Benign Prostatic Hyperplasia & Prostate Cancer: A Review on the Treatment Strategies

Submitted By

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A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

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Declaration

It is hereby declared that

1. The thesis submitted is my original work while completing my degree at BRAC University.

2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.

3. The thesis does not contain material that has been accepted or submitted, for any other degree or diploma at a university or other institution.

4. I have acknowledged all main sources of help.

Student's Full Name & Signature:

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Approval

The thesis titled "Benign Prostatic Hyperplasia & Prostate Cancer: A Review on the Treatment Strategies" submitted by Tahera Alam (18346004), of Summer 2022 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy.

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Ethics Statement:

The thesis was done without any unethical work. No human or animal tests are involved in this study.

Abstract

About 15% of prostate cancer diagnoses are due to high-risk conditions and the best way to treat this patient are always changing. To allow the accurate identification of high-risk illnesses and the creation of more effective treatment pattern, a new classification method is necessary. The Food & Drug Administration has authorized the newest innovative prostate-specific membrane antigen Pluvicto as a prostate cancer therapy. A percent of old citizens that do meet the criteria for the prostate-specific membrane antigen and have prostate cancer which is known as metastatic castration-resistant prostate cancer are now advised to use Pluvicto. Biomarkers are substances that are used to reveal either regular or irregular bodily activities for determining prostate cancer by prostate-specific antigen, 4 Kallikreins score, and prostate cancer gene 3 level. Moreover, this project highlights the advanced treatment strategies along with their mechanisms to cure prostate cancer and benign prostatic hyperplasia.

Keywords: Prostate cancer; benign prostatic hyperplasia; prostate-specific antigen.

Dedication

My parents and older brother deserve special thanks for their unwavering support and unwavering trust in me during my four-year quest to get my bachelor of pharmacy degree, thus I choose to devote my project to them.

Acknowledgment

The completion of this thesis could not have been possible without the expertise of Faruque Azam, our beloved project supervisor. I want to thank the program director, assistant, and dean of academics Dr. Hasina Yasmin and Dr. Eva Rahman Kabir for supporting my project and contributing to the jury.

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Not least among my gratitude goes to my parents, without whom I could not have accomplished all of this.

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List of Acronyms

BPH   Benign Prostatic Hyperplasia

PSA   Prostate Specific Antigen

ADT   Androgen Deprivation Therapy

EBERT   External Beam Radio Therapy

SWOG   Southwest Oncology Group

MCRPC   Metastatic Castration-Resistant Prostate Cancer

AR   Androgen Receptor

PSMA   Prostate-Specific Membrane Antigen

EAU   European Association of Urology

EPIC   European Multidisciplinary Investigations into Cancer and Nutrition

% FPSA   Percent-free PSA

PHI   Prostate Health Index

PCA3   Prostate Cancer Gene 3

hK2   Human Kallikrein 2

BTD   Break Through Therapy designation

FDA   US Food and Drug Administration

CTC   Circulating Tumor Cell

DD3   Prostate Cancer Gene 3

BRCA1/2 Breast Cancer Gene 1/2

Chapter 1

Introduction

In terms of incidence and mortality, tumors are a worldwide representation of the effects of all cancers. The incidence and fatality rates of prostate cancer vary greatly by region. Examining trends in the frequency and mortality of prostate cancer across communities and over time is necessary to comprehend the contribution of particular factors and community detection practices to the epidemiological statistics of this illness (Sekhoacha et al. 2022).

Carcinoma is a clinically diverse disorder. Although some individuals have an acute form of the illness, the majority of men with prostate tumors have a slow-moving or indolent variety.

The underlying etiology of this condition matches the clinical variance as well. Several risk factors have different correlations with deadly versus indolent disease, as detailed in the chapters following (Dai et al. 2016).

Making this distinction between risk factors for terminal or early-stage disease and risk factors for prostate cancer as a whole is critical in prostate cancer epidemiology (Kaplan 2005).

Biologically speaking, hazards for prostate cancer should distinguish from those for the wider public for prostate cancer because it is less aggressive. In addition, men who take part in clinical assessment tend to be generally healthier, independent of a diagnosis of prostate cancer. Therefore, prostate specific antigen testing could have conflicting results (Sekhoacha et al. 2022).

When analyzing randomized trials on prostate cancer, it is crucial to consider how much information on prostate specific antigen screening is incorporated into the studies.

Aims of the Study

There are some specific aims for this study which includes-

1. To create awareness towards prostate cancer disease and benign prostatic hyperplasia which is very crucial for modern days.

2. To make a progress in diagnosis of the disease which is done at a later stage due to unwillingness and less knowledge.

3. Making a practice to check the health of prostate time to time, especially in late 60s.

Objectives of the Study

There are some objectives which we want to achieve in order to fight against prostate cancer and benign prostatic hyperplasia. They are mentioned below-

1. To obtain the best opportunities for advanced treatment options available for patients.

2. To review the staging and treatment guidelines for high-risk prostate cancer patients.

3. To identify the mechanism of metastasis of prostate cancer.

Chapter 2

Benign Prostatic Hyperplasia

As men age, they are more likely to develop prostate gland hypertrophy, which is another name for benign prostatic hyperplasia. Inconvenient symptoms in the urinary system, such as the bladder being unable to empty its contents, might result from an oversized male reproductive gland. In addition, it could lead to issues with renal disturbance and Urinary tract infection. BPH affects roughly 20% of males in their 40s and a percentage of old male patients in their late sixties according to several postmortem studies carried out worldwide. Despite the fact that by their sixth century of life, nearly all men will have microscopic anatomy or morphological indications of BPH, the condition does not require treatment unless it presents a symptom.

2.1 Symptoms of Benign Prostatic Hyperplasia

Benign prostatic hyperplasia has frequent occurrences of inadequate or intermittent urine flow as well as frequent urination, especially at night. They can also face difficulties in entirely emptying the bladder, urinary discomfort or burning and lastly urine or sperm containing blood.
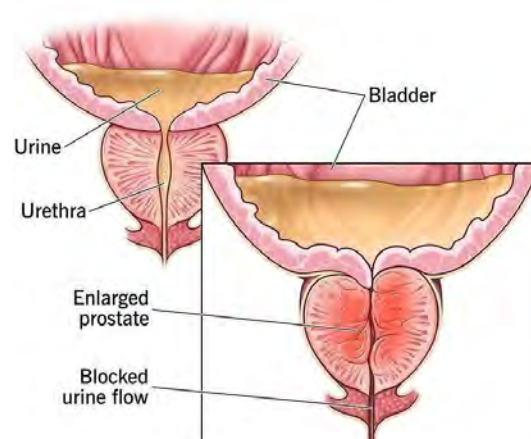
Figure 1: Benign prostatic hyperplasia. Retrieved from Guneyli et al. 2016.

2.2 Medication Used for Benign Prostatic Hyperplasia

Medication is the most frequent form of therapy for severe to moderate prostate enlargement symptoms. The choices consist of:

Alpha (α-blockers): These types of medications relax the tissues in the urethra and prostate, making urination more relaxing. In males, alpha-blockers such as alfuzosin (Uroxatral), doxazosin (Cardura), tamsulosin (Flomax), and silodosin (Rapaflo), typically take effect immediately. Dizziness is one of the possible side effects, as a benign disease is where the penis does not open fully and the semen returns to the bladder (retrograde ejaculation).

