

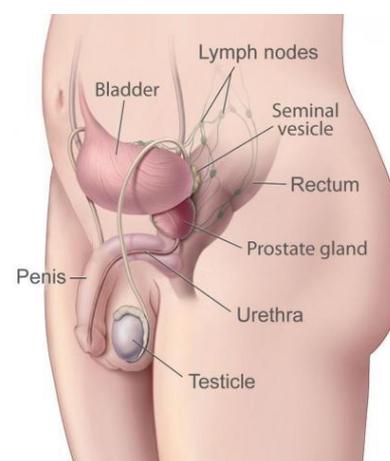
Cancer Association of South Africa (CANSA)



Fact Sheet on Prostate Cancer

Introduction

The prostate gland is about the size of a walnut. It is situated between the base of the penis and the rectum immediately below the bladder. It is a compound muscular alveolar gland and is part of the male reproductive system. It secretes a slightly alkaline fluid during ejaculation – the alkalinity assists in neutralising the normal acidic environment in the female vagina prolonging the lifespan of sperm. It also contains smooth muscle which assists in ejaculation. The prostate gland surrounds a portion of the urethra, a tube that carries urine from the bladder to the tip of the penis. It is an important part of the male reproductive system.



[Picture Credit: Prostate Gland]

Prostate Cancer

Excluding melanoma of the skin and non-melanoma skin cancers, prostate cancer is the most common cancer of men.

Normally all human cells grow and divide to form new cells as the body needs them. As cells grow old or become damaged, they die (apoptosis), and new cells are required to take their place. In the case of prostate cancer, this orderly process of cell division breaks down and cells start to divide in an uncontrolled manner to form growths called tumours. Cancerous tumours are malignant – they can spread into, or invade, nearby tissues. Apart from this, as the tumours grow, cancer cells can break off from the original cancer and spread to distant parts of the body through the blood or lymphatic system to form new tumours. This is referred to as metastasis.

Important Information for Men Who are at High Risk of Prostate Cancer

Recent research recommends that because men with BRCA2 gene mutations have such a high risk of aggressive prostate cancers that they should be offered annual prostate screening inclusive of PSA testing.

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Any man of 40 years of age or older, to whom any of the undermentioned apply, should be referred for genetic counselling and if identified with BRCA2 gene mutation should receive annual full screening for prostate cancer:

- Has a first- or second-degree relative (male or female) diagnosed with Breast Cancer
- Has a first- or second-degree relative diagnosed with Prostate Cancer
- Is aware of a first- or second-degree relative (male or female) who has tested positive for BRCA2 gene mutation

A **first-degree relative** is defined as a close blood relative which includes the individual's parents, full siblings, or children.

A **second-degree relative** is defined as a blood **relative** which includes the individual's grandparents, grandchildren, aunts, uncles, nephews, nieces or half-siblings.

Incidence of Prostate Cancer in South Africa

According to the outdated National Cancer Registry (2014) known for under reporting the following number of prostate cancer cases was histologically diagnosed in South Africa during 2014:

Group - Males 2014	No of Cases	Lifetime Risk	Percentage of All Cancers
All males	7 057	1:19	19.18%
Asian males	184	1:27	10.79%
Black males	2 833	1:30	25.57%
Coloured males	803	1:14	19.08%
White males	3 238	1:10	15.73%

N.B. 'Histologically diagnosed' means that a biopsy (removal of a specimen of tissue) was performed and that a diagnosis of Prostate Cancer was confirmed by a qualified pathologist.

The frequency of histologically diagnosed cases of prostate cancer in South Africa for 2014 was as follows (National Cancer Registry, 2014):

Group - Males 2014	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	0	1	14	192	1 308	2 717	2 071	593
Asian males	0	0	1	4	25	77	56	12
Black males	0	1	9	90	539	1 065	753	228
Coloured males	0	0	0	22	155	316	232	59
White males	0	0	4	73	572	1 245	992	283

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

According to **Bruni, et al.**, (2019), the burden of prostate cancer for South Africa for 2018 is estimated as (based on Globocan estimates):

- Annual number of prostate cancer cases 12 452
- Annual number of prostate cancer deaths 4 400

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Bleyer, A., Spreafico, F. & Barr, R. 2019. Prostate cancer in young men: an emerging young adult and older adolescent challenge. *Cancer*. DOI: 10.1002/cnr.32498.

Background: Recent observations suggest that prostate cancer is an increasing disease among older adolescents and young adults.

Method: Incidence, mortality, and survival data were obtained from the United States National Cancer Institute Surveillance, Epidemiology, and End Results program and the Institute for Health Metrics and Evaluation Global Burden of Disease database.

Results: worldwide, the incidence of prostate cancer has increased in all groups between ages 15 and 40 years and increased globally at a steady rate averaging 2% per year since 1990 (P < .01). In the United States, this age group was >6 times more likely than older men to have distant disease at diagnosis. Stage for stage, their survival rate improved less than in older men. Whereas the overall 5-year relative survival rate in the United States for men diagnosed between ages 40 and 80 years was between 95% and 100%, it was 30% in those aged 15 to 24 years, 50% in those aged 20 to 29 years, and 80% in those aged 25 to 34 years.

Conclusion: Prostate cancer in older adolescents and young adult men has increased in most countries. There is some evidence that this may be caused in part by underdiagnosis, Prostate-specific Antigen screening, and overdiagnosis. It also may be caused by trends in obesity, physical inactivity, HPV infection, substance exposure, environmental carcinogens, and/or referral patterns. How the biology of these cancers differs from that in older men and how these etiologies vary from country to country remain to be determined. **Cancer. 2019;0:1-12.**

Cancer of the Prostate

Prostate cancer is a malignant tumour that begins in the prostate gland. Some prostate cancers grow very slowly and may not cause symptoms or problems for years. However, most prostate cancer cells make excessive amounts of a protein called prostate specific antigen (PSA). PSA is also found in higher-than-normal levels in men with various other prostate conditions, such as benign prostatic hyperplasia (BPH) and prostatitis, in addition to prostate cancer.

