of one lobe or less (T2a) (see figure 1). This stage indicates a favorable prognosis with minimal risk [1, 2, 13], as the malignancy is entirely localized within the prostate without invasion of adjacent structures. Stage II disease remains organ-confined but demonstrates greater histologic heterogeneity, increased tumor volume, or elevated PSA values. It is further subdivided into Stage II A, Stage II B, and Stage II C based on tumor characteristics. Stage II A encompasses T1 – T2a tumors with PSA levels between 10 and 20 ng/mL and a Gleason score of 6. Stage II B includes T2b–T2c tumors or those with a Gleason score of 7 (Grade Groups 2–3), whereas Stage II C refers to any T1–T2 tumor with a Gleason score 8 (Grade Group 4). Although curative management remains possible, patients in Stage II require more exhaustive risk assessment, vigilant monitoring, and, in some cases, early therapeutic intervention to mitigate disease progression. Stage III, Figure 2 defined as locally advanced disease, is characterized by extraprostatic extension involving the seminal vesicles or surrounding tissues (T3). Clinical indicators include PSA concentrations exceeding 20 ng/mL and Gleason scores ranging from 8 to 10 (Grade Groups 4–5), often accompanied by evidence of capsular penetration or seminal vesicle invasion. Given the heightened likelihood of recurrence, treatment at this stage generally necessitates a multimodal approach incorporating radiation therapy, androgen deprivation, and other systemic regimens. Stage IV represents advanced or metastatic prostate cancer and is subdivided into Stage IVA and Stage IVB. In Stage IVA, the disease extends to regional lymph nodes (N1) without distant metastasis (M0), whereas Stage IVB signifies dissemination to distant sites such as non-regional lymph nodes, bone, or visceral organs (M1). This stage denotes a severe and high-grade malignancy with the poorest prognosis. Management typically involves systemic treatment modalities, including androgen deprivation therapy, cytotoxic chemotherapy, radioligand therapy, or emerging targeted therapeutics, with the primary goals of disease control, symptom palliation, and prolongation of survival.



**Figure 2: Four Stages of prostate cancer in the prostate gland**

### Symptoms

Early-stage prostate cancer frequently exhibits no symptoms, developing gradually without any discernible signs. Urinary symptoms, including increased frequency of urination, especially nocturia (nighttime urination), a weak or intermittent urine stream, difficulty starting or stopping urination, and occasionally blood in the urine, are common as the disease progresses [19, 21, 22]. Erectile dysfunction (the inability to get or keep an erection), ejaculatory pain, and a discernible decrease in ejaculate volume are examples of sexual symptoms that may also appear. Patients may report general malaise, exhaustion, inexplicable weight loss, and discomfort from metastases that impact the lower back, thighs, hips, or pelvis in more systemic or advanced stages [25, 26]. These symptoms are non-specific, though, because benign illnesses like prostatitis or benign prostatic hyperplasia (BPH) can cause comparable symptoms [20, 22, 25]. It is impossible to overestimate the significance of screening because early prostate cancer is often asymptomatic. For those at higher risk, routine screening techniques such as digital rectal examinations (DRE) or blood testing for prostate-specific antigen (PSA) are especially advised [44, 9, 12, 14]. In the end, prompt medical examination is essential for precise diagnosis and for differentiating between benign and malignant conditions [19, 14, 12].

### 2.1 Risk Factors

Age significantly raises the risk of prostate cancer, especially after the age of 50 [4, 25, 21]. Another important contributing factor is family history; men who have close relatives with a young diagnosis, such as a father, brother, or cousin, are far more likely to get the disease [1, 47]. Race and ethnicity are also important factors; Asian and Hispanic men often show reduced susceptibility, while African American men have a significantly higher incidence and mortality rate and are frequently identified at more late stages [4, 44, 9]. The risk may be further increased by inherited genetic mutations, particularly in the genes BRCA1, BRCA2, PTEN, and TMPRSS2-ERG. An increased risk of aggressive prostate cancer types has been associated with obesity [2, 23, 21]. Furthermore, dietary and lifestyle choices affect the risk of disease; diets high in red meat and high-fat dairy products but low in fruits and vegetables may increase vulnerability, and poor nutrition and sedentary behaviour can exacerbate inflammation and hormone imbalances [27, 23]. Chemical exposure, whether occupational or environmental, may increase the risk of prostate cancer, though more research is required to fully understand this relationship. Chronic prostate inflammation (prostatitis) is also being studied as a possible contributing factor [28, 25].

### 2.2 Diagnosis and Treatment

Recent advancements in prostate cancer diagnosis and treatment include computational modelling, genomic analysis, and improved imaging. Lesion localisation and PSMA-expressing cancer detection are improved by multiparametric MRI (mpMRI) and 18F-DCFPyL PET/CT [5]. Together with genomic profiling, genomic biomarkers like PCA3 and AR-V7 allow for more accurate treatment resistance prediction and therapeutic customisation [6, 15, 28]. In order to balance early detection with decreased over-diagnosis, the ProScreen trial implemented a multistep screening paradigm utilising PSA, kallikreins, and MRI [13, 20]. Predictive diagnostics is now aided by statistical models and machine learning, such as Cox and Kaplan-Meier analyses, with deep learning approaches demonstrating greater accuracy [21, 22]. Darolutamide dramatically increases survival in both non-metastatic and metastatic cases, according to the ARAMIS and ARASENS trials in therapeutics [3, 18]. Precision oncology advances target specific genetic mutations to customise treatments [15, 28], and new grading schemes

like GUPS 2019 encourage uniformity in diagnosis [33, 44]. Individualised and evidence-based treatment decisions are increasingly supported by the multimodal integration of imaging, biomarkers, and AI-based predictions [12, 18].