2a	2b

Figure 2a & 2b: Cialis 20 mg oral tablet. Retrieved from Maki et al. 2022. Tamsulosin HCl tablet. Retrieved from Korstanje, Krauwinkel, and van Doesum-Wolters 2011.

Inhibitors of 5-alpha reductase: These medications shrink your prostate by reversing the hormonal shifts that cause it to grow. This could take as long as six months for these drugs, which comprises dutasteride (Avodart) and finasteride (Proscar), to start working. Retrograde ejaculation is one of the side effects.

Chapter 3

Prostate Cancer

An abnormal growth that develops in the prostate is referred to as prostate cancer. The prostate is a tiny gland that looks walnut sized and appears to be found in males that produce viable sperm, which nourishes or transports sperm in the semen (Sekhoacha et al. 2022). Prostate cancer is the largest and most prominent cancer in the male anatomy. Many prostate cancers have a sluggish growth rate because they are only found in the prostate gland, where they cannot represent a serious hazard. While some prostate tumors are aggressive and roll out quickly, others develop slowly and may not even need treatment. The best opportunity for effective treatment is when the prostate tumor is discovered early when it is still contained in the prostate gland (Patel and Klein 2009).
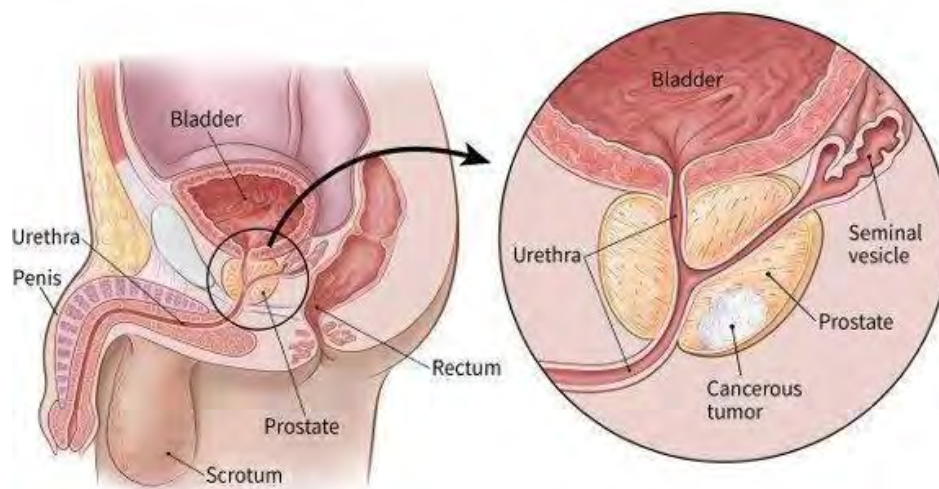
Figure 3: Prostate cancer or cancerous tumor in the prostate gland. Retrieved from Taneja 2004.

3.1 Difference between Prostate Cancer and Benign Prostatic Hyperplasia

Prostate cancer and benign prostatic hyperplasia both are different from each other and they show variety of symptoms which are not similar. These differences between them are given below:

Table 1: Difference between prostate cancer and benign prostatic hyperplasia

Prostate Cancer	Benign Prostatic Hyperplasia
1. Cancerous cells are present and may spread	1. Cells are not cancerous and do not spread
2. Sides of the prostate is affected	2. Central portion of the prostate is affected
3. PSA and alkaline phosphates are increased	3. PSA levels are increased
4. It can be life-threating	4. It is not life-threatening
5. Abnormal enlargement of the prostate gland	5. Enlargement of prostate due to aging

Chapter 4

Prostate Cancer Geographical Predominance

Only three variables have been proven to increase the likelihood of developing prostate cancer: maturity level, African-American ethnicity, and genetic history of the illness. Genome wide association studies known as GWAS has lately provided more evidence of a hereditary proclivity to prostate cancer. More than 180 genetic risk loci in persons of various races or ethnicities have been found (Giovannucci et al. 2007). Thus, according to reliable statistics, being taller may also increase the likelihood of acquiring all forms of prostate cancer (MacInnis and English 2006).

While these features cannot be modified, they highlight the probable pathways connected to prostate cancer development and could be employed to classify individuals more prone to getting the disease (Patel and Klein 2009).

The assumption that a person's risk of having prostate cancer is affected by a genetic history of the illness is backed up by compelling data from family studies. Men who have a bloodline connection such as who are recently been diagnosed with the disease have a two to multiple greater risk, whereas those who have both have a nine-fold increased risk.

An analogous connection has been seen for the chance of developing prostate cancer. According to Brandt et al. (2011), men who are suffering from prostate cancer have a family history of the conditions are twice as likely to pass away than, men who have never experienced the disease. Prostate diagnostic accuracy and mortality rates differ considerably throughout groups of race and ethnicity (D'Elia et al. 2022).
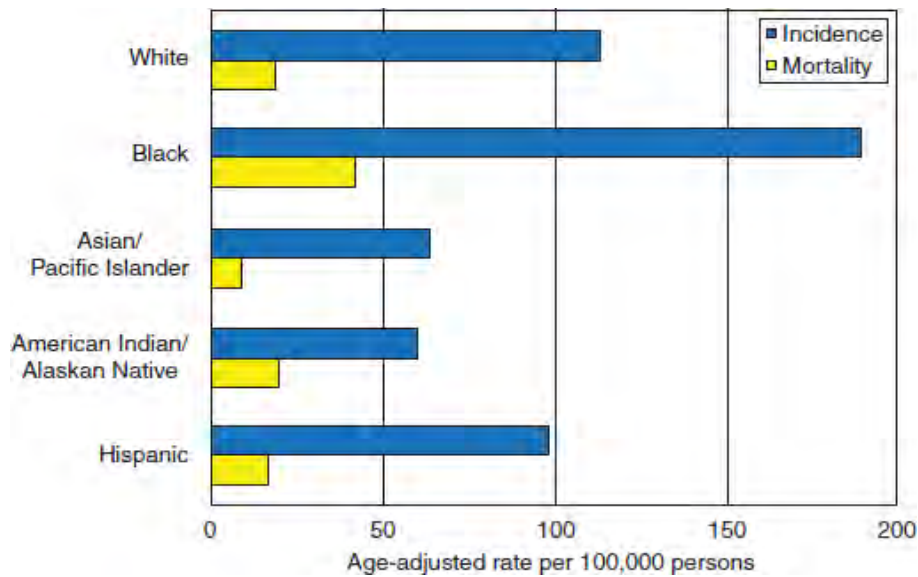
Figure 4: Prostate cancer incidence and mortality rates. Retrieved from Pernar et al. 2018.

4.1 Risk Factors of Prostate Cancer

Research papers proved that there are several reasons which play a vital role in prostate cancer. Among them major factors are discussed as they are very common as well as popular. Factors that increase the risk of prostate cancer is given below:

Table 2: Factors that increase the risk of prostate cancer

Increases risk	Evidence
Height (BMI ≥ 30)	Highly affirmative
Lipid level (≥ 100 mg/dl)	Affirmative
Dairy product intake (≥ 430 gm)	Affirmative
Smoking (1-10 cigarettes per day)	Highly affirmative
Calcium intake (≥2000 mg/day)	Affirmative
Obesity (23.0 ≤ BMI < 25)	Highly affirmative

4.2 Height

Height plays an important role in prostate cancer and it is good evidence for progressive disease. Taller stature was linked to progressed and deadly prostate cancer but not to overall prostate cancer. However, a retrospective study of a multicultural population found no correlation between tall size and the incidence of primary or metastatic tumors. Height is not thought to be a prostate cancer risk factor that can be changed, but its significance in the illness sheds light on its underlying biology. Growing taller as you age may be related to exposure to androgens like insulin-like growth factor 1 as a youngster, which might be one explanation for this link (IGF-1).