Differential Diagnosis

The following table provides an overview of the signs and symptoms of prostate problems. Individuals with any of the symptoms listed below should contact a medical professional:

Symptom	Acute Prostatitis	Chronic Prostatitis	Benign Enlarged Prostate	Prostate Cancer
Pain or burning sensation when urinating (dysuria)	x	x	x	
Difficulty urinating, such as dribbling or hesitant urination	x	x	x	x
Frequent urination, particularly at night (nocturia)	x	x	x	x
Urgent need to urinate	x	x	x	x
A urinary stream that starts and stops	x	x	x	x
Pain in abdomen, groin or lower back	x	x	x	x
Pain or discomfort of the penis or testicles	x	x		x
Pain in the area between the scrotum and rectum (perineum)	x			
Painful orgasms (ejaculation)	x	x		x
Flulike symptoms (with bacterial prostatitis)	x	x		
Feels like bladder does not empty completely		x	x	
Erectile dysfunction	x	x	x	x
Decreased urinary stream	x	x	x	x
Blood in semen	x	x		x

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Blood in urine	x	x	x	x
Raised Prostate Specific Antigen (PSA)	x	x	x	x
Bone pain				x

Types of Prostate Cancer

It is said that by the age of about 50, around half of all men have small changes in the size and shape of the cells in the prostate. This is called prostatic intraepithelial neoplasia (PIN). Some research has indicated these cellular changes may eventually develop into prostate cancer. This is controversial and preventive treatment is not recommended.

If PIN is present, then careful follow-up screening with a PSA blood test and digital rectal examination (DRE) is usually recommended.

More than 9 out of 10 prostate cancers (90%) are a type called acinar adenocarcinoma. It starts from gland cells in the prostate. There are other types of adenocarcinoma, which include atrophic, foamy, colloid and signet ring carcinoma.

The remaining prostate cancers include the following types:

- Ductal adenocarcinoma
- Transitional cell (or urothelial) cancer
- Squamous cell cancer
- Carcinoid
- Small cell cancer
- Sarcomas and sarcomatoid cancer

Because these cancers are so rare, there is sometimes very little information about which treatments work best.

Ductal adenocarcinoma - this type of prostate cancer starts in the cells that line the ducts of the prostate gland. It tends to grow and spread more quickly than acinar adenocarcinoma. This is why some men have an advanced prostate cancer when they are diagnosed. This type of cancer is usually less sensitive to hormone therapy than acinar adenocarcinoma.

Transitional cell (urothelial cancer) - this type of prostate cancer also starts in the cells that line the urethra. More commonly, this type of cancer may start in the bladder and spread into the prostate.

Squamous cell cancer - squamous cell prostate cancer starts from the squamous cells covering the prostate gland. Squamous cell prostate cancer tends to grow and spread more quickly than adenocarcinoma of the prostate. This may be why some men have an advanced prostate cancer when they are diagnosed.

Carcinoid of the prostate - carcinoid tumours start from cells of the neuroendocrine system, which is made up of specialised nerve and gland cells. These tumours are very rare and seem to be slow growing, although some of them may be more aggressive. They may not cause any symptoms for many years.

Small cell cancer - this is a type of neuroendocrine tumour and is made up of small round cells. This type of cancer often cause a raised prostate specific antigen (PSA) test. Many men are diagnosed when it is already

advanced. Small cell prostate cancer tends to grow and spread more quickly than adenocarcinoma of the prostate. Hormone therapy usually does not work for this type of prostate cancer.

Sarcoma and sarcomatoid cancer - sarcomas start from muscle cells. They often grow quite quickly. The most common type of prostate sarcoma in adult men is leiomyosarcoma. It tends to occur in men between the ages of 35 and 60. Sarcomatoid cancers have a mixture of sarcoma and adenocarcinoma cells.

Oligometastatic Prostate Cancer

Cancer progresses in a stepwise fashion. Oligometastatic prostate cancer is defined as up to five extrapelvic lesions on conventional imaging. There are controversies surrounding the management of this malignancy, but retrospective and population-based studies suggest a role for radical prostatectomy. Despite insufficient data to draw conclusions regarding the effectiveness of aggressive therapies on overall or cancer-specific survival of patients with oligometastatic prostate cancer, current studies suggest that surgery decreases tumour burden, disease-related morbidity, and the need for palliative surgical intervention, while increasing the period of time to development of castration-resistant disease.

Risk Factors for Prostate Cancer

Age is the strongest risk factor for prostate cancer. Prostate cancer is very rare before the age of 40, but the chance of having prostate cancer rises rapidly after age 50.

Other possible risk factors include:

- Family history: Prostate cancer seems to run in some families, and scientists have found several inherited genes that seem to raise prostate cancer risk

Risk Group	Relative Risk for Prostate Cancer (95% Confidence Index) *
Brother(s) with prostate cancer diagnosed at any age	3.14 (2.37 – 4.15)
Father with prostate cancer diagnosed at any age	2.35 (2.02 – 2.72)
One affected first-degree relative diagnosed at any age	2.48 (2.25 – 2.74)
Affected first-degree relatives diagnosed <65 years	2.87 (2.21 – 3.74)
Affected first-degree relatives diagnosed ≥65 years	1.92 (1.49 – 2.47)
Second-degree relatives diagnose at any age	2.52 (0.99 – 6.46)
Two or more affected first-degree relatives diagnosed at any age	4.39 (2.61 – 7.39)

(*) Adapted from Kiciński, at al (2011)

- Race/ethnicity: Prostate cancer occurs more often in African-American men than in men of other races. Current evidence shows that this is applicable to South African black men. In black men, prostate cancer is also said to be more aggressive or advanced. It is not clear why this is so.
- If there is a family history of the BRCA1 or BRCA2 gene mutation or a very strong history of women with breast cancer, the risk for prostate cancer may be higher
- Nationality: Prostate cancer is most common in North America, north western Europe, Australia, Africa and Caribbean island and less common in Asia, Central America, and South America
- Diet: Men who eat a lot of red meat or high-fat dairy products appear to have a slightly higher risk of getting prostate cancer. Insufficient consumption of fruit, vegetables and legumes
- Obesity: Obese men diagnosed with prostate cancer may be more likely to have advanced disease that is more difficult to treat – with specific reference to belly fat

- Use of Anabolic Steroids: The use of anabolic steroids may have the following side effects:
 - Infertility (low sperm count)
 - Impotence
 - Testicular shrinkage
 - Baldness
 - Testicular/prostate cancer
 - Enlarged breast tissue
- High alcohol intake – Alcohol was declared a Group 1 carcinogen by the International Agency for Research on Cancer (IARC) in the 1980s
- Use of tobacco products

Rider, J.R., Wilson, K.M., Sinnott, J.A., Kelly, R.S., Mucci, L.A. & Giovannucci, E.L. 2016.