### 2.3 Datasets

Prostate cancer research depends on data to understand disease aetiology, improve diagnostic precision, forecast patient outcomes, and direct treatment plans [17, 15], [19, 12]. Reviews of 50 studies demonstrate the extensive use of a variety of data sources, such as imaging results, clinical records, genetic biomarkers, and socioeconomic indices [29]. Tumour stage, Gleason score, PSA levels, age, ethnicity, and family history are among the clinical and demographic data that are essential to prostate cancer research. Large datasets from WHO registries, GLOBOCAN, and SEER highlight racial and age-related disparities [4, 23], [6, 22]. For instance, between 2003 and 2016, age-standardized incidence rates in Indian males increased dramatically from 5.1 to 9.0 per 100,000 people as shown Fig. 3, highlighting a serious public health concern [52]. Diagnosis and staging are aided by imaging and histopathological data from mp MRI, PET/CT, and ultrasound; however, multiparameters MRI (Fig. 4) has limited sensitivity in the transitional zone where 20–30 percent of prostate cancers begin [5], [13], [18]. Precision oncology is supported by molecular and genomic data, including biomarkers like miR-21, AR-V7, and mutations in BRCA1/2, PTEN, and TMPRSS2-ERG, as databases like TCGA, COSMIC, and OncoKB enable research; In cases of prostate cancer, TP53 mutations occur most frequently (13 percent) (Fig. 5). [29], [52], cite Cimadamore A., Sartor O.. Survey-derived behavioural and epidemiological data evaluate screening methods and awareness that are essential for early detection and intervention [14]. Primary data sources, such as SEER for epidemiology, TCGA-PRAD for genomics, GLOBOCAN for worldwide incidence, clinical trials like ARASENS/ARAMIS, and imaging databases PROstateX and PROMISE [4, 23], [29], are ranked in Table 1. Feature engineering, normalisation, and labelling are preprocessing steps in data curation; augmentation is required for tiny imaging datasets. Logistic regression, survival analysis, chi-square tests, and machine learning methods like support vector machines, random forests, and deep learning—which can get accuracy as high as 97 percent—are examples of analytical techniques. Hazard ratios, odds ratios, relative risk, and AUC are examples of prognostic and diagnostic metrics. Data heterogeneity, under-representation in low-to-middle-income countries that hinders generalisability, inconsistent pathology reporting, a lack of clinical validation for novel biomarkers, and data privacy concerns that restrict sharing are among the challenges.

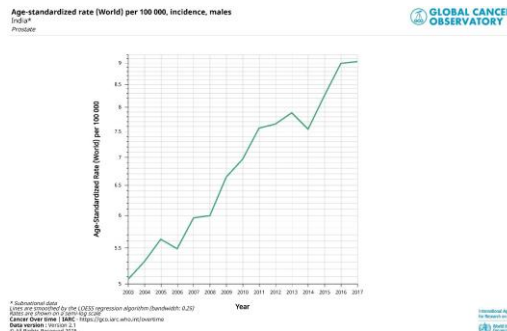


Figure 3: Age-standardized incidence rate of prostate cancer among Indian males (2003–2016) [52]

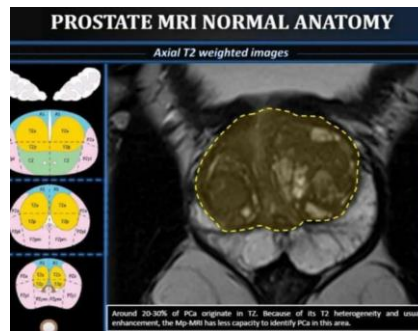


Figure 4: Axial T2-weighted MRI image showing normal prostate anatomy

#### 2.3.1 Data Preprocessing and Curation, Analytical Technique, Challenges

Data processing for prostate cancer research includes careful preprocessing and curation, including feature engineering (e.g., computing PSA density or composite risk scores), normalisation of clinical variables like PSA, and careful labelling of imaging and genetic markers. Data augmentation is often used for imaging datasets with small sample numbers, and systematic evaluations

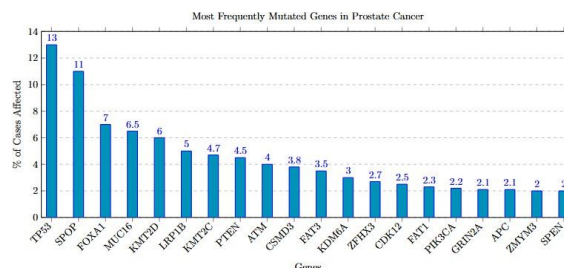


Figure 5: Most Frequently Mutated Genes [52]

**Table 1: Primary Data Sources for Prostate Cancer Research**

Rank	Data Source	Main Use
1	SEER	Epidemiology, survival analysis
2	TCGA-PRAD	Genomics, biomarkers, machine learning
3	GLOBOCAN / WHO	Global incidence, mortality rates
4	ARASENS / ARAMIS	Clinical trials, treatment outcomes
5	ProstateX, PROMISE	Imaging diagnostics (MRI, PET)

often identify pretreatment technique variability as a significant source of bias. Traditional statistics like logistic regression, Kaplan-Meier estimators, Cox proportional hazards models, and chi-square tests are examples of analytical approaches. More sophisticated methods include meta-analysis and the application of machine learning models like support vector machines, random forests, and deep learning, with multilayer perceptrons sometimes reaching accuracy rates as high as 97 percent. Hazard ratios, odds ratios, relative risk, and area under the curve (AUC) are important metrics for measuring prognostic power and diagnostic value. Significant challenges still exist despite methodological advancements: data heterogeneity in imaging, histopathology, and population attributes; under-representation of LMICs, which affects the generalisability of findings; inconsistent pathology reporting standards, particularly for novel biomarkers; a lack of robust clinical validation for many biomarkers, including miR-21, PCA3, and AR-V7; and privacy concerns that restrict the sharing of sensitive clinical and genetic data.

### MATHEMATICAL MODELS

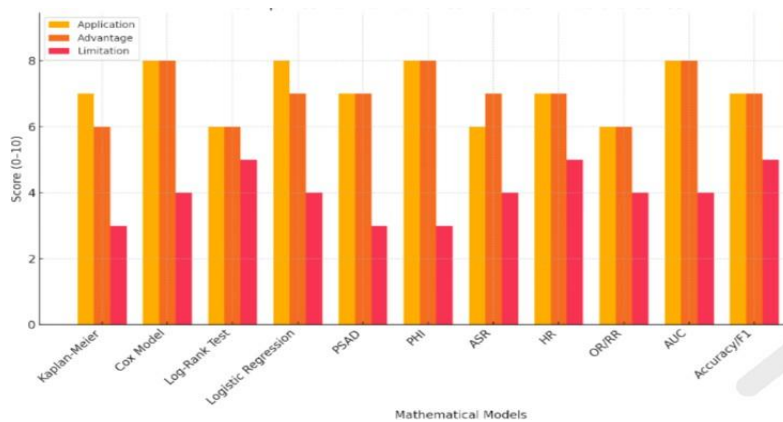
Quantitative prostate cancer research is built on mathematical and computational models that integrate clinical, genomic, and population-level data to enable sophisticated biological mechanism simulation, accurate diagnosis, and outcome prediction. While machine learning techniques, such as neural networks, logistic regression, and support vector machines, support robust prognosis, personalised risk stratification, and optimal treatment selection, deterministic, stochastic, and agent-based models efficiently capture tumour dynamics, response variability, and therapeutic effects. Using techniques like the Kaplan-Meier estimator to estimate survival probability over time, the Cox proportional hazards model to evaluate covariate effects on hazard, and the Log-Rank test to compare survival distributions across patient groups, survival analysis plays a crucial role. These techniques are frequently employed, with Kaplan-Meier appearing in 40 percent of studies, Cox models in 35 percent, and Log-Rank in 25 percent. PSA density (PSAD), Prostate Health Index (PHI), and age-standardized rate (ASR) are examples of diagnostic and prognostic indicators used in biomarker-driven models. These parameters help distinguish between benign and malignant disease, guide clinical decisions about biopsy and treatment, and allow for standardised comparisons across populations. Important statistical metrics that are essential for validating clinical and molecular biomarkers include sensitivity, specificity, predictive values, hazard ratio (HR), odds ratio (OR), and relative risk (RR). These metrics offer quantitative assessments of therapeutic efficacy, risk estimation, and diagnostic accuracy. Risk prediction, patient classification, and biomarker evaluation are made easier by predictive and prognostic frameworks, especially logistic regression (probability modelled by a logistic function). Supporting metrics like area under the ROC curve (AUC), accuracy, and F1 score describe model discrimination and performance on imbalanced datasets (see 2). In prostate cancer research, these statistical techniques and mathematical tools collectively support modern evidence-based approaches that direct clinical care, epidemiological comparison, biomarker validation, and personalised therapy.

