# COMPREHENSIVE REVIEW OF PROSTATE CANCER: CURRENT INSIGHTS AND ADVANCES

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## ABSTRACT

Prostate cancer stands out as a significant contributor to rising mortality rates among men globally. Diagnosis of prostate cancer involves methods such as prostate biopsies, digital rectal examinations, and prostate-specific antigen (PSA) analyses, which determine whether the cancer is localized or advanced at the time of detection. This review aims to comprehensively cover the pathogenesis, progression, and treatment options for prostate cancer. The onset, development, and spread of prostate cancer are closely linked to genetic mutations. Treatment strategies for localized prostate cancer typically include ablative radiation therapy, radical prostatectomy, and active surveillance. For metastatic prostate cancer or cases of relapse, chemotherapy, salvage radiation therapy, and androgen deprivation therapy (ADT) are commonly employed. Despite these treatments, prostate cancer remains incurable, highlighting the need for combined therapeutic approaches. Ongoing research explores alternative treatment modalities such as gene therapy, traditional medicine, and nanotechnologies, aimed at addressing drug resistance and mitigating side effects associated with current treatments. This review provides insights into the genetic factors influencing prostate cancer, current treatment options, and the evolving landscape of complementary therapies.

**Keywords:** Prostate cancer, prostate cancer diagnosis, genetics of prostate cancer, prostate specific antigen (PSA).

## Introduction

Prostate cancer predominantly affects men aged 45 to 60 and stands as a leading cause of cancer-related mortality in Western countries. Diagnostic methods such as prostate biopsy, PSA testing, digital rectal examination, MRI, and health screenings are commonly employed to detect prostate cancer[1]. Risk factors include age, weight, race, family history, and environmental factors, contributing to varying epidemiological patterns globally. Research indicates a strong hereditary component in prostate cancer, supported by studies on genetic predisposition and familial inheritance. Genetic diversity in androgen production, metabolism, and function, including chromosome rearrangements and gene mutations, are implicated in cancer development[2]. The androgen receptor signalling pathway plays a crucial role in prostate cancer cell growth, highlighting potential targets for biomarker-driven therapies. Treatment options range from active surveillance to surgery and chemotherapy, tailored based on tumor characteristics and patient factors. Despite advances, current treatments are associated with significant side effects and high costs, underscoring the need for novel, cost effective therapies with improved efficacy. This study provides a comprehensive overview of prostate cancer, covering diagnosis, treatment strategies, genetic factors influencing disease onset and progression, and emerging therapeutic alternatives [3].

**Epidemiology**

Prostate cancer ranks among the most common cancers in men worldwide. In 2018, there were approximately 1,276,106 new cases of prostate cancer globally, leading to 358,989 deaths, with higher incidence rates observed in industrialized nations. Annually, there are around 190,000 new cases and 80,000 deaths from prostate cancer globally. Incidence rates vary geographically and among ethnic groups, with black males exhibiting the highest documented rates globally and notably higher rates among Black Americans compared to White men in the United States. Countries with widespread PSA testing and high awareness of prostate cancer typically report the highest incidence rates. As the global population continues to age, with a significant increase in men aged 65 and older, projections suggest that by 2030, prostate cancer could lead to nearly 1.7 million new cases and 499,000 deaths worldwide [4].

**Diagnosis**

The primary contributors to prostate cancer's high mortality rates include treatment failure and late-stage diagnoses. Diagnosis often involves a digital rectal examination (DRE), which assesses prostate size and detects abnormalities through rectal probing. Despite advancements, the prostate-specific antigen (PSA) test remains pivotal for screening, detecting PSA levels in blood samples. A PSA level exceeding 4 ng/mL typically prompts further testing, as values between 4 and 10 ng/mL may indicate a heightened risk for prostate cancer, particularly if exceeding 10 ng/mL. Elevated PSA levels can also result from benign conditions such as benign prostatic hyperplasia (BPH) or prostatitis, complicating diagnostic interpretation. Confirmation through prostate tissue biopsy is often necessary to differentiate cancer from benign conditions [5].