BACKGROUND: Evidence suggests that ejaculation frequency may be inversely related to the risk of prostate cancer (PCa), a disease for which few modifiable risk factors have been identified.

OBJECTIVE: To incorporate an additional 10 yr of follow-up into an original analysis and to comprehensively evaluate the association between ejaculation frequency and PCa, accounting for screening, clinically relevant disease subgroups, and the impact of mortality from other causes.

DESIGN, SETTING, AND PARTICIPANTS: A prospective cohort study of participants in the Health Professionals Follow-up Study utilizing self-reported data on average monthly ejaculation frequency. The study includes 31925 men who answered questions on ejaculation frequency on a 1992 questionnaire and followed through to 2010. The average monthly ejaculation frequency was assessed at three time points: age 20-29 yr, age 40-49 yr, and the year before questionnaire distribution.

OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Incidence of total PCa and clinically relevant disease subgroups. Cox models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs).

RESULTS AND LIMITATIONS: During 480831 person-years, 3839 men were diagnosed with PCa. Ejaculation frequency at age 40-49 yr was positively associated with age-standardized body mass index, physical activity, divorce, history of sexually transmitted infections, and consumption of total calories and alcohol. Prostate-specific antigen (PSA) test utilization by 2008, number of PSA tests, and frequency of prostate biopsy were similar across frequency categories. In multivariable analyses, the hazard ratio for PCa incidence for ≥ 21 compared to 4-7 ejaculations per month was 0.81 (95% confidence interval [CI] 0.72-0.92; $p < 0.0001$ for trend) for frequency at age 20-29 yr and 0.78 (95% CI 0.69-0.89; $p < 0.0001$ for trend) for frequency at age 40-49 yr. Associations were driven by low-risk disease, were similar when restricted to a PSA-screened cohort, and were unlikely to be explained by competing causes of death.

CONCLUSIONS: These findings provide additional evidence of a beneficial role of more frequent ejaculation throughout adult life in the etiology of PCa, particularly for low-risk disease.

PATIENT SUMMARY: We evaluated whether ejaculation frequency throughout adulthood is related to prostate cancer risk in a large US-based study. We found that men reporting higher compared to lower ejaculatory frequency in adulthood were less likely to be subsequently diagnosed with prostate cancer.

According to Harvard Health, 2019.

The Harvard ejaculation study

The Health Professionals Follow-Up Study has been collecting information about a large group of volunteers since 1986. All the men are health care providers, including dentists, pharmacists, veterinarians, optometrists, ophthalmologists, and podiatrists. Most are white. In 1992, 29,342 men between the ages of 46 and 81 provided information about their average number of ejaculations per month in young adulthood (age 20–29), middle age (40–49), and in the most recent year. Ejaculations included sexual intercourse,

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nocturnal emissions, and masturbation. The volunteers provided comprehensive health and lifestyle data every two years until the study concluded in 2000.

The scientists found no evidence that frequent ejaculations mark an increased risk of prostate cancer. In fact, the reverse was true: High ejaculation frequency was linked to a decreased risk. Compared to men who reported 4–7 ejaculations per month across their lifetimes, men who ejaculated 21 or more times a month enjoyed a 31% lower risk of prostate cancer. And the results held up to rigorous statistical evaluation even after other lifestyle factors and the frequency of PSA testing were taken into account.

Ejaculation: data from Down Under

An Australian study of 2,338 men examined the impact of sexual factors on the occurrence of prostate cancer before the age of 70. Like the Harvard research, the Australian investigation evaluated total ejaculations rather than sexual intercourse itself. Like the American men, the Australians who ejaculated most frequently enjoyed a reduced risk of prostate cancer. The effect was strongest for the frequency of ejaculations in young adulthood, even though prostate cancer was not diagnosed until many decades later. Even so, the apparent protection extended to all age groups. In all, men who averaged 4.6–7 ejaculations a week were 36% less likely to be diagnosed with prostate cancer before the age of 70 than men who ejaculated less than 2.3 times a week on average.

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Husby, A., Wohlfahrt, J. & Melbye, M. 2020.

BACKGROUND: A man's risk of prostate cancer has been linked to his prior reproductive history, with low sperm quality, low ejaculation frequency, and a low number of offspring being associated with increased prostate cancer risk. It is, however, highly controversial whether vasectomy, a common sterilization procedure for men, influences prostate cancer risk.

METHODS: We established a cohort of all Danish men (born between 1937 and 1996) and linked information on vasectomy, doctor visits, socioeconomic factors, and cancer from nationwide registries using unique personal identification numbers. Incidence risk ratios for prostate cancer by time since vasectomy and age at vasectomy during the follow-up were estimated using log-linear Poisson regression.

RESULTS: Overall, 26 238 cases of prostate cancer occurred among 2 150 162 Danish men during 53.4 million person-years of follow-up. Overall, vasectomized men had an increased risk of prostate cancer compared with nonvasectomized men (relative risk = 1.15, 95% confidence interval = 1.10 to 1.20). The increased risk of prostate cancer following vasectomy persisted for at least 30 years after the procedure and was observed regardless of age at vasectomy and cancer stage at diagnosis. Adjustment for the number of visits to the doctor and socioeconomic factors did not explain the association.