The absence of a relationship between birth weight and the chance of developing tumors shows that the important period for origination may be during adolescence when the prostate undergoes rapid growth (Chang et al. 2014).

Even though the robust exercise was associated with a decreased risk among all fatalities in a survey, neither vigorous nor non-vigorous activity was that harmful. Brisk walking showed a similar connection, with a decreased risk of recurrence for males who walked at least three hours briskly each week compared to those less briskly (easy walking) each week (Suresh 2022). Although the mechanism by which exercise may lower the incidence of prostate cancer is uncertain, it may include changes in sex hormone levels such as those of testosterone, progesterone, and estrogen with the IGF axis, and other sex hormones (Pernar et al. 2018).

4.2 Obesity

Numerous studies have been conducted on the intricate association between both body weight and the prevalence of prostate cancer. Obesity is linked to an increased likelihood of prostate cancer death and recurrence. The potential processes by which obesity may impact the development of prostate cancer has been identified using biomarkers. Men who had elevated

levels of C-peptide, a measure of insulin production in the blood, in a prospective study with factors that may influence drops of blood, had higher rates of cancer-specific death. This connection, however, was not validated in two prospective trials for the risk of aggressive illness (Merriel, Funston, and Hamilton 2018). Since it is considered that the waist contains more active metabolism fat cells, the hip circumference is a frequently used indicator of adiposity. A greater risk of advanced prostate carcinoma was associated with a larger waist measurement, according to a controlled study of European male volunteers. In contrast to the Health Study, the Melbourne Multidisciplinary Cohort Study supported this finding (Suresh 2022).

4.3 Calcium Intake, Dairy Products

In various prospective studies, the relationship between serum calcium levels and the risk of prostate cancer has been investigated. High blood calcium was linked to an increased risk of deadly prostate cancer in two concentric research papers on Swedish males (Preble et al. 2019). The observations on serum calcium should be inter because circulating levels are heavily restricted and are only altered by food at high amounts of dietary intake (Cary and Cooperberg 2013).

Milk-based food items which have calcium as a primary factor and a good amount of dairy or milk consumption have been linked to an increased risk of prostate cancer. In contrast to the majority of research. Subsequent studies have found a link between increased milk or dairy consumption and a higher risk of developing advanced or fatal prostate cancer. It is challenging to distinguish between the individual impacts of these compounds because of the link between cow's milk and other minerals, such as calcium (Cary and Cooperberg 2013).

4.3 Smoking

According to a 2014 report by the U.S. Surgeon General, there is "provocative" evidence linking smoking to a doubled risk of dying from prostate carcinoma and an increased risk of developing the disease (U.S. Department of Health and Human Services 2014). 526 cancer-related departures from life were reported in the largest study on this topic which included 5366 men with prostate carcinoma who were significantly ramifications for 22 years, HPFS conducted this investigation. The risk of dying from prostate carcinoma was higher for smoking compared to non-smokers after taking into account all pertinent factors. After adjusting for prostate cancer stage and grade, the correlation with cigarette smokers remained largely unchanged (D'Elia et al. 2022). This mitigation shows that grade and severity may inflate hence the overall effects of smoking on prostatic cancer death. According to Byrne et al. (2010), current smokers are less likely to report having their PSA tested than nonsmokers, which may lead to delayed cancer detection and treatment among smokers. There are several factors that decrease the risk of prostate cancer which are mentioned below:

Table 3: Factors that decrease the risk of prostate cancer

Decreases risk	Evidence
Physical activity	Highly affirmative
Coffee (1-3 cup per day)	Limited
Tomatoes (5-6 times a week)	Affirmative
Fish (5 servings of fish per week)	Highly affirmative
Vitamin D (4000 IU per day)	Highly affirmative
Statins (10 - 40 mg/day)	Affirmative

4.4 Physical Activity

A somewhat negative connection between physical exercise and the hazard of prostate cancer that has spread and is deadly has been found by findings from prospective cohort research. However, The European Multidisciplinary Investigations into Cancer and Nutrition known as EPIC cohort discovered an indirect link between work activities and risks but no linkage between recreational exercise and the risk of severe prostate carcinoma (Suresh 2022).

Physical exercise has been associated with enhanced longevity and lower prostate cancer development in males with prostate cancer. In comparison to men who engaged in less than one hour of vigorous activity each week, the few who engaged in intensive exercise for at least three hours per week used to have a 61% reduced risk of prostate cancer-specific death, according to the research on 2,705 male persons with prostate cancer. Although the vigorous exercise was connected to a decreased risk of prostate cancer-specific fatality, both vigorous and non-vigorous activity were linked to a lower risk among all death rates in this sample. A comparable link was seen for light exercise, with men who walked mostly for more than 2 hours in seven days having a decreased probability of recurrence contrasted to those who walked less than 3 hours a week. Although doing some sort of bodily fitness activity may lower the hazard of prostate cancer is yet unknown, it may do so by affecting the anti-inflammatory pathways and the levels of sex hormones known as testosterone, estrogen, or the IGF axis (Gann et al. 1996).

4.5 Vitamin D Intake

One possible mechanism behind the calcium relationship is suppression. Di-hydroxy vitamin D (1,25 (OH)2D), in the dietary sources of vitamin D are just reliable data, with the majority coming from the endogenous synthesis in the skin as a consequence of sun exposure. Although

1,25(OH)2D is the most physiologically active form, 25(OH)D is more abundant and may be a good predictor of sun and food exposure (Wang et al. 2018).

4.6 Coffee

Coffee has a wide range of physiologically active chemicals, which may explain the relationship with prostate cancer growth. One of the most effective antioxidant foods is coffee, which has been related in clinical and preclinical studies to enhanced glucose metabolism and insulin secretion (Pernar et al. 2018).

4.6 Fish

According to an analysis done by experts of four prospective studies, eating more fish overall was associated with a 63% reduction in prostate cancer-specific mortality. Even while one study found an enhanced risk of prostate carcinoma with a higher blood level of long-chain omega-3 which is a fatty acid found in male persons, this is probably because these cases tend to be early-stage illnesses and those who consume more fish are more likely to get PSA screening. According to one study, eating two more meals of fish each week after receiving a prostate cancer diagnosis decreased the risk of recurrence by 17% (Joseph et al. 2021). A second study of post-diagnostic fish diet found no connection. Long marine omega-3 polyunsaturated fatty acids found in fish may lower the risk of prostate carcinoma through anti-inflammatory pathways, while the exact mechanism is unknown.

4.6 Statins

Statins have little impact on the frequency of Benign prostatic hyperplasia. However, they can minimize the risk of BPH in individuals above the age of fifty (Pernar et al. 2018).

Chapter 5

Biomarkers of Prostate Cancer

Biomarkers are "substances" that can reveal either regular or irregular bodily activities. The best-known of them is prostate-specific antigen. The PSA test has been utilized for centuries to evaluate prostate cancer and perhaps identify it soon. It identifies astonishingly high blood levels of PSA (Cary and Cooperberg 2013).