**Table 2: Mathematical Models Used in Prostate Cancer: Types, Applications, Advantages, and Limitations**

Model	Type	Application	Advantage	Limitation
Kaplan-Meier Estimator	Survival Analysis	Estimate survival probabilities; compare outcomes across treatment groups	Handles censored data, intuitive interpretation	Limited to univariate analysis; doesn't adjust for covariates
Cox Proportional Hazards Model	Semi-parametric Survival Model	Assess impact of covariates on survival time	Adjusts for multiple variables; widely used	Assumes proportional hazards; sensitive to violations
Log-Rank Test	Hypothesis Testing	Compare survival distributions between patient groups	Non-parametric; suitable for group comparison	No adjustment for covariates; assumes proportional hazards
PSA Density (PSAD)	Diagnostic Index	Differentiates prostate cancer from benign conditions using PSA per prostate volume	Increases specificity over PSA alone; simple calculation	Requires accurate prostate volume estimation
Prostate Health Index (PHI)	Biomarker Composite Index	Stratifies risk in patients with ambiguous PSA levels	Improves detection accuracy; reduces unnecessary biopsies	Limited availability; costlier than PSA test
Age-Standardized Rate (ASR)	Epidemiological Metric	Compare incidence/mortality rates across regions	Standardized across populations; useful in public health	Doesn't capture individual-level risk
Logistic Regression	Predictive Statistical Model	Predict presence or progression of cancer from clinical features	Interpretable coefficients; fast training	Assumes linearity in log-odds; not ideal for non-linear problems

Area Under Curve (AUC)	Model Performance Metric	Evaluate classifier performance in prediction tasks	Summarizes sensitivity vs. specificity across thresholds	Does not reflect calibration or decision threshold impact
Accuracy and F1 Score	Evaluation Metrics	Measure classification performance (balanced/unbalanced data)	Easy to compute; F1 is useful for imbalance	Misleading in imbalanced datasets (accuracy); lower interpretability (F1)
Hazard Ratio (HR)	Risk Metric	Compare event risk between treatment/control groups	Intuitive for clinical interpretation	Assumes consistent hazard over time
Odds Ratio (OR) and Relative Risk (RR)	Association Metrics	Quantify association between risk factors and outcomes	Standard in case-control and cohort studies	Misinterpretation common; OR may overestimate risk in frequent outcomes

Three primary criteria—application, benefit, and limitation—are used to compare and assess the different mathematical models used in prostate cancer research in Fig. 6. Prostate health index (PHI), PSA density (PSAD), and the Cox model all received excellent application and perceived benefit scores, demonstrating their wide range of usefulness and efficacy in clinical decision-making. On the other hand, models such as the Log-Rank Test and the Odds Ratio (OR/RR) showed higher restriction scores, which indicated difficulties with generalizability or interpretability. The significance of striking a balance between clinical application and statistical robustness when using prediction methods for the treatment of prostate cancer is highlighted by this study.



**Figure 6: Comparison of Mathematical Models in Prostate Cancer Based on Application, Advantage, and Limitation Scores**

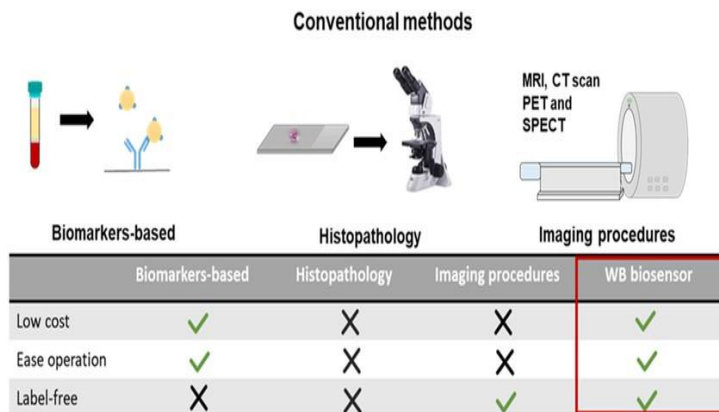
### COMPARISON OF DIFFERENT METHODOLOGIES

One of the most often diagnosed cancers in males worldwide is prostate cancer (PCa), which varies greatly in its course, molecular makeup, and re-sponse to treatment. Timely diagnosis and specialized treatment plans are essential for the effective management of PCa. A new age of personalized medicine has begun with the development of diagnostic tools and the incorporation of genetic profiling into clinical practice. A multidisciplinary strategy is necessary for the diagnosis, treatment, and management of prostate cancer since it is a complicated and diverse illness. Patient outcomes have been improved by the development and application of a broad range of approaches, including clinical, imaging, molecular, computational, and artificial intelligence-based techniques. Based on the therapeutic goals, available resources, and illness stage, each approach has certain benefits and drawbacks. The many approaches to prostate cancer research and treatment are compared in this chapter (see 3), with an emphasis on their guiding concepts, uses, and contributions to the development of precision medicine.