CONCLUSIONS: Vasectomy is associated with a statistically significantly increased long-term risk of prostate cancer. The absolute increased risk following vasectomy is nevertheless small, but our finding supports a relationship between reproductive factors and prostate cancer risk.

Signs and Symptoms of Prostate Cancer

Signs and symptoms of prostate cancer may include the following:

Urinary symptoms of prostate cancer - because of the proximity of the prostate gland in relation to the bladder and urethra, prostate cancer may be accompanied by a variety of urinary symptoms. Depending on the size and location, a tumour may press on and constrict the urethra, inhibiting the flow of urine. Some prostate cancer signs related to urination include:

- Stranguria - a slow and painful discharge of urine, drop by drop, produced by spasmodic muscular contraction of the urethra and bladder
- Dysuria
- Pollakiuria - abnormally frequent urination
- Haematuria
- Trouble starting and stopping while urinating
- Nocturia - frequent urges to urinate at night
- Loss of bladder control
- Decreased flow or velocity of urine stream

Other prostate cancer signs & symptoms - prostate cancer may metastasise to nearby tissues or bones. Other prostate cancer symptoms include:

- Blood in semen
- Erectile dysfunction
- Painful ejaculation
- Swelling in legs or pelvic area
- Numbness or pain in the hips, legs or feet
- Bone pain that does not go away, or leads to fractures

Diagnosis of Prostate Cancer

Caught in its early stages whilst still confined to the prostate gland prostate increases effective treatment. Testing through a Prostate Specific Antigen (PSA) blood test and Digital Rectal Examination (DRE) and subsequent prostate biopsy are currently mostly employed to detect the presence of prostate cancer.

Early detection is key to enabling better outcomes and potential cure of prostate cancer. Accordingly, it is recommended that men over age 50, or 40 with a family history of prostate cancer, should talk to a doctor about testing for prostate cancer using the PSA test and DRE as part of their annual health check-up. Men should make an individual informed decision about testing based on the latest available evidence on the benefits and potential harms of testing and subsequent treatment for prostate cancer.

It can be life threatening to wait for symptoms to appear before seeking assessment.

Most men seek testing for prostate cancer for the following reasons:

- As part of a general check-up - usually after 50 years of age
- Due to a recent experience with a relative or friend who has suffered from prostate cancer
- A family history of prostate cancer
- A recent onset of urinary symptoms

The Prostate Specific Antigen (PSA) Test

The PSA blood test looks for the presence in the blood of a protein that is produced specifically by prostate cells called Prostate Specific Antigen (PSA). The presence of an elevated PSA does not necessarily mean prostate cancer is present as there are other medical conditions that can lead to a PSA result outside the normal range.

The result of a PSA test needs expert evaluation by an experienced doctor. As a general rule, the higher the PSA result the greater the chance that prostate cancer is present. Where cancer is present, the PSA can predict the volume of disease. Where the PSA is less than 10, the cancer is commonly confined to the prostate. If the PSA is above 30, it is very likely the cancer has spread beyond the prostate and is, therefore, less likely to be curable.

If the PSA test reveals a slightly elevated PSA, a doctor should recommend the test be repeated from time to time to establish the rate of change, if any, before recommending a biopsy.

The Digital Rectal Examination (DRE)

The DRE involves the insertion a gloved finger in the anus, where it is possible to feel part of the surface of the prostate. Irregularities include swelling or hardening of the prostate, or lumps on the surface that may indicate development of a tumour, or other problems. The drawback to this test is that one can feel only part of the prostate, so may miss irregularities beyond reach. There are views that a DRE is not a requirement in the diagnosis of prostate cancer.



Biopsy

A Biopsy is a small tissue sample taken with a spring loaded needle. This is normally conducted by a urologist. A small probe containing an ultrasound generator and sampling needles (known as Trans Rectal Ultra Sound or TRUS) is inserted in the anus.

The ultrasound generates an image of the prostate on a computer screen and guides the urologist to insert the sampling needle into selected areas of the prostate. The biopsy samples are analysed by a pathologist to determine the stage and grade of the cancer.

There are four likely results of a prostatic biopsy:

- The tissue is normal benign prostate tissue
- A condition called atypia or dysplasia where the cells do not look typical of either normal or cancerous cells
- Prostatic intraepithelial neoplasia (PIN) where the cells appear to be in the transitional stage between normal and cancer
- Prostate cancer - which are currently graded on a numerical scoring system call the Gleason Score and the Stage of cancer

PET/CT for Prostate Cancer

Improvements in cancer care have been closely linked to advances in imaging technologies, as these have allowed for more accurate diagnosis, staging, and surveillance of the disease. Prostate cancer (PCa) has been unique in its reliance on a serum biomarker, prostate-specific antigen (PSA), as the major player for disease diagnosis, treatment, and surveillance. Until recently, the use of imaging in PCa was limited to transrectal ultrasonography (TRUS) for guidance of prostate biopsies and computed tomography (CT) and ⁹⁹Tc bone scans for staging of the disease. Over the last 10 years, advances in magnetic resonance imaging (MRI) technology and the development of novel nuclear medicine radiotracers have revolutionised PCa management.



[Picture Credit: PET Radio Tracers]

Trabulsi, E.J., Rumble, R.B., Jadvar, H., Hope, T., Pomper, M., Turkbey, B., Rosenkrantz, A.B., Verma, S., Margolis, D. J., Froemming, A., Oto, A., Purysko, A., Milowsky, M.M., Schlemmer, H-P., Eiber, M., Morris, M.J. Choyke, P.L., Padhani, A., Oldan, J., Fanti, S., Jain, S., Pinto, P.A., Keegan, K.A., Porter, C.R., Coleman, J.A., Bauman, G.S., Jani, A.B., Kamradt, J.M., Sholes, W. & Vargas, H.A. 2020. PURPOSE: Provide evidence- and expert-based recommendations for optimal use of imaging in advanced prostate cancer. Due to increases in research and utilization of novel imaging for advanced prostate cancer, this guideline is intended to outline techniques available and provide recommendations on appropriate use of imaging for specified patient subgroups.