**Prostate Cancer and Genetics**

Prostate cancer exhibits a strong familial association, with individuals having close relatives diagnosed with the disease facing a 50% higher risk compared to those without such family history. Early-onset prostate cancer often manifests in first-degree relatives, indicating a hereditary predisposition. Epidemiological studies underscore the inheritable nature of genes contributing to prostate cancer risk, supported by case-control, twin, and family studies. Specific gene mutations, such as those affecting DNA repair genes like ATM, BRCA1, and BRCA2, increase susceptibility to hereditary prostate cancer. Genetic profiling through multigene sequencing aids in assessing genetic inheritance patterns among men diagnosed with or at high risk of prostate cancer. Racial factors and environmental influences, including

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migration and dietary habits, also play roles in prostate cancer susceptibility, particularly among African males [6].
Mutations such as single nucleotide polymorphisms (SNPs), somatic copy number alterations (SCNAs), and point mutations alter DNA sequences, contributing to prostate cancer development. These mutations can activate oncogenes and deactivate tumor suppressor genes, promoting uncontrolled cell division in prostate cells. Mutations may be acquired during an individual's lifetime or inherited across generations, occurring predominantly during DNA replication in the nucleus. Biomarkers such as ATM gene, RNase L (HPC1, lq22), HOX genes, BRCA genes, MSR1 (8p), and ELAC2/HPC2 (17p11) are commonly used in prostate cancer diagnosis, staging, and treatment monitoring, highlighting their diagnostic and prognostic value. Advances in profiling technologies, including precision medicine, have led to the discovery of new biomarkers such as the prostate health index (PHI), TMPRSS2-ERG fusion gene, 4K tests, and PCA3, which improve the specificity and sensitivity of PSA testing, reducing unnecessary biopsies and minimizing over diagnosis [7].

## Treatment Options

Precision medicine represents a burgeoning field aimed at developing gene-specific therapies for individuals with advanced prostate cancer. Utilizing genetic and environmental biomarkers, precision medicine enables tailored diagnoses, prognostic assessments, and precise treatment dosages [8]. Genome sequencing is pivotal in identifying patients with tumors featuring actionable targets, facilitating informed treatment decisions.

Gene mutations play a crucial role in guiding treatment strategies for metastatic castration-resistant prostate cancer (mCRPC). Individuals harboring mutations in genes such as BRCA1, BRCA2, ATM, CDK12, CHECK2, CHECK1, PALB2, PP2R2A, and RAD54L have shown positive responses to therapies like rucaparib and olaparib [9]. Research involving 1302 individuals, including 67 with BRCA mutations, has demonstrated poorer treatment outcomes, including increased metastasis and reduced survival rates following radiation therapy or prostatectomy in mutation carriers [10].

Studies have identified specific mutations, such as the BRCA1 c.4211C > G mutation prevalent in Chinese patients, which significantly enhance responses to radiation and androgen deprivation therapy (ADT) in prostate cancer treatment [83]. Conversely, mutations like F876L and W741L/C in the androgen receptor (AR) present challenges in developing effective treatments for castration-resistant prostate cancer (CRPC) by altering ligand binding and promoting AR activation [11]. These insights underscore the importance of precision medicine in tailoring therapies based on genetic profiles, thereby optimizing treatment efficacy and outcomes in prostate cancer management[12].

## CONCLUSIONS

Prostate cancer stands as a leading cause of male mortality worldwide, second only to lung disease. Biomarkers altered genes, proteins, and pathways associated with increased prostate cancer risk play crucial roles in diagnosing and staging the disease. They also guide treatment decisions by specifying the type of therapy needed. However, current treatments often affect patients' quality of life due to significant side effects and limited efficacy, leading to drug resistance in chemotherapy, radiation therapy, and hormonal treatments. In response, ongoing research explores therapeutic plants, gene therapy, and nanotechnology to mitigate side effects and restore sensitivity to chemotherapy in resistant tumor cells. Promising approaches include targeted medications that exploit specific cellular pathways, genetic material delivered via nanocarriers for controlled release, and bioactive compounds derived from medicinal plants. These advancements aim to enhance treatment effectiveness and improve outcomes for prostate cancer patients.

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