**Table 3: Comparison of Methodologies Used in Prostate Cancer Research and Diagnosis**

Methodology	Type	Examples	Strengths	Limitations	Clinical Utility
Conventional Detection [4, 12, 13, 10, 9], (Fig. 7)	Clinical Screening	PSA test, DRE, TRUS, systematic biopsy	Widely available; PSA test is non-invasive; forms foundation of diagnosis	Overdiagnosis; low specificity (PSA ~20%); invasive biopsy risks	Initial screening and staging
Multiparametric MRI (mpMRI) [2, 18, 5, 17], (Figs. 4, 8, 9)	Imaging	T2-weighted, DWI, DCE-MRI	High sensitivity/specificity; guides targeted biopsy; non-invasive	Expensive; operator dependent; limited access	Tumor localization, staging, active surveillance

MRI-Targeted Biopsies [12, 10, 17, 26] Fig. 10	Imaging Biopsy +	Fusion-guided or in-bore MRI biopsy	Improved detection of clinically significant PCa; fewer unnecessary biopsies	Requires mpMRI and fusion tech; skill-intensive	More accurate diagnosis
PET Imaging (e.g., PSMA PET)	Molecular Imaging	<sup>18</sup> F-DCFPyL, <sup>68</sup> Ga-PSMA-11	Detects recurrence at low PSA; high accuracy in metastatic staging	Costly; limited availability; requires nuclear medicine infrastructure	Recurrent/metast PCa detection
Biomarker Assays [12, 10, 17, 26], Fig. 10	Molecular Testing	PCA3, PHI, 4Kscore, SelectMDx	Non-invasive (often urine/blood); improves risk stratification	Limited sensitivity; not yet widely adopted	Adjunct to PSA screening
Liquid Biopsy	Molecular Testing	Circulating tumor DNA, miR-21, exosomes	Minimally invasive; enables real-time monitoring	Still under validation; costly; technical variability	Risk assessment, prognosis, therapy monitoring
Genomic Testing	Molecular Profiling [1, 10, 17], Fig. 13	BRCA1/2, ATM, CHEK2, TMPRSS2-ERG fusions	Identifies hereditary risk; guides targeted therapy	Limited to high-risk/advanced PCa; inconsistent gene panels	Therapy selection; clinical trials eligibility
Artificial Intelligence (AI/ML) [10, 27, 18, 20], Fig. 13	Predictive Models	SVMs, CNNs, Ensemble models	High accuracy (>90% in some models); integrates imaging/genomics	Requires large, curated datasets; interpretability challenges	Risk prediction, treatment planning
Radioligand Therapy	Therapeutic	<sup>177</sup> Lu-PSMA-617	Targeted treatment for mCRPC; extends survival	Toxicity concerns; limited access and high cost	Advanced/metast disease
Genetically Targeted Therapy	Therapeutic	PARP inhibitors (olaparib, rucaparib)	Effective in BRCA-mutant or HR-deficient PCa	Requires confirmed genetic mutation; resistance can develop	Precision oncology for select patients
Screening Innovations (e.g., ProScreen) [12, 18, 5, 9], Figs. 11, 9	Combined Strategy	PSA + kallikrein panel + MRI	Reduces unnecessary biopsies; high accuracy in detecting significant PCa	Multi-step process; cost and complexity	Population screening trials



**Figure 7: Comparison of conventional diagnostic methods**

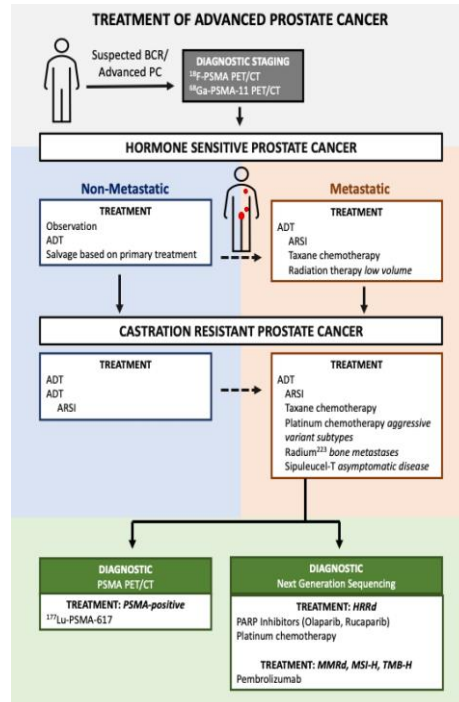


Figure 8: Treatment Algorithm for Advanced Prostate Cancer

## CURRENT TRENDS, CHALLENGES AND FUTURE DI-RECTION

### 5.1 Current Trends

One of the leading causes of cancer-related mortality among men is prostate cancer (PCa), which remains a serious global health concern. The burden of PCa is increasing, particularly in older populations, with over 1.4

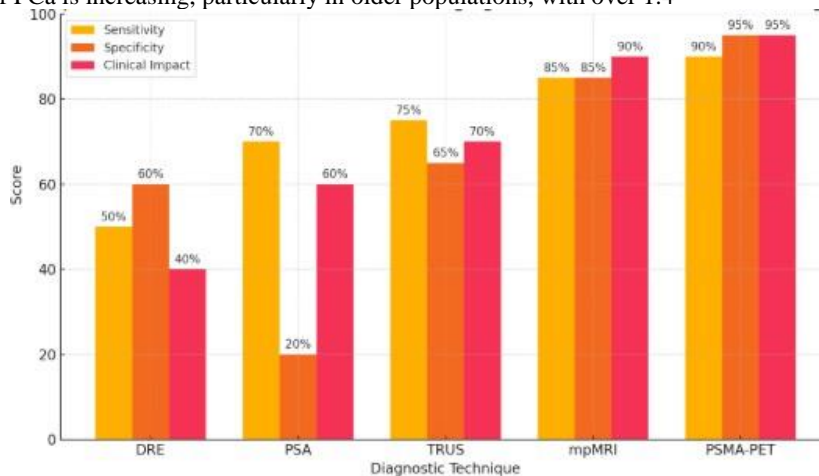


Figure 9: Comparison of Conventional and Advanced imaging Modalities in Prostate Cancer diagnosis

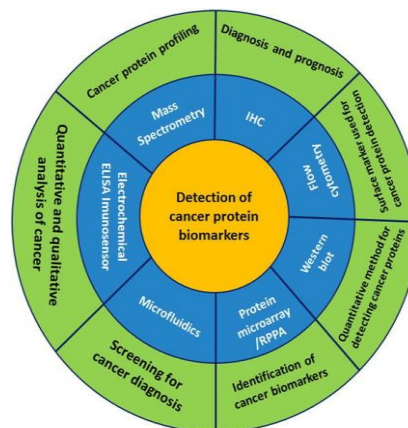


Figure 10: Methodology and Applications in the Detection of Cancer Protein Biomarkers

million new cases reported each year [24],[19]. The current state of PCa re- search is being shaped by developments in genetics, diagnostics, treatments, and digital health[5]. Based on a thorough analysis of 50 research publi- cations, this chapter examines current trends and projects where prostate cancer research will go in the future[25, 3].