METHODS: An Expert Panel was convened with members from ASCO and the Society of Abdominal Radiology, American College of Radiology, Society of Nuclear Medicine and Molecular Imaging, American Urological Association, American Society for Radiation Oncology, and Society of Urologic Oncology to conduct a systematic review of the literature and develop an evidence-based guideline on the optimal use of imaging for advanced prostate cancer. Representative index cases of various prostate cancer disease states are presented, including suspected high-risk disease, newly diagnosed treatment-naïve metastatic disease, suspected recurrent disease after local treatment, and progressive disease while undergoing systemic treatment. A systematic review of the literature from 2013 to August 2018 identified fully published English-language systematic reviews with or without meta-analyses, reports of rigorously conducted phase III randomized controlled trials that compared ≥ 2 imaging modalities, and noncomparative studies that reported on the efficacy of a single imaging modality.

RESULTS: A total of 35 studies met inclusion criteria and form the evidence base, including 17 systematic reviews with or without meta-analysis and 18 primary research articles.

RECOMMENDATIONS: One or more of these imaging modalities should be used for patients with advanced prostate cancer: conventional imaging (defined as computed tomography [CT], bone scan, and/or prostate magnetic resonance imaging [MRI]) and/or next-generation imaging (NGI), positron emission tomography [PET], PET/CT, PET/MRI, or whole-body MRI) according to the clinical scenario. J Clin Oncol 38. © 2020 by American Society of Clinical Oncology

The Gleason Score

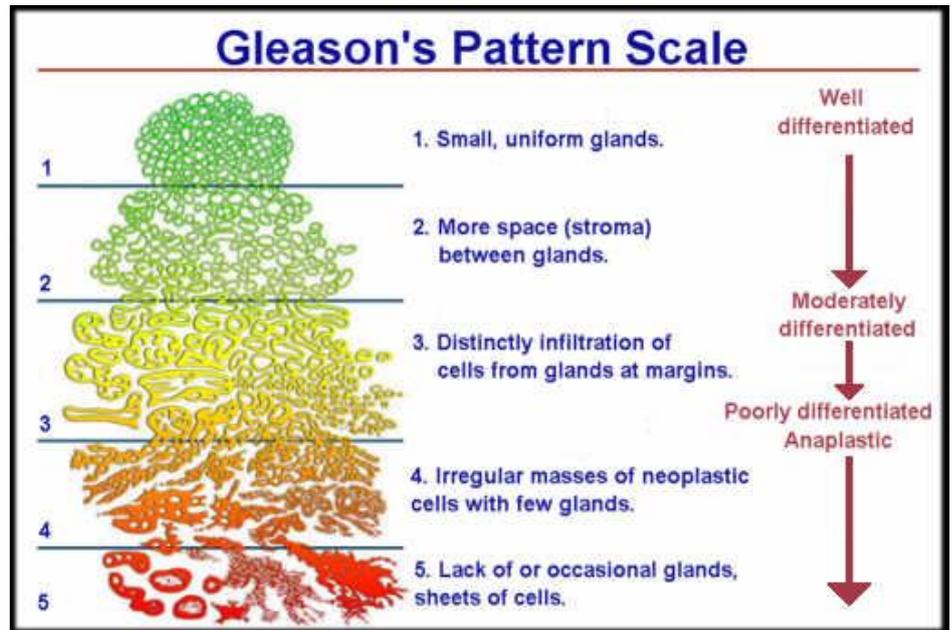
The Gleason score is used to help determine how quickly a tumour may grow or spread. It may seem confusing because with the Gleason system (the most common system used), there's both a 'grade' and a 'score'.

The Gleason grade uses numbers 1 to 5.

[Picture Credit: Gleason Score]

A number is assigned to two of the areas of the prostate that have the most cancer (based on biopsy core samples that are taken). This is because the cancer may look different in each of those two areas.

Once those two numbers are determined, they are added together to come up with the Gleason score, which ranges from 2 to 10.



What the Gleason grades mean :

Grade 1: The cells look almost like normal cells (called *well differentiated*) and are uniformly spaced in a tight mass.

Grade 2: The cancer cells are still well differentiated, but are arranged more loosely, are more irregular in shape, and some cells have spread to other prostatic tissue.

Grade 3: The cancer is moderately differentiated; cells vary in size from small to large; and more cells have invaded other prostatic tissue.

Grade 4: The cancer cells are irregular, distorted, and look less like normal cells (called *poorly differentiated*), and there is considerable spread (called *invasion*) to other prostatic tissue.

Grade 5: The cancer cells do not look anything like normal cells and have spread in haphazard 'clumps' of all different shapes and sizes through the prostate.

What the Gleason scores mean:

- If the score is less than 6, the cancer may be considered to be well-differentiated or low-grade cancer
- A score of 7 may be considered to be moderately differentiated or intermediate-grade cancer
- A score of 8 to 10 may be considered to be poorly differentiated or high-grade cancer

According to the American Urological Association, the lowest Gleason score that is usually found after a biopsy is 5. The cancer is considered to be more aggressive as the score rises. Scores of 8 to 10 are

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considered to be the most aggressive, which means that the cancer is more likely to grow and spread more quickly.

The biopsy results (called the *pathology report*) will contain other important information that helps to assess how aggressive the cancer may be.

This includes:

- How many biopsy core samples were positive for cancer
- How much cancer was in each core sample (this is given as a percentage)
- Whether cancer was found in just one side of the prostate gland or in both sides (which is referred to as *bilateral*)

Biopsy of the Prostate

A PSA test on its own cannot tell if a patient has prostate cancer (many patients with prostate cancer in fact may not have an abnormal PSA level) – it is only an indicator, although generally a reliable one. As a result, further investigation is required. This involves tests in the form of an MRI scan and/or a biopsy, which are usually performed to give the oncologist/urologist a much clearer picture and firm data about the presence of any possible cancer.

An MRI scan on its own is also not necessarily sufficient. Although MRI scanning is getting close to being able to reliably predict the presence of a significant (Gleason grade 7 or higher) prostate cancer, it is still only 80% accurate. One can, therefore, not rely on it on its own. Only prostate cancer seen under a microscope by a trained pathologist can be taken as incontrovertible proof of the presence of cancer within a prostate gland, and this requires a biopsy to be performed.