The prostate-specific antigen test is flawed in two ways. First, the level can indicate that something is wrong with the prostate, albeit it may not always be cancer (Cary and Cooperberg 2013). Elevated concentrations might indicate more benign prostatic problems known as Benign prostatic hyperplasia. Second, even if high prostate-specific antigen levels are the consequence of prostate cancer, the prostate specific antigen level by itself cannot tell you which tumors are fast-growing and require intensive therapy and which are sluggish and may be treated more cautiously.

5.1 Prostate Specific Antigen

Prostate specific antigen known as PSA is exceptional in that it is utilized at all of the primary stages of the detection of prostate cancer. and patient care, including scanning, risk assessment for recurring, observation after diagnosis, and treatment observation. The prostate-specific antigen test quantifies the level of PSA in your blood (Cary and Cooperberg 2013). The prostate is a little gland that resides under the bladder in males, produces PSA both from malignant and non-cancerous cells. Lack of specificity is one of the key issues using PSA as a prostate cancer screening tool. Numerous supplementary or supplementary tests have been suggested to increase precision and thereby decrease the frequency of unwanted biopsies and repeat

biopsies. They are as follows: percent-free PSA, prostate health index and four Kallikreins score (Cary and Cooperberg 2013).

5.1 Percent-free Prostate Specific Antigen

The percentage of PSA that is circulated freely concerning the overall PSA level is known as the percent-free PSA (% fPSA). Those with prostate cancer have a smaller share of free PSA than men without the disease (Cary and Cooperberg 2013). When a man's blood prostate-specific antigen level is 2.5 ng/mL or lower, the percent free prostate-specific antigen is a strong predictor of his risk of developing prostate cancer (Catalona 2018).

5.2 Prostate Health Index

It is a quick full blood count that has FDA approval, and aids in estimating the likelihood that biopsies may find prostate cancer. The likelihood of discovering a clinically relevant condition increases with the score. In contrast, a phi score of more than 55 indicates that there is a 50% chance of discovering cancer during a biopsy. A phi spectrum between 0 to 26.9 correlates to about 10% likelihood of cancer. However, prostate cancer testing methods frequently involve the PSA test. A more accurate tool is required for the identification of prostate cancer due to the PSA test's low cancer specificity. When determining which patients require a biopsy, the phi score offers superior risk classification (Cary and Cooperberg 2013).

5.2 Four Kallikreins Score

The prostate specific antigen, % free prostate specific antigen, Human kallikrein 2 and many others are determined by the 4 kallikreins score levels and any past biopsies results. One of the 4K score's main therapeutic uses is the opportunity to reduce the number of unnecessary biopsies (Duffy 2020).

5.2 Prostate Cancer Gene 3

Sometimes referred to as DD3 or PCA3 (prostate cancer gene 3) is a non-coding mRNA specifically for the prostate. After an electronic examination of the rectum, the most well-known PCA3 test (Progensa PCA3, The United States of America, Marlborough, MA) detects mRNA for PCA3 and PSA in the first urinate. The USFDA has approved the PROGENSA PCA3 test for use in conjunction with other patient records to assist males younger than 50 who have had one or more prior not affirmative biopsies and would be indicated by a doctor using the current advised treatment (Cary and Cooperberg 2013).

5.3 Therapy Predicative Biomarkers

There are now several tissue biomarkers tests that may be used to assess the high progressiveness of a patient's prostate carcinoma and forecast their prognosis. The development of prostate cancer therapy forecast biomarkers has started. Among these are the DNA CTC (circulating tumor cell) for forecasting tolerance to radiation and the AR splice variant (androgen receptor splice variant 7), AR-V7 detected in CTC for indicating susceptibility to enzalutamide and abiraterone. Lastly, the therapy of BRCA1/2 known as breast cancer gene 1/2, gene-mutated metastatic castrate-resistant prostate cancer patients who have previously had taxane-based chemotherapy, abiraterone, or enzalutamide, the US Food and Drug Administration (FDA) awarded Olaparib Break Through Therapy designation (BTD) in 2016.

Chapter 6

Treatment Options for Prostate Cancer

The basic concept of treatment for high-risk prostate cancer is that the main tumor must be treated first, not only for local control but also to avoid additional seeding of locally advanced or metastatic locations. External beam radiation (EBRT) in combination with ADT outperforms both ADT and EBRT used independently (Levine et al. 2010). Three options are known as Androgen deprivation treatment and Radiation therapy, Long-term versus short-term hormone therapy and Intermittent versus Continuous hormone therapy.

6.1 Androgen Deprivation Treatment and Radiation Therapy

To spread the prostate cancer, it requires testosterone. The male body produces a high amount of testosterone which should be decreased to temporarily stop the growth of cancer or perhaps cause it to shrink. Androgen deprivation therapy is the medical term for this procedure since testosterone is an androgen, or male sex hormone (Levine et al. 2010).

For individuals at high risk, the addition of radiotherapy to complete testosterone-blocking boosted longevity rates and plaque survival rates, according to the randomized phase III study from Scandinavia. The first principle, which emphasizes that treating the main tumor is crucial, does not have an age restriction. According to a recent study, elderly men are not likely to obtain comprehensive therapy and have a greater likelihood to have high-risk illnesses. Even older men with high-grade illness, however, have a significant likelihood of passing away due to prostate cancer and will be benefited from possibly curative therapy when co-morbidities are taken into account. The mixture is well-established in high-risk illnesses, even though ADT itself is not as effective as radiation in this setting (Gomella et al. 2010).

The second principle is that, compared to radiation alone, long-term ADT is associated with better results, particularly survival. Invasion of the seminal vesicles and positive margins were present in 15% of these individuals who had had a radical prostatectomy. Results for those who had ADT together with radiation were better than for those who underwent radiotherapy alone (Levine et al. 2010).

6.2 Long-term Versus Short-term Hormone Therapy

Wherever cancer has spread inside the body, hormone treatment reduces it in size and stops its growth. Although it cannot treat cancer, it may typically keep it under control for years. Furthermore, it can aid in treating aggressive cancer signs including bone discomfort (Gomella et al. 2010).

Rather than having to consider other therapies, hormone therapy can bring your cancer under management for several months or years. But with time, your cancer can begin to spread once more. While you can keep receiving your first hormone therapy, there are alternative options as well. Male serum testosterone will gradually build up again if you stop taking hormone treatment, and certain adverse symptoms will go away. After you discontinue hormone therapy, your side effects might not go away right away; they can take many months. The consequences of testicular surgery (orchiectomy), which cannot be undone, are long-lasting (Levine et al. 2010).

6.3 Intermittent Versus Continuous Hormone Therapy

Intermittent androgen deprivation also known as ADT therapy involves cyclical ADT, enabling hormonal healing throughout non-treatment times. Delaying the advancement of castration tolerance might enhance the quality of life for patients not receiving therapy. The main idea is that individuals can maintain their susceptibility to testosterone depletion by discontinuing ADT while they are still responding and enabling any tumor cells to survive to grow again under androgen stimulation when testosterone levels increase. Furthermore, it was hypothesized that ADT-related hazards would be decreased during the "off" times, leading to a net improvement in general life satisfaction (Gomella et al. 2010). A recent Southwest Oncology Group (SWOG) experiment examined the patients getting intermittent ADT to patients getting continuous ADT and found that among fatalities whose cause could be determined, prostate cancer-specific death rates preferred continuous treatment and non-cancer-related deaths favored the interval group; nevertheless, the researchers state that equivalency was not established in this analysis (Gomella et al. 2010).