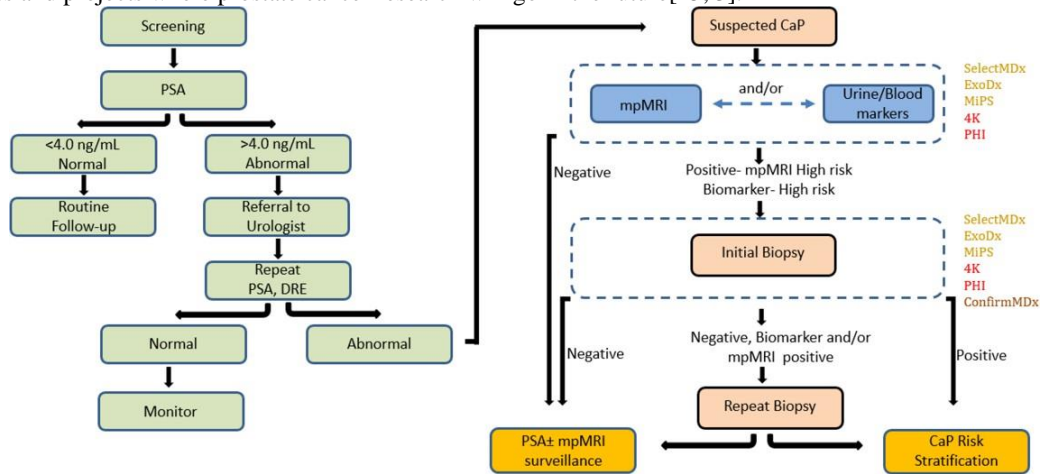


Figure 11: Prostate Cancer Diagnostic Pathway

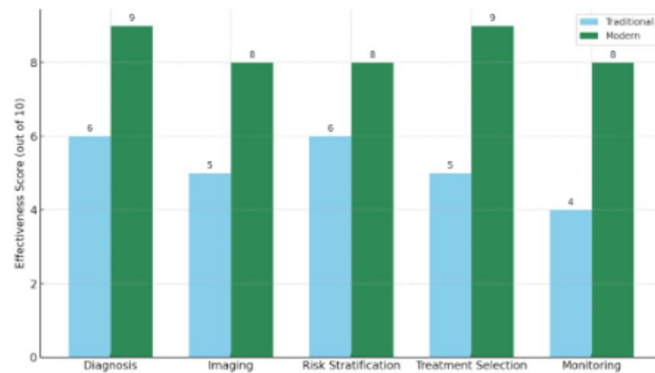


Figure 12: Comparison of Traditional vs. Modern Prostate Cancer Methodologies Based on Effectiveness Scores

The current trends and future directions in important areas of prostate cancer research and treatment are succinctly summarized in this Table 4. It demonstrates how the industry is moving away from conventional methods and toward more sophisticated, individualized strategies. It is anticipated that the present use of BRCA1/2 and PTEN profiling in genetics will de- velop into thorough multi-omics integration. Standard imaging techniques such as PSMA-PET and mpMRI are opening the door for liquid biopsy and AI-enhanced diagnostics in diagnostics. Future research will concentrate

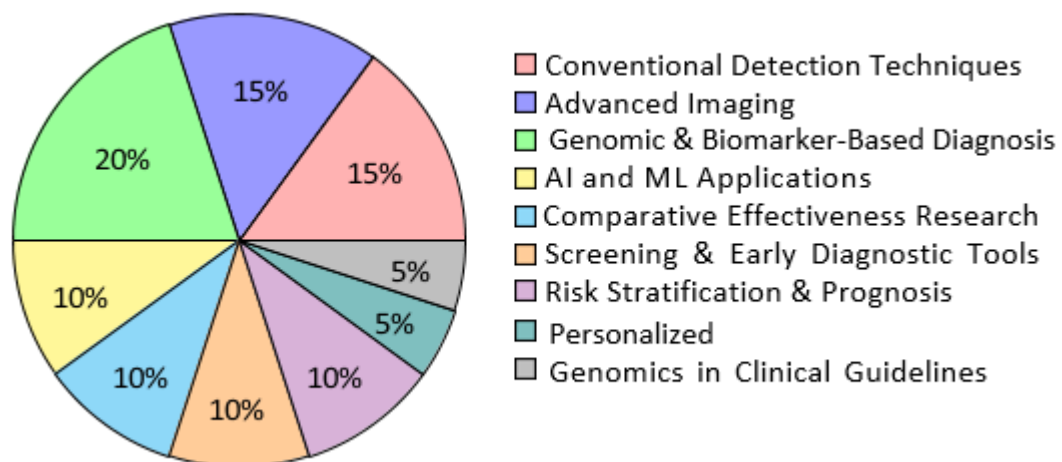


Figure 13: Functional Roles of Prostate Cancer Methodologies

on immunotherapy combinations, even though PARP inhibitors and next- generation androgen receptor blockers like darolutamide are now being used therapeutically. Basic prognostic models are giving way to real-time clinical decision support systems in AI.

Table 4: Overview of current trends and future directions

Area	Current Trends	Future Directions
Genetics	BRCA1/2, PTEN profiling	Multi-omics integration
Diagnostics	mpMRI, PSMA-PET	Liquid biopsy, AI support
Therapy	PARP inhibitors, darolutamide	Immunotherapy combinations
AI	Prognostic modeling	Clinical decision support tools
Public Health	Awareness programs	Global screening equity

### 5.1.1 Precision Medicine and Genetic Profiling

Genetic profiling in prostate cancer is driving precision medicine more and more, allowing for more individualized and successful treatment plans. According to current trends, individuals who are at higher risk or who could benefit from targeted medicines like PARP inhibitors (e.g., olaparib) can be identified by testing for germline and somatic mutations in genes including BRCA1/2, ATM, CHEK2, and TP53, as well as TMPRSS2-ERG fusions. Especially in cases of advanced and castration-resistant prostate cancer (CRPC), these genetic insights inform therapy choices. Furthermore, panel testing and next-generation sequencing (NGS) are being incorporated into clinical workflows to aid in prognostic prediction, medication selection, and risk stratification. Accessibility, standardization, and clinical interpretation continue to be obstacles, despite the good results, particularly in areas with limited resources [17, 10, 26].

### 5.1.1 Advanced Imaging and Diagnostics

The current advancements in prostate cancer advanced imaging and diagnostics are centered on increasing early detection, decreasing needless biopsies, and boosting accuracy. A common tool for local tumor identification, staging, and directing targeted biopsies, multiparametric MRI (mpMRI) offers more sensitivity and specificity than conventional techniques. Even at low PSA levels, PSMA-PET imaging (e.g., 68Ga-PSMA-11, 18F-DCFPyL) is being utilized more and more to detect metastatic disease and biochemical recurrence with exceptional precision [12]. A common addition to these imaging developments is MRI-targeted biopsies, which reduce overdiagnosis while increasing the detection of clinically relevant prostate cancer. Additionally, new molecular diagnostics are becoming popular for non-invasive risk assessment and monitoring. These include liquid biopsies (like ctDNA and exosomes) and biomarker tests (like PHI, 4Kscore, and PCA3) [5].