There are two methods of performing a prostate biopsy, namely a transrectal biopsy and a transperineal prostate biopsy.

Transrectal biopsy method - prostate biopsy has traditionally been done via the transrectal route – i.e. via the rectum. This is because before the advent of transrectal ultrasound (where an ultrasound probe is placed in the rectum to provide a visual of the prostate as the needles were inserted into it), the biopsies were finger-guided. This means that the biopsy needle was placed alongside a gloved finger placed in the rectum, which allowed the operator to feel which part of the prostate to guide the needle into. The advent of the transrectal ultrasound probe allowed urologists to see exactly where the needle was within the prostate before the biopsy was taken, allowing a much greater degree of accuracy than with the finger-guided approach.

However, even with the probe to help, problems remain with transrectal prostate biopsies. These may include:

- An infection rate of 10-20% due to needles penetrating the rectal wall, and faecal matter contaminating other parts of the body.
- A serious infection (septicaemia or blood poisoning) rate of 1-2%.
- The development of antibiotic-resistant strains of bacteria causing infection.
- Pain during biopsy.
- Inability to accurately place the biopsy needle within the prostate in 3 dimensions.

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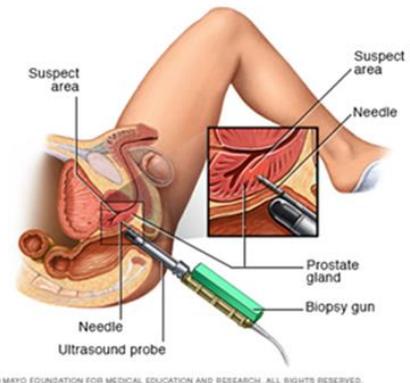
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In addition, perhaps the biggest downside of the transrectal approach is that it is harder/impossible to reach the part of the prostate (the anterior, or frontal aspect) that is furthest away from the biopsy needle. This leads to poor 'sampling' – in that the tissue samples collected by the needles may miss any cancer found in this part of the prostate, leading to an inaccurate biopsy.

A transrectal approach might miss the cancer in the anterior, with the biopsy coming back clear from the other parts of the prostate. In essence, all parts of the prostate need to be sampled completely for the most accurate biopsy result.

Transperineal biopsy method - the answer to the above problems lies in using a transperineal approach to inserting the needles – meaning that the needles go through the perineum (the area behind the scrotum and in front of the anus) instead of through the rectum. A brachytherapy grid is placed over the perineum to allow accurate placement of the biopsy needle within the prostate, together with the use of an ultrasound probe to direct the urologist. This allows better sampling of all parts of the prostate, including the anterior section.

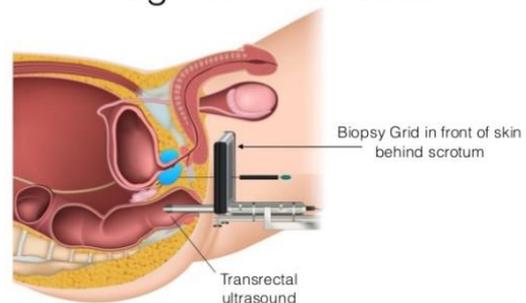


[Picture Credit: Transrectal Prostate Biopsy]

[Picture Credit: Transperineal Prostate Biopsy]

Targeting the biopsy accurately using MRI - by doing an MRI scan before a transperineal biopsy, one can identify the suspicious areas to be specifically targeted during the biopsy – increasing the accuracy of the biopsy. This can either be done by comparing the MRI scan with the transrectal ultrasound view during the biopsy process (cognitive targeting) or by overlaying the 2 images in real-time using computer software: fusion biopsy. Because patients are asleep under a general anaesthetic for transperineal biopsy, discomfort during the biopsy process is not an issue, allowing many more samples to be taken and so increasing the detection rate. And because the biopsies are not taken via the rectum, infection-related complications are much less common.

Transperineal biopsies: through skin not rectum



In summary - the point of a biopsy is to accurately determine the grade of prostate cancer, and so one must be able to access the whole of the prostate to do so. A quick overview of the main points of comparison is found below.

Item:	Transrectal Prostate Biopsy	Transperineal Prostate Biopsy
Anaesthetic	Local	General
Hospital stay	Outpatient	Day case
Discomfort during procedure	Moderate	None
Discomfort after procedure	Ache	Ache
Infection risk	10 – 20%	1 – 2%
Serious infection risk	1 – 2%	Less than 1%
Ability to sample anterior prostate	Limited	Full
Allows systematic sampling (prostate mapping)	No	Yes

Staging of Prostate Cancer

Like other forms of cancer, the prognosis for prostate cancer depends on how far the cancer has spread at the time it is diagnosed.

A system of staging is used to describe prostate cancer spread.

Accurately identifying the prostate cancer stage is extremely important.

Prostate cancer staging helps to determine the optimal treatment as well as prognosis.

Treatment of Prostate Cancer

The main treatments for prostate cancer are surgery, radiotherapy and hormone therapy. Chemotherapy is also sometimes used.

A number of different factors needs to be taken into consideration when deciding on treatment. The most important of these are how fast the cancer is likely to grow and how far it has already grown.

It is generally recommend that treatment is considered individually for every man with prostate cancer.

Patients often query their treatment when they come across other men with prostate cancer who are having different treatment to what they are receiving. They should be informed that it is because they have a different stage or grade of cancer.

- Active Surveillance -The concept of active surveillance, or watchful waiting, has increasingly emerged in recent years as a viable option for men who decide not to undergo immediate surgery or radiation therapy.

During active surveillance, prostate cancer is carefully monitored for signs of progression. A PSA blood test and digital rectal exam (DRE) are usually administered periodically along with a repeat biopsy of the prostate at one year and then at specific intervals thereafter. If symptoms develop, or if tests indicate the cancer is growing, treatment might be warranted.