Chapter 7

Advanced Treatment for Prostate Cancer

The FDA has authorized the newest innovative Pluvicto as a prostate cancer therapy. PSMA Pluvicto is now suggested for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) who test positive for the PSMA membrane antigen. According to the current recommendations, individuals must have received at least one taxane-based chemotherapy for androgen receptor (AR) pathway suppression before being eligible for the PSMA Pluvicto therapy (Keam 2022).

Through an IV, medication is administered into the circulation during PSMA treatment. The medication uses a targeting chemical to find cancer in the system and administer a tiny quantity of radiation specifically to the tumor cells, destroying or injuring them with little injury to the healthy tissue around them. The entire PSMA therapy consists of six infusions spaced six weeks apart. Users will continue to get supervision from their cancer specialist throughout the course of the therapy (Keam 2022).

7.1 Mechanism of Pluvicto in the Body

In the body pluvicto is administered via an IV route. After that pluvicto looks for prostate cells which are spread throughout the body. Pluvicto then binds to prostate tumors and gives the cancer cells a little dose of radiation. The radiation destroys the cancerous cells while sparing the healthy tissue around them (Keam 2022).

Figure 5: Pluvicto, a newly FDA approved radiopharmaceutical drug used for prostate-specific membrane antigen-positive metastatic castration-resistant prostate cancer. Retrieved from Keam 2022.

Radiotherapy has advantages over other treatment. Because it uses intense radiation to kill cancer cells by irreversibly damaging their DNA. Radiation causes transient cell damage in surrounding healthy cells, but these cells are typically capable of repairing the damage to DNA and carry on growing normally. High doses of radiation are delivered directly into a tumor during radiation therapy. The radiation beams cause the tumor to shrink or die by altering the DNA structure of the tumor. Since it only affects one part of the body, this form of cancer treatment is less harmful than chemotherapy. Radiation might be the best option, due to the fact that radiation may produce less harm and that the affected bodily part may function better after therapy. However, radiation can also harm surrounding cells and induce harmful effects spanning from skin irritation and exhaustion to significant organ damage, besides saving lives by eradicating tumor.

Chapter 8

Outcomes of Radiotherapy for Prostate Cancer

In radiotherapy, radiation is utilized to kill cancerous cells. This approach can be used to destroy cancer cells that have not rolled out outside of the prostate or not too far. Chemo treatment can also be used to treat prostate carcinoma that is rolling out to lessen the discomfort and slow the disease's progression (Chang et al. 2014).

8.1 Radical Prostatectomy

According to the European Association of Urology (EAU) recommendations, radical prostatectomy is a second choice for individuals with very risky prostate carcinoma patients (Chen1 et al. 2019). So, for the betterment of the high-risk group in particular, the surgery necessitates four steps. First of all, systematically separating a large number of pelvic lymph nodes, verifying intraoperatively that the surgical borders are not positive on the frozen section and total removal of the gland itself. Lastly, the treatment is best carried out by a skilled and high-volume surgeon who has been found to produce superior results overall.

8.2 Extended Pelvic Lymph Node Dissection

A pelvic lymph node dissection is performed to examine the lymph nodes in the pelvis for signs of malignancy. To determine the number of lymph nodes that have cancer in them, the extent of cancer's spread there, and the diameter of the lymph nodes. Cancerous lymph nodes should be removed. Pelvic Efferent lymphatic nodes empty and cleanse the lymph that is present in the pelvis and the surrounding areas. In cancer patients, surgeons may extract pelvic lymph nodes close to a tumor to check for signs that the illness has advanced (Kawahara, Miyoshi, and Uemura 2020).

Lastly, selective alpha-blockers have dominated pharmacological treatment for simple benign prostatic hyperplasia for the past ten years. The alpha-blockers are the first-line treatment for all males in the absence of limitations. Dual treatment with a 5-alpha-reductase inhibitor and an alpha-blocker has been demonstrated to be more effective in treating males with greater prostate sizes (Vietri et al. 2021).

8.3 Radical Prostatectomy and Radiation Therapy Difference

The two methods which are known as the best treatment for prostate cancer are radiation and surgery. Both are equally sound and safe to perform. Since, side effects are major part after surgery, it is very obvious to face some serious side effects as differentiate to radiation therapy. The major differences between radical prostatectomy and radiation therapy is given below:

Table 4: Difference between radical prostatectomy and radiation therapy

Radical Prostatectomy (Surgery)	Radiation Therapy
1. An incision made by surgeons in the body to completely eradicate the prostate gland	1. Prostate cancer cells are destroyed using radiation beams with high energy
2. It is not palliative care because the patient cannot take the pain during invasive surgery	2. It is palliative case care because pain is relieved by lowering the appearance of the tumor
3. Surgeries of cancerous cells can be completely removed from the body	3. It is non-invasive and works well when surgery is not possible
4. It increases the life expectancy of the patients	4. Life expectancy is lower than surgery
5. Erection problem and urinary difficulty can occur as a result of side effects	5. Bowel and bladder-related problems can occur as side effects

Chapter 9

Conclusion

Prostate cancer is a serious health concern that affects men all over the world. Despite the challenges associated with its diagnosis and treatment, advances in medical research and technology have greatly improved the prognosis and quality of life for those who are diagnosed with this disease.

Through early detection and treatment, many cases of prostate cancer can be successfully managed and even cured. Additionally, there are several effective treatment options available, including surgery, radiation therapy, hormone therapy, and chemotherapy (Sivanand 2019).

Furthermore, awareness campaigns and education initiatives have helped to increase public understanding of prostate cancer and its risk factors, encouraging men to seek medical attention and undergo regular screening to catch the disease in its early stages (Storck et al. 2022).

In conclusion, while prostate cancer remains a serious health concern, there is much reason for hope. With continued research, awareness, and access to effective treatment options, we can work towards better outcomes and improved quality of life for those affected by this disease (Hayden, Catton, and Pickles 2010).

Reference:

Cary, K. Clint, and Mathew R. Cooperberg. 2013. "Biomarkers in Prostate Cancer Surveillance and Screening: Past, Present, and Future." *Therapeutic Advances in Urology* 5(6):318–29. doi: 10.1177/1756287213495915.

Catalona, William J. 2018. "Prostate Cancer Screening." *Medical Clinics of North America* 102(2):199–214. doi: 10.1016/j.mcna.2017.11.001.

Chang, Albert J., Karen A. Autio, MacK Roach, and Howard I. Scher. 2014. "High-Risk Prostate Cancer-Classification and Therapy." *Nature Reviews Clinical Oncology* 11(6):308–23. doi: 10.1038/nrclinonc.2014.68.

Chen1, Rui, Xin Cheng1 Lei Wang1 *. Xia Sheng1 Shu-Guang Piao1 Xin-Wen Nian1, Tie Zhou1, Hui-Zhen Li1, Ya-Wei Liu2, Guang-An Xiao1 Chen1 Guang-Hua Chun-Lei Zhang1 De-Pei Kong1, Xin Lu1, Zhen-Yu Jia1 Zhi-Yong Liu1, and Ying-Hao Sun. 2019. "Prostate Cancer Risk Prediction Models in Eastern Asian Populations: Current Status, Racial Difference, and Future Directions." *Asian Journal of Andrology* 21(July):1–4. doi: 10.4103/aja.aja.