### 5.1.2 Novel Therapeutic Modalities

Targeted and customized therapies are the focus of recent developments in prostate cancer therapy, which aims to improve outcomes for advanced and resistant disease stages. BRCA1/2 and other DNA repair gene mutations are treated with PARP inhibitors (e.g., olaparib, rucaparib). Agents like 177 Lu-PSMA-617 have demonstrated notable effectiveness in radioligand treatment for metastatic castration-resistant prostate cancer (mCRPC) [15]. Furthermore, survival is increasing with fewer adverse effects because to next-generation androgen receptor inhibitors such as apalutamide and darolutamide. Immunotherapy is gaining popularity, especially checkpoint inhibitors and combination approaches (such as immunotherapy + androgen deprivation treatment), while research is still being done to see how successful they are for prostate cancer. Adaptive clinical trials, genomic-guided precision medicine, and AI-driven therapy selection are also influencing a more customized approach to treatment [25, 3].

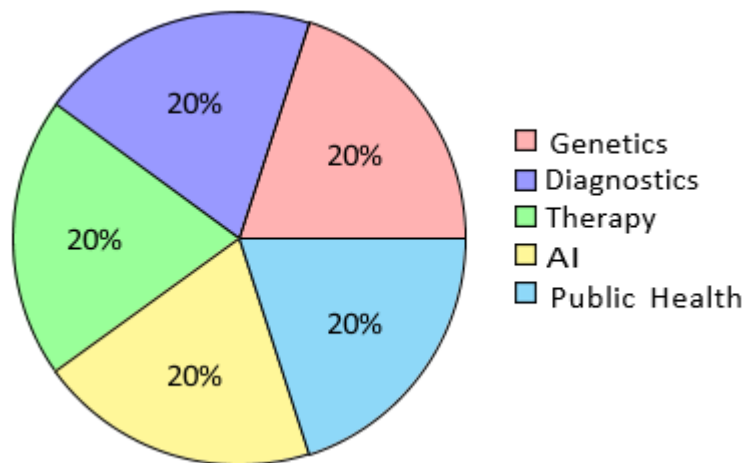
### 5.1.3 Digital Health and Artificial Intelligence

Prostate cancer treatment is fast changing due to digital health and artificial intelligence, with a particular emphasis on data-driven precision medicine. These days, prognosis prediction, imaging interpretation (e.g., mpMRI, PSMA-PET), and biopsy guiding are all done with AI models, such as support vector machines (SVMs), convolutional neural networks (CNNs), and multilayer perceptrons (MLPs), which frequently achieve diagnostic accuracies above 90%. Continuous care and real-time decision-making are supported by digital health solutions such as telemedicine platforms, remote patient monitoring, and algorithms incorporated into electronic health records (EHR). Notwithstanding encouraging outcomes, there are still issues, such as poor clinical integration, inconsistent validation, and a dearth of broad demographic representation in training datasets. These technologies do, however, mark a significant advancement in automated, scalable, and customized prostate cancer treatment [27].

### 5.1.4 Global Disparities and Public Health

Variations in PCa outcomes according to socioeconomic class and access to healthcare are revealed by epidemiological studies. Stronger health-care infrastructure in Southeast Asia is associated with better survival outcomes [22], while in Africa, rural awareness initiatives are crucial [14].

An equal distribution of prostate cancer research priority areas is shown in Fig. 14, with five key domains—Genetics, Diagnostics, Therapy, Artificial Intelligence (AI), and Public Health—each accounting for 20% of the overall emphasis. Current PCa research is interdisciplinary, which is reflected in this balanced categorization. It emphasizes how enhanced imaging, therapy innovation, AI-driven analytics, molecular profiling, and fair healthcare delivery must all be combined. A thorough emphasis like this is necessary to make significant improvement in the outcomes of prostate cancer.



**Figure 14: Research Focus Areas**

## 5.2 Challenges in Prostate Cancer Management

### 5.2.1 Diagnostic Limitations

Testing for prostate-specific antigen (PSA) has poor specificity, which frequently leads to false positive results and needless biopsies. Prostate lesion localization is improved by multiparametric MRI (mpMRI), although diagnostic consistency is impacted by the wide variation in mpMRI interpretation throughout institutions [12, 18].

Further limiting the broad use of precision diagnostic tools in clinical settings is the absence of standardized, clinically validated biomarkers [17, 10].

1. **Low Specificity of PSA Testing:** The prostate-specific antigen (PSA) test frequently produces false positives due to benign conditions like prostatitis or BPH, resulting in unnecessary biopsies and patient anxiety.
2. **Overdiagnosis and Overtreatment:** Many prostate cancers are indolent and may never become life-threatening, but current diagnostic tools frequently cannot reliably distinguish aggressive from low-risk disease.
3. **Biopsy Sampling Error:** Traditional transrectal ultrasound (TRUS)-guided biopsies can miss clinically significant tumors, particularly in anterior or apical regions of the prostate.
4. **Imaging Variability:** While mpMRI improves detection, its accuracy is highly dependent on operator expertise and interpretation, resulting in inconsistent results across centers.
5. **Limited Access to Advanced Diagnostics:** PSMA-PET and genomic testing may not be available in resource-limited settings, limiting equitable care.
6. **Low Access to Advanced Diagnostics:** Equitable care may be hampered in settings with low resources by the lack of technologies such as PSMA-PET and genetic testing.
7. **Absence of Validated Biomarkers:** In spite of continuous study, many genetic or imaging biomarkers that may reliably predict the aggressiveness of a disease and direct treatment are still lacking.
8. **Uneven Guidelines:** Different diagnostic thresholds and procedures in different areas or institutions may result in uneven treatment and a delayed diagnosis.

These difficulties underscore the need for more accurate, easily available, and standardized diagnostic instruments to enhance prostate cancer risk assessment and early diagnosis.

### 5.2.2 Therapeutic Challenges

One of the most challenging phases of prostate cancer to treat is castration-resistant prostate cancer (CRPC). Even with improvements in targeted therapy and second-generation androgen receptor inhibitors, CRPC frequently results in metastases and higher death rates [11, 2]. Additionally, the high prices and infrastructure requirements, particularly in low- and middle-income countries, limit access to new medicines such as PARP inhibitors and radioligand therapy employing <sup>177</sup>Lu-PSMA-617 [15, 29].

1. **Castration-resistant prostate cancer (CRPC):** A significant obstacle since, in spite of androgen deprivation therapy, the illness frequently advances, reducing available treatments and survival.
2. **Therapy Resistance:** As time passes, resistance to common medicines including PARP inhibitors, chemotherapy, and androgen receptor inhibitors grows, decreasing their long-term effectiveness.
3. **Limited Access in LMICs:** In low- and middle-income countries, advanced treatments such as genetic testing, PSMA-targeted therapy, and radioligand treatment are either unavailable or prohibitively expensive.
4. **Exorbitant Treatment Costs:** Patients and healthcare systems are put under financial duress by the high cost of new targeted medicines and immunotherapies.
5. **Toxicity and Side Effects:** The quality of life of patients may be negatively impacted by severe side effects from treatments like chemotherapy and radiation.
6. **Lack of Predictive Biomarkers:** It is challenging to implement individualized therapy due to the lack of trustworthy biomarkers that can forecast treatment response.
7. **The disease's heterogeneity:** Because prostate cancer differs greatly from patient to patient, specialized treatments are needed, but they are not yet completely developed or available.