- **Surgery –**

A surgical approach to treating prostate cancer will remove all or part of the prostate. Typically, men with early-stage disease or cancer that’s confined to the prostate will undergo radical prostatectomy - removal of the entire prostate gland, plus some surrounding tissue. Other surgical procedures may be performed on men with advanced or recurrent disease.

APPROACH PROSTATE CANCER
with
ACTIVE SURVEILLANCE

Active surveillance is a strategy that involves monitoring your prostate cancer closely and choosing to undergo treatment if it advances. It's an option for men who have "low-risk" prostate cancer.

Criteria:

- PSA level is under 10ng/ml
- Gleason score of 6 or less
- Cancer stage T2a or lower
- Your age and overall health

How to monitor your prostate cancer

 <p>Regular DREs Regular digital rectum exams help monitor any tumor growth.</p>	 <p>Periodic PSA Testing To check for increases in blood levels that may indicate progression of the cancer.</p>
 <p>MRI Scans If needed, an MRI helps your doctor visualize portions of the prostate gland they can't feel during DREs.</p>	 <p>Biopsy Generally done once a year or so.</p>

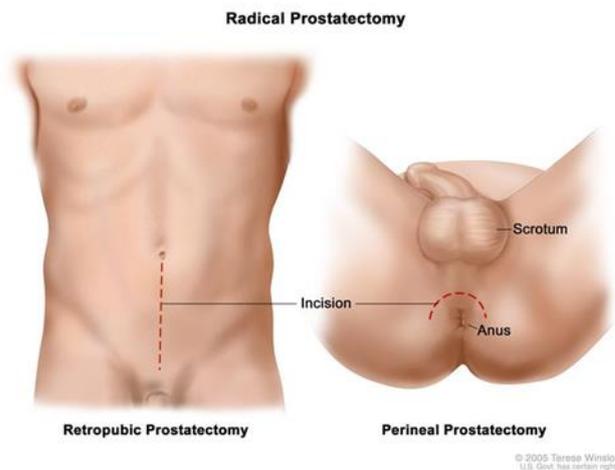
The most common types of prostatectomy include:

Radical Retropubic Prostatectomy - an incision is made in the abdomen and the prostate is removed from behind the pubic bone. The surgeon then stitches the urethra directly to the bladder so urine is able to flow.

[Picture Credit: Radical Prostatectomy Incision]

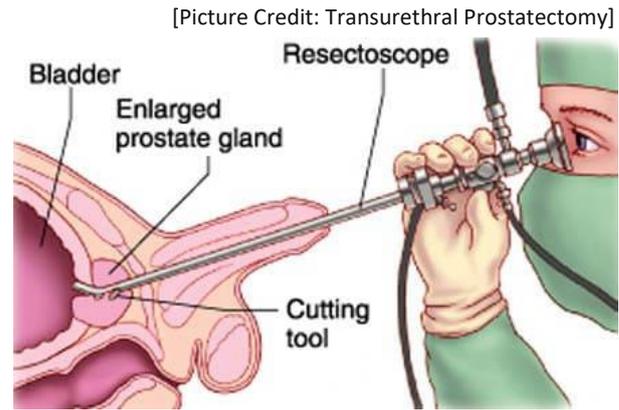
Radical Perineal Prostatectomy - A perineal prostatectomy is done through a cut in the area between the testicles and back passage, the perineum.

Transurethral prostatectomy – transurethral resection of the prostate (TURP) is a type of prostate surgery done to relieve moderate to severe urinary symptoms caused by an enlarged prostate, a condition known as benign prostatic hyperplasia (BPH).



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During TURP, a combined visual and surgical instrument (resecto-scope) is inserted through the tip of the penis and into the tube that carries urine from the bladder (urethra). The urethra is surrounded by the prostate. Using the resectoscope, the doctor trims away excess prostate tissue that is blocking urine flow and increases the size of the channel that allows one to empty one's bladder.



TURP is one of the most effective options for treating urinary symptoms caused by BPH. To determine whether TURP or another treatment is the right choice, the doctor will consider how severe the patient's symptoms are, what other health problems he has, and the size and shape of the prostate.

- Radiation therapy - it involves the killing of cancer cells and surrounding tissues with directed radioactive exposure. The use of radiation therapy as an initial treatment for prostate cancer is described below. Some forms of radiation therapy can also be used in men with advanced or recurrent prostate cancer.

Although technological advancements have made radiation therapy (RT) treatment more specific to the prostate, surrounding structures such as the bladder and rectum can still be affected. Close to 70% of all cancers are treated with radiation; depending on the location of the involved organ, radiation colitis can be a common complication outside of prostate cancer. Yet up to 20% of patients with prostate cancer treated with RT (external or internal via brachytherapy) will develop radiation colitis.

Radiation colitis can present in 2 ways: acute (within 6 weeks of RT) and chronic (within 9 months after RT and for up to 30 years thereafter). Patients with acute and chronic radiation colitis have similar symptoms, although chronic can cause more gastrointestinal bleeding. A patient's bowel movements will contain more mucus and will be less formed; they may experience diarrhoea as well as urgency. Tenesmus is another common symptom.

Chronic inflammation of the rectum over many years can lead to stricturing of the left side of the colon, which may present with changes in stool calibre or constipation.

[Picture Credit: Brachytherapy]

- External Beam Radiation Therapy - this is the most common type of radiation therapy. CT scans and MRIs are used to map out the location of the tumour cells, and X-rays are targeted to those areas. With 3-D conformal radiotherapy, a computerised program maps out the exact location of the prostate tumours so the highest dose of radiation can reach the cancer cells within the gland.

Intensity-modulated radiation therapy (IMRT) allows the radiation doctors to modulate, or change, the intensity of the doses and radiation beams to better target the radiation delivered to the prostate, while simultaneously delivering lower doses to the tumour cells that are immediately adjacent to the bladder and rectal tissue. These techniques are always improving, including the use of guidance markers (fiducial markers), which may be able to reduce the risks to the bowel and bladder over time.

Because the treatment planning with these types of radiation therapy is far more precise, higher—and more effective—doses of radiation can be used with less chance of damaging surrounding tissue. Also, because radiation works slowly, toxicities to the normal surrounding tissues can also develop slowly.