D'Elia, Giovanna, Gemma Caliendo, Maria Myrsini Tzioni, Luisa Albanese, Luana Passariello, Anna Maria Molinari, and Maria Teresa Vietri. 2022. "Increased Risk of Hereditary Prostate Cancer in Italian Families with Hereditary Breast and Ovarian Cancer Syndrome Harboring Mutations in BRCA and in Other Susceptibility Genes." *Genes* 13(10):1–13. doi: 10.3390/genes13101692.

Dai, Xiaoyu, Xiangming Fang, Ying Ma, and Jianbo Xianyu. 2016. "Benign Prostatic Hyperplasia and the Risk of Prostate Cancer and Bladder Cancer a Meta-Analysis of Observational Studies." *Medicine (United States)* 95(18):e3493. doi: 10.1097/MD.0000000000003493.

Duffy, Michael J. 2020. "[14374331 - Clinical Chemistry and Laboratory Medicine (CCLM)]

Biomarkers for Prostate Cancer_ Prostate-Specific Antigen and beyond.Pdf." 58(3):326–39.

Giovannucci, Edward, Yan Liu, Elizabeth A. Platz, Meir J. Stampfer, and Walter C. Willett. 2007. "Risk Factors for Prostate Cancer Incidence and Progression in the Health Professionals Follow-up Study." *International Journal of Cancer* 121(7):1571–78. doi: 10.1002/ijc.22788.

Gomella, Leonard G., Jaspreet Singh, Costas Lallas, and Edouard J. Trabulsi. 2010. "Hormone Therapy in the Management of Prostate Cancer: Evidence-Based Approaches." *Therapeutic Advances in Urology* 2(4):171–81. doi: 10.1177/1756287210375270.

Hayden, A. J., C. Catton, and T. Pickles. 2010. "Radiation Therapy in Prostate Cancer: A Risk-Adapted Strategy." 18–24.

Joseph, Diya B., Anne E. Turco, Chad M. Vezina, and Douglas W. Strand. 2021. "Progenitors in Prostate Development and Disease." *Developmental Biology* 473:50–58. doi: 10.1016/j.ydbio.2020.11.012.

Kaplan, Steven A. 2005. "Benign Prostatic Hyperplasia." *Journal of Urology* 174(1):221–22. doi: 10.1097/01.ju.0000164803.79620.97.

Kawahara, Takashi, Yasuhide Miyoshi, and Hiroji Uemura. 2020. "Re: Current Treatment Strategies for Advanced Prostate Cancer." *International Journal of Urology* 27(6):571. doi: 10.1111/iju.14237.

Keam, Susan J. 2022. "Lutetium Lu 177 Vipivotide Tetraxetan: First Approval." *Molecular Diagnosis and Therapy* 26(4):467–75. doi: 10.1007/s40291-022-00594-2.

Levine, Glenn N., Anthony V. D'Aamico, Peter Berger, Peter E. Clark, Robert H. Eckel, Nancy L. Keating, Richard V. Milani, Arthur I. Sagalowsky, Matthew R. Smith, and Neil Zakai. 2010. "Androgen-Deprivation Therapy in Prostate Cancer and Cardiovascular Risk: A Science Advisory from the American Heart Association, American Cancer Society, and

American Urological Association." *Circulation* 121(6):833–40. doi: 10.1161/CIRCULATIONAHA.109.192695.

Merriel, Samuel W. D., Garth Funston, and Willie Hamilton. 2018. "Prostate Cancer in Primary Care." *Advances in Therapy* 35(9):1285–94. doi: 10.1007/s12325-018-0766-1.

Patel, Amit R., and Eric A. Klein. 2009. "Risk Factors for Prostate Cancer." *Nature Clinical Practice Urology* 6(2):87–95. doi: 10.1038/ncpuro1290.

Pernar, Claire H., Ericka M. Ebot, Kathryn M. Wilson, and Lorelei A. Mucci. 2018. "The Epidemiology of Prostate Cancer." *Cold Spring Harbor Perspectives in Medicine* 8(12):1–18. doi: 10.1101/CSHPERSPECT.A030361.

Preble, Isabella, Zhenzhen Zhang, Ryan Kopp, Mark Garzotto, Gerd Bobe, Jackilen Shannon, and Yumie Takata. 2019. "Dairy Product Consumption and Prostate Cancer Risk in the United States." *Nutrients* 11(7):1–12. doi: 10.3390/nu11071615.

Sekhoacha, Mamello, Keamogetswe Riet, Paballo Motloung, Lemohang Gumenku, Ayodeji Adegoke, and Samson Mashele. 2022. "Prostate Cancer Review: Genetics, Diagnosis, Treatment Options, and Alternative Approaches." *Molecules* 27(17):1–33. doi: 10.3390/molecules27175730.

Storck, William K., Allison M. May, Thomas C. Westbrook, Zhi Duan, Colm Morrissey, Joel A. Yates, and Joshi J. Alumkal. 2022. "The Role of Epigenetic Change in Therapy-Induced Neuroendocrine Prostate Cancer Lineage Plasticity." *Frontiers in Endocrinology* 13(July):1–14. doi: 10.3389/fendo.2022.926585.

Suresh, Kishanrao. 2022. "Prostate Health in India (BPH & Prostate Cancer)." *Archives of Cancer Science and Therapy* 6(1):009–017. doi: 10.29328/journal.acst.1001028.

Vietri, Maria Teresa, Giovanna D'elia, Gemma Caliendo, Marianna Resse, Amelia

Casamassimi, Luana Passariello, Luisa Albanese, Michele Cioffi, and Anna Maria Molinari. 2021. "Hereditary Prostate Cancer: Genes Related, Target Therapy and Prevention." *International Journal of Molecular Sciences* 22(7). doi: 10.3390/ijms22073753.

Wang, Guocan, Di Zhao, Denise J. Spring, and Ronald A. Depinho. 2018. "Prostate Cancer Biology 2018." *Genes & Development* 32:1105–40. doi: 10.1101/gad.315739.118.GENES.

Cary, K. Clint, and Mathew R. Cooperberg. 2013. "Biomarkers in Prostate Cancer Surveillance and Screening: Past, Present, and Future." *Therapeutic Advances in Urology* 5(6):318–29. doi: 10.1177/1756287213495915.

Catalona, William J. 2018. "Prostate Cancer Screening." *Medical Clinics of North America* 102(2):199–214. doi: 10.1016/j.mcna.2017.11.001.

Chang, Albert J., Karen A. Autio, MacK Roach, and Howard I. Scher. 2014. "High-Risk Prostate Cancer-Classification and Therapy." *Nature Reviews Clinical Oncology* 11(6):308–23. doi: 10.1038/nrclinonc.2014.68.