8. Trial Underrepresentation: Clinical trials frequently include a low representation of older persons and minority groups, which restricts the applicability of treatment results.

### 5.2.3 Health System Barriers

Widespread myths, misunderstandings, and low public knowledge of prostate cancer and its risk factors prevent many people in developing nations from getting screened [14]. Furthermore, financial position, geography, and racial inequality all contribute to notable differences in care that impact early detection, access to treatment, and results[24, 23].

1. Limited Access to Screening and Diagnosis: PSA testing, mpMRI, and biopsy services are hard to come by in many low- and middle-income countries (LMICs), which results in late-stage diagnosis.
2. Resource Constraints: The high expense of sophisticated diagnostics (like PSMA-PET and genetic testing) and therapies (such as PARP inhibitors and radioligand therapy) restricts access, particularly in health systems with limited funding.
3. Workforce Shortages: Timely and correct diagnosis and treatment are hampered by a shortage of qualified urologists, oncologists, radiologists, and pathologists.
4. Geographic Disparities: In order to receive specialist prostate cancer care, those living in rural and isolated areas sometimes have to drive farther, wait longer, and have fewer facilities.
5. Fragmented Care Pathways: Inadequate communication between oncology experts, diagnostic services, and general care leads to delays and less than ideal results.
6. Lack of Standardized Guidelines: Consistent, evidence-based therapy is hampered by clinical practice variability, particularly in areas with low resources.
7. Data Gaps: It is challenging to track results, spot inequities, and direct policy when there are insufficient electronic health systems and cancer registries.
8. Health Literacy and Awareness: Men in underprivileged groups, in particular, are less likely to use preventative care due to a lack of knowledge about prostate cancer signs and screening.

### 5.3 Future Directions

A strategic roadmap for the future paths of prostate cancer (PCa) research is presented in Figure 17. It stresses a step-by-step strategy that begins with early detection and progresses to sophisticated imaging methods like mpMRI and PSMA-PET. Targeted treatments like PARP inhibitors and androgen deprivation therapy (ADT) are made possible by the incorporation of biomarkers like BRCA1/2 and PTEN, which facilitates AI-driven prognostic prediction. The focus for the future includes immunotherapy, liquid biopsy, and multi-omics, demonstrating a move toward more individualized and accurate oncologic care.

From early detection and advanced imaging to biomarker discovery, AI-based prognostic modeling, and personalized therapy, this Fig. 15 of the prostate cancer (PCa) research pipeline highlights important phases and points to upcoming advancements including multi-omics, liquid biopsy, and immunotherapy.

#### 5.3.1 Integrated Multi-Omics Approaches

A potential area for future research and precision therapy in prostate cancer is the use of integrated multi-omics techniques. By combining information from radiomics, proteomics, metabolomics, transcriptomics, and genomes, these techniques offer a thorough molecular profile of the illness. Through the simultaneous examination of several biological layers, multi-omics can reveal new therapeutic targets, molecular subtypes, and biomarkers that are not visible with single-omics study. This comprehensive approach improves

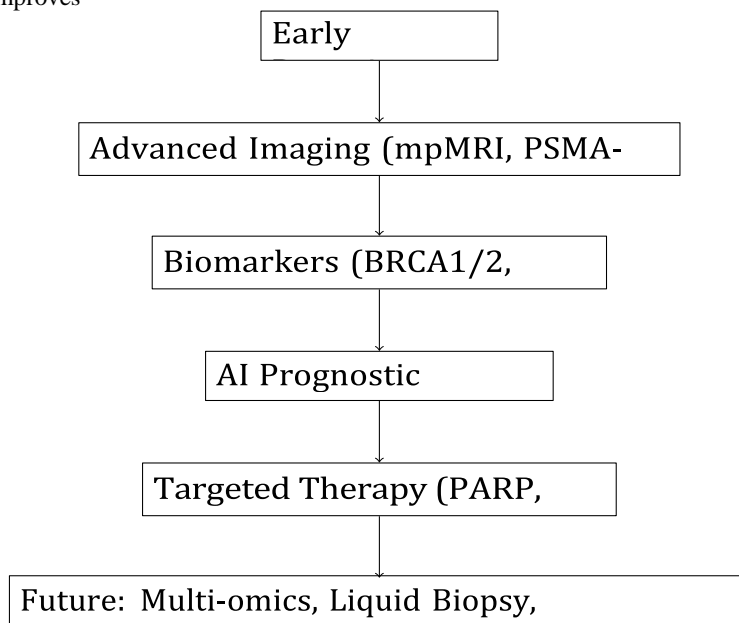


Figure 15: PCa Research

the capacity to differentiate between aggressive and indolent cancers, forecast therapy response, and customize treatments. Furthermore, more precise diagnostic and prognostic tools are made possible by the integration of AI and machine learning models with clinical and imaging data. Even if there are still issues like data harmonization, cost, and computational complex-

ity, multi-omics techniques have the potential to transform prostate cancer therapy by developing really customized treatment plans [19].

### 5.3.2 Immunotherapy and Combination Strategies

Prostate cancer immunotherapy is showing promise as a future therapeutic option, especially for advanced and treatment-resistant patients. Although prostate cancer has historically been regarded as immunologically "cold," research is still being conducted to determine how adoptive T-cell treatments, cancer vaccines like sipuleucel-T, and checkpoint inhibitors like anti-PD-1 and anti-CTLA-4 can improve the immune response. These strategies are being studied more and more in conjunction with other treatments including radiation, PARP inhibitors, and androgen deprivation therapy (ADT) in order to overcome resistance and enhance results. Prostate cancer immunotherapy's future depends on tailored combinations that determine which individuals are most likely to benefit based on immunological and genetic profiling. Precision immuno-oncology may be advanced by incorporating AI-driven systems to improve treatment planning and track response [2].

### 5.3.3 Liquid Biopsy and Non-Invasive Monitoring

The detection and treatment of prostate cancer, liquid biopsy and non-invasive monitoring offer a bright future. With liquid biopsies, as opposed to standard tissue biopsies, circulating tumor components such circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), exosomes, and microRNAs are examined from bodily fluids like blood or urine. For early identification, prognosis, therapy selection, and real-time tracking of illness development or treatment response, these instruments provide a reproducible, less intrusive approach. In advanced or metastatic prostate cancer, when tumor heterogeneity and development can be dynamically watched, they are very useful. The integration of liquid biopsy data with AI and multi-omics platforms has the potential to greatly enhance precision oncology, lower the dangers associated with biopsies, and provide individualized, flexible treatment plans as technology develops [17].