Chen1, Rui, Xin Cheng1 Lei Wang1 *. Xia Sheng1 Shu-Guang Piao1 Xin-Wen Nian1, Tie Zhou1, Hui-Zhen Li1, Ya-Wei Liu2, Guang-An Xiao1 Chen1 Guang-Hua Chun-Lei Zhang1 De-Pei Kong1, Xin Lu1, Zhen-Yu Jia1 Zhi-Yong Liu1, and Ying-Hao Sun. 2019. "Prostate Cancer Risk Prediction Models in Eastern Asian Populations: Current Status, Racial Difference, and Future Directions." *Asian Journal of Andrology* 21(July):1–4. doi: 10.4103/aja.aja.

D'Elia, Giovanna, Gemma Caliendo, Maria Myrsini Tzioni, Luisa Albanese, Luana Passariello, Anna Maria Molinari, and Maria Teresa Vietri. 2022. "Increased Risk of Hereditary Prostate Cancer in Italian Families with Hereditary Breast and Ovarian Cancer Syndrome Harboring Mutations in BRCA and in Other Susceptibility Genes." *Genes*

13(10):1–13. doi: 10.3390/genes13101692.

Dai, Xiaoyu, Xiangming Fang, Ying Ma, and Jianbo Xianyu. 2016. "Benign Prostatic Hyperplasia and the Risk of Prostate Cancer and Bladder Cancer a Meta-Analysis of Observational Studies." *Medicine (United States)* 95(18):e3493. doi: 10.1097/MD.0000000000003493.

Duffy, Michael J. 2020. "[14374331 - Clinical Chemistry and Laboratory Medicine (CCLM)] Biomarkers for Prostate Cancer_ Prostate-Specific Antigen and beyond.Pdf." 58(3):326–39.

Giovannucci, Edward, Yan Liu, Elizabeth A. Platz, Meir J. Stampfer, and Walter C. Willett. 2007. "Risk Factors for Prostate Cancer Incidence and Progression in the Health Professionals Follow-up Study." *International Journal of Cancer* 121(7):1571–78. doi: 10.1002/ijc.22788.

Gomella, Leonard G., Jaspreet Singh, Costas Lallas, and Edouard J. Trabulsi. 2010. "Hormone Therapy in the Management of Prostate Cancer: Evidence-Based Approaches." *Therapeutic Advances in Urology* 2(4):171–81. doi: 10.1177/1756287210375270.

Hayden, A. J., C. Catton, and T. Pickles. 2010. "Radiation Therapy in Prostate Cancer: A Risk-Adapted Strategy." 18–24.

Joseph, Diya B., Anne E. Turco, Chad M. Vezina, and Douglas W. Strand. 2021. "Progenitors in Prostate Development and Disease." *Developmental Biology* 473:50–58. doi: 10.1016/j.ydbio.2020.11.012.

Kaplan, Steven A. 2005. "Benign Prostatic Hyperplasia." *Journal of Urology* 174(1):221–22. doi: 10.1097/01.ju.0000164803.79620.97.

Kawahara, Takashi, Yasuhide Miyoshi, and Hiroji Uemura. 2020. "Re: Current Treatment Strategies for Advanced Prostate Cancer." *International Journal of Urology* 27(6):571. doi: 10.1111/iju.14237.

Keam, Susan J. 2022. "Lutetium Lu 177 Vipivotide Tetraxetan: First Approval." *Molecular Diagnosis and Therapy* 26(4):467–75. doi: 10.1007/s40291-022-00594-2.

Levine, Glenn N., Anthony V. D'Aamico, Peter Berger, Peter E. Clark, Robert H. Eckel, Nancy L. Keating, Richard V. Milani, Arthur I. Sagalowsky, Matthew R. Smith, and Neil Zakai. 2010. "Androgen-Deprivation Therapy in Prostate Cancer and Cardiovascular Risk: A Science Advisory from the American Heart Association, American Cancer Society, and American Urological Association." *Circulation* 121(6):833–40. doi: 10.1161/CIRCULATIONAHA.109.192695.

Merriel, Samuel W. D., Garth Funston, and Willie Hamilton. 2018. "Prostate Cancer in Primary Care." *Advances in Therapy* 35(9):1285–94. doi: 10.1007/s12325-018-0766-1.

Patel, Amit R., and Eric A. Klein. 2009. "Risk Factors for Prostate Cancer." *Nature Clinical Practice Urology* 6(2):87–95. doi: 10.1038/ncpuro1290.

Pernar, Claire H., Ericka M. Ebot, Kathryn M. Wilson, and Lorelei A. Mucci. 2018. "The Epidemiology of Prostate Cancer." *Cold Spring Harbor Perspectives in Medicine* 8(12):1–18. doi: 10.1101/CSHPERSPECT.A030361.

Preble, Isabella, Zhenzhen Zhang, Ryan Kopp, Mark Garzotto, Gerd Bobe, Jackilen Shannon, and Yumie Takata. 2019. "Dairy Product Consumption and Prostate Cancer Risk in the United States." *Nutrients* 11(7):1–12. doi: 10.3390/nu11071615.

Sekhoacha, Mamello, Keamogetswe Riet, Paballo Motloung, Lemohang Gumenku, Ayodeji Adegoke, and Samson Mashele. 2022. "Prostate Cancer Review: Genetics, Diagnosis, Treatment Options, and Alternative Approaches." *Molecules* 27(17):1–33. doi: 10.3390/molecules27175730.

Storck, William K., Allison M. May, Thomas C. Westbrook, Zhi Duan, Colm Morrissey, Joel

A. Yates, and Joshi J. Alumkal. 2022. "The Role of Epigenetic Change in Therapy-Induced Neuroendocrine Prostate Cancer Lineage Plasticity." *Frontiers in Endocrinology* 13(July):1–14. doi: 10.3389/fendo.2022.926585.

Suresh, Kishanrao. 2022. "Prostate Health in India (BPH & Prostate Cancer)." *Archives of Cancer Science and Therapy* 6(1):009–017. doi: 10.29328/journal.acst.1001028.

Vietri, Maria Teresa, Giovanna D'elia, Gemma Caliendo, Marianna Resse, Amelia Casamassimi, Luana Passariello, Luisa Albanese, Michele Cioffi, and Anna Maria Molinari. 2021. "Hereditary Prostate Cancer: Genes Related, Target Therapy and Prevention." *International Journal of Molecular Sciences* 22(7). doi: 10.3390/ijms22073753.

Wang, Guocan, Di Zhao, Denise J. Spring, and Ronald A. Depinho. 2018. "Prostate Cancer Biology 2018." *Genes & Development* 32:1105–40. doi: 10.1101/gad.315739.118.GENES.

Cary, K. Clint, and Mathew R. Cooperberg. 2013. "Biomarkers in Prostate Cancer Surveillance and Screening: Past, Present, and Future." *Therapeutic Advances in Urology* 5(6):318–29. doi: 10.1177/1756287213495915.

Catalona, William J. 2018. "Prostate Cancer Screening." *Medical Clinics of North America* 102(2):199–214. doi: 10.1016/j.mcna.2017.11.001.

Chang, Albert J., Karen A. Autio, MacK Roach, and Howard I. Scher. 2014. "High-Risk Prostate Cancer-Classification and Therapy." *Nature Reviews Clinical Oncology* 11(6):308–23. doi: 10.1038/nrclinonc.2014.68.

Chen1, Rui, Xin Cheng1 Lei Wang1 *. Xia Sheng1 Shu-Guang Piao1 Xin-Wen Nian1, Tie Zhou1, Hui-Zhen Li1, Ya-Wei Liu2, Guang-An Xiao1 Chen1 Guang-Hua Chun-Lei Zhang1 De-Pei Kong1, Xin Lu1, Zhen-Yu Jia1 Zhi-Yong Liu1, and Ying-Hao Sun. 2019. "Prostate Cancer Risk Prediction Models in Eastern Asian Populations: Current Status,

Racial Difference, and Future Directions." *Asian Journal of Andrology* 21(July):1–4. doi: 10.4103/aja.aja.

D'Elia, Giovanna, Gemma Caliendo, Maria Myrsini Tzioni, Luisa Albanese, Luana Passariello, Anna Maria Molinari, and Maria Teresa Vietri. 2022. "Increased Risk of Hereditary Prostate Cancer in Italian Families with Hereditary Breast and Ovarian Cancer Syndrome Harboring Mutations in BRCA and in Other Susceptibility Genes." *Genes* 13(10):1–13. doi: 10.3390/genes13101692.

Dai, Xiaoyu, Xiangming Fang, Ying Ma, and Jianbo Xianyu. 2016. "Benign Prostatic Hyperplasia and the Risk of Prostate Cancer and Bladder Cancer a Meta-Analysis of Observational Studies." *Medicine (United States)* 95(18):e3493. doi: 10.1097/MD.0000000000003493.

Duffy, Michael J. 2020. "[14374331 - Clinical Chemistry and Laboratory Medicine (CCLM)] Biomarkers for Prostate Cancer_ Prostate-Specific Antigen and beyond.Pdf." 58(3):326–39.

Giovannucci, Edward, Yan Liu, Elizabeth A. Platz, Meir J. Stampfer, and Walter C. Willett. 2007. "Risk Factors for Prostate Cancer Incidence and Progression in the Health Professionals Follow-up Study." *International Journal of Cancer* 121(7):1571–78. doi: 10.1002/ijc.22788.

Gomella, Leonard G., Jaspreet Singh, Costas Lallas, and Edouard J. Trabulsi. 2010. "Hormone Therapy in the Management of Prostate Cancer: Evidence-Based Approaches." *Therapeutic Advances in Urology* 2(4):171–81. doi: 10.1177/1756287210375270.

Hayden, A. J., C. Catton, and T. Pickles. 2010. "Radiation Therapy in Prostate Cancer: A Risk-Adapted Strategy." 18–24.

Joseph, Diya B., Anne E. Turco, Chad M. Vezina, and Douglas W. Strand. 2021. "Progenitors in Prostate Development and Disease." *Developmental Biology* 473:50–58. doi:

10.1016/j.ydbio.2020.11.012.

Kaplan, Steven A. 2005. "Benign Prostatic Hyperplasia." *Journal of Urology* 174(1):221–22. doi: 10.1097/01.ju.0000164803.79620.97.

Kawahara, Takashi, Yasuhide Miyoshi, and Hiroji Uemura. 2020. "Re: Current Treatment Strategies for Advanced Prostate Cancer." *International Journal of Urology* 27(6):571. doi: 10.1111/iju.14237.

Keam, Susan J. 2022. "Lutetium Lu 177 Vipivotide Tetraxetan: First Approval." *Molecular Diagnosis and Therapy* 26(4):467–75. doi: 10.1007/s40291-022-00594-2.

Levine, Glenn N., Anthony V. D'Aamico, Peter Berger, Peter E. Clark, Robert H. Eckel, Nancy L. Keating, Richard V. Milani, Arthur I. Sagalowsky, Matthew R. Smith, and Neil Zakai. 2010. "Androgen-Deprivation Therapy in Prostate Cancer and Cardiovascular Risk: A Science Advisory from the American Heart Association, American Cancer Society, and American Urological Association." *Circulation* 121(6):833–40. doi: 10.1161/CIRCULATIONAHA.109.192695.

Merriel, Samuel W. D., Garth Funston, and Willie Hamilton. 2018. "Prostate Cancer in Primary Care." *Advances in Therapy* 35(9):1285–94. doi: 10.1007/s12325-018-0766-1.

Patel, Amit R., and Eric A. Klein. 2009. "Risk Factors for Prostate Cancer." *Nature Clinical Practice Urology* 6(2):87–95. doi: 10.1038/ncpuro1290.

Pernar, Claire H., Ericka M. Ebot, Kathryn M. Wilson, and Lorelei A. Mucci. 2018. "The Epidemiology of Prostate Cancer." *Cold Spring Harbor Perspectives in Medicine* 8(12):1–18. doi: 10.1101/CSHPERSPECT.A030361.

Preble, Isabella, Zhenzhen Zhang, Ryan Kopp, Mark Garzotto, Gerd Bobe, Jackilen Shannon, and Yumie Takata. 2019. "Dairy Product Consumption and Prostate Cancer Risk in the United States." *Nutrients* 11(7):1–12. doi: 10.3390/nu11071615.

Sekhoacha, Mamello, Keamogetswe Riet, Paballo Motloung, Lemohang Gumenku, Ayodeji

Adegoke, and Samson Mashele. 2022. "Prostate Cancer Review: Genetics, Diagnosis, Treatment Options, and Alternative Approaches." *Molecules* 27(17):1–33. doi: 10.3390/molecules27175730.

Storck, William K., Allison M. May, Thomas C. Westbrook, Zhi Duan, Colm Morrissey, Joel A. Yates, and Joshi J. Alumkal. 2022. "The Role of Epigenetic Change in Therapy-Induced Neuroendocrine Prostate Cancer Lineage Plasticity." *Frontiers in Endocrinology* 13(July):1–14. doi: 10.3389/fendo.2022.926585.

Suresh, Kishanrao. 2022. "Prostate Health in India (BPH & Prostate Cancer)." *Archives of Cancer Science and Therapy* 6(1):009–017. doi: 10.29328/journal.acst.1001028.

Vietri, Maria Teresa, Giovanna D'elia, Gemma Caliendo, Marianna Resse, Amelia Casamassimi, Luana Passariello, Luisa Albanese, Michele Cioffi, and Anna Maria Molinari. 2021. "Hereditary Prostate Cancer: Genes Related, Target Therapy and Prevention." *International Journal of Molecular Sciences* 22(7). doi: 10.3390/ijms22073753.

Wang, Guocan, Di Zhao, Denise J. Spring, and Ronald A. Depinho. 2018. "Prostate Cancer Biology 2018." *Genes & Development* 32:1105–40. doi: 10.1101/gad.315739.118.GENES.

Sekhoacha, Mamello, Keamogetswe Riet, Paballo Motloung, Lemohang Gumenku, Ayodeji Adegoke, and Samson Mashele. 2022. "Prostate Cancer Review: Genetics, Diagnosis, Treatment Options, and Alternative Approaches." *Molecules* 27(17):1–33. doi: 10.3390/molecules27175730.

Suresh, Kishanrao. 2022. "Prostate Health in India (BPH & Prostate Cancer)." *Archives of Cancer Science and Therapy* 6(1):009–017. doi: 10.29328/journal.acst.1001028.

Vietri, Maria Teresa, Giovanna D'elia, Gemma Caliendo, Marianna Resse, Amelia Casamassimi, Luana Passariello, Luisa Albanese, Michele Cioffi, and Anna Maria Molinari. 2021. "Hereditary Prostate Cancer: Genes Related, Target Therapy and Prevention." *International Journal of Molecular Sciences* 22(7). doi: 10.3390/ijms22073753.