### 5.3.4 Global Health Equity and Policy Implementation

Global efforts are being made to standardize screening and care, particularly in areas with limited resources. Addressing inequities still requires data inclusion. [24].

This Fig. 16 offers a thorough summary of the changing field of prostate cancer research, including both recent developments and expected future paths. Advances in genetics (e.g., BRCA1/2, PTEN profiling), improved diagnostics using mpMRI and PSMA-PET, and innovative treatment approaches such PARP inhibitors and immunotherapy combinations are important areas of research. In addition, public health initiatives including awareness campaigns and worldwide screening equality are highlighted, as is the importance of AI in prognostic modeling and clinical decision assistance. Expanding liquid biopsy applications, integrating multi-omics, and creating combination therapy plans are the goals of future initiatives.

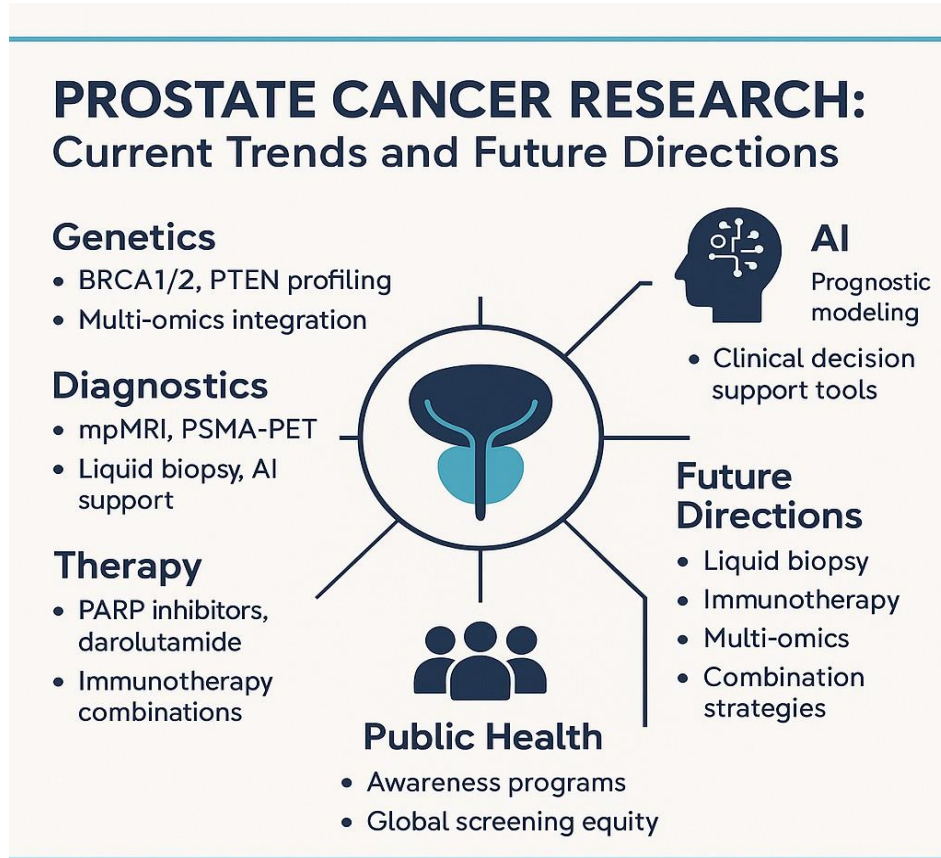


Figure 16: Overview of current trends and future directions

The current trends, challenges, and future directions in the major fields of prostate cancer are thoroughly compared in this Table 5. In addition to highlighting advancements in genetics, diagnostics, treatments, AI, and public health, it examines obstacles including the standardization of biomarkers, restricted access in LMICs, and the incorporation of AI into clinical practice. Future directions include global equality in screening and care, liquid biopsy, combination medicines, AI-driven decision tools, and multi-omics integration. It represents, in general, the trend toward technology-driven, globally inclusive, and individualized prostate cancer treatment.

**Table 5: Comparison of Current Trends, Challenges, and Future Directions**

Area	Current Trends	Challenges	Future Directions
Genetics & Precision Medicine	BRCA1/2, PTEN, TMPRSS2-ERG profiling; PARP inhibitors; AR-targeted therapies	Lack of standardized biomarkers; limited access in LMICs	Integrated multi-omics (genomics, proteomics, metabolomics, radiomics)
Diagnostics	mpMRI, PSMA-PET (e.g., $^{18}\text{F}$ -DCFPyL PET/CT); detection of biochemical recurrence	PSA test low specificity; variability in mpMRI interpretation; lack of validated biomarkers	Liquid biopsy; ctDNA; exosome analysis; AI-assisted diagnostics
Therapeutics	Darolutamide, PARP inhibitors, radioligand therapy ( $^{177}\text{Lu}$ -PSMA-617) for CRPC and mHSPC	CRPC remains challenging; high cost; infrastructure barriers in LMICs	Immunotherapy; combination strategies (e.g., ADT + checkpoint inhibitors)
AI & Digital Health	ML models (e.g., SVM, MLP) for prognostic prediction with >90% accuracy	Limited integration in clinical workflows; lack of diverse datasets	AI-based clinical decision support; real-time monitoring; multi-modal data platforms
Public Health	Rural awareness programs; better outcomes in Southeast Asia	Low awareness in Africa; disparities due to geography, race, and income	Global screening equity; policy standardization for early detection and care

## CONCLUSION

Prostate cancer research is undergoing a transformative shift, driven by advancements in genetics, imaging, artificial intelligence, and personalized medicine. Precision diagnostics, such as PSMA-PET and genomic profiling, are enhancing early detection and patient stratification, while novel therapies—including PARP inhibitors and radioligand treatments—are improving survival outcomes in advanced disease stages. Artificial intelligence is emerging as a powerful tool for prognostic modeling and clinical decision support, demonstrating predictive accuracies exceeding 90% in some applications.

Despite these advancements, significant challenges remain. These include limited specificity of traditional diagnostic tools like PSA testing, therapeutic resistance in castration-resistant prostate cancer (CRPC), and systemic inequities in access to care across regions. The lack of standardized biomarkers and global representation in clinical datasets further impedes equitable and effective prostate cancer management.

Looking ahead, the future of prostate cancer research lies in integrated multi-omics approaches, non-invasive diagnostics like liquid biopsies, and the clinical integration of AI technologies. Efforts to standardize care, expand awareness, and ensure global health equity will be critical in closing existing gaps. A multidisciplinary, data-driven, and globally inclusive framework is essential to translate scientific innovation into tangible improvements in patient outcomes worldwide.

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