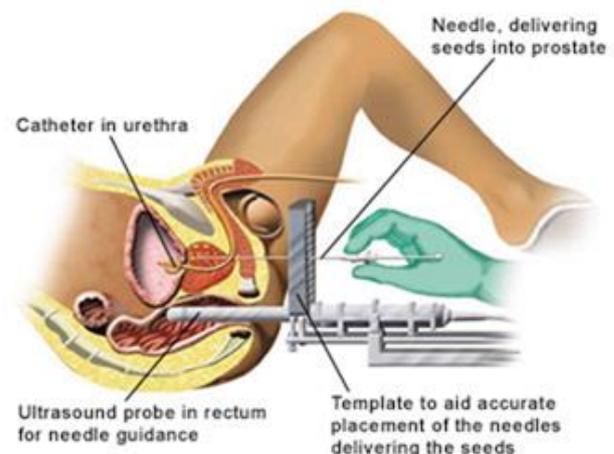
- Proton Therapy

The advantage of using protons over other external beam sources is precision. Protons of energetic particles can hit a targeted prostate cancer tumour without affecting surrounding tissue. This direct attack on cancerous cells ultimately causes their death, as the cells are particularly vulnerable to attack due to their rapid division.

Proton treatment is notably valuable for treating localized, isolated, solid tumours before they spread to other tissues and the rest of the body. However, to date, proton beam therapy has never been compared directly to standard IMRT techniques, so we do not truly know if this offers an advantage over standard approaches.

- Brachytherapy

With brachytherapy, tiny metal pellets containing radioactive iodine or palladium are inserted into the prostate via needles that enter through the skin behind the testicles. As with 3-D conformal radiation therapy, careful and precise maps are used to ensure that the seeds are placed in the proper locations.



Over the course of several months, the seeds give off radiation to the immediate surrounding area, killing the prostate cancer cells. By the end of the year, the radioactive material degrades, and the seeds that remain are harmless.

Compared with external radiation therapy, brachytherapy is less commonly used, but some patients prefer this option primarily because it doesn't require daily visits to the treatment centre. Side effects can include erectile dysfunction, urinary frequency and obstruction, and rarely rectal injury.

- **Hormone Therapy** - Prostate cancer cells are like other living organisms—they need fuel to grow and survive. Because the hormone testosterone serves as the main fuel for prostate cancer cell growth, it's a common target for therapeutic intervention in men with the disease.

- Hormone therapy, also known as androgen-deprivation therapy or ADT, is designed to stop testosterone from being released or to prevent it from acting on the prostate cells. Although hormone therapy plays an important role in men with advancing prostate cancer, it is increasingly being used before, during, or after local treatment as well.

- **Orchidectomy** - About 90% of testosterone is produced by the testicles. So orchidectomy (the surgical removal of the testicles) is an effective solution to blocking testosterone release. This approach has been used successfully since the 1940s. Because it is permanent and irreversible, most men opt for drug therapy instead.

- LHRH Agonists - LHRH, or luteinizing-hormone releasing hormone, is one of the key hormones released by the body before testosterone is produced. (Note that LHRH is sometimes called GnRH, or gonadotropin-releasing hormone.)
- Chemotherapy - The term 'chemotherapy' refers to any type of therapy that uses chemicals to kill or halt the growth of cancer cells. The drugs work in a variety of ways, but are all based on the same simple principle: stop the cells from dividing and you stop the growth and spread of the tumour.
- Other treatment options - Surgery and radiation therapy remain the standard treatment for localised prostate cancer, but other, less popular treatment options might be beneficial as well. As time goes on and the benefits of these treatment options are further explored, it's possible that they will move more into the mainstream. For now, though, none are seen as standard treatments for localized prostate cancer.
- Cryotherapy - Cryotherapy, also known as cryosurgery or cryoablation, has been around for years, but until a few years ago, it was rarely used. With this approach, probes are inserted into the prostate through the perineum (the space between the scrotum and the anus), and argon gas or liquid nitrogen is delivered to the prostate, literally freezing to death the prostate cells and any prostate tumours.

Over the years, a number of modifications were made to avoid freezing damage to the nearby structures, but the rates for both erectile and urinary dysfunction remain high, and data on long-term outcomes are limited.

- Primary Hormone Therapy - Prostate cancer cells are like other living organisms—they need fuel to grow and survive. Because the hormone testosterone serves as the main fuel for prostate cancer cell growth, it's a common target for therapeutic intervention in men with the disease. Hormone therapy, also known as androgen-deprivation therapy or ADT, is designed to stop testosterone from being released or to prevent it from acting on the prostate cells.

Although hormone therapy plays an important role in men with advancing prostate cancer, it is also increasingly being used before, during, or after local treatment. In some cases, hormone therapy may be used in conjunction with radiation therapy. If so, treatment with ADT is generally given before, during and after radiation therapy in the form of an LHRH agonist. LHRH, or luteinizing hormone releasing hormone, is one of the key hormones involved in the production of testosterone. This medicine works through a complicated feedback loop to lower the body's testosterone. Note that LHRH is sometimes called GnRH, or gonadotropin-releasing hormone. Although there is little, if any, data to show that hormone therapy alone is an effective treatment strategy for men with localized prostate cancer, it is increasingly being used in this setting.

Because it is not invasive, it is possible that the therapy is seen as a middle ground between active surveillance and local therapy. For men who are not good candidates for surgery or radiation, and who require immediate therapy, primary hormonal therapy is a reasonable option. However, hormonal therapy has a long list of side effects, and thus, the main question is whether therapy can be safely deferred in men who are not candidates for immediate surgery or radiation. Primary hormonal therapy is also a reasonable option in men who have metastatic disease (cancer spread beyond the prostate) when the diagnosis of prostate cancer is made. In these men, hormonal therapy will shrink the prostate gland and cancer and may delay any need for local therapy.

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- Targeted Therapies - Chemotherapy drugs can play an important role in improving the lives of men with advanced prostate cancer, but they often don't distinguish between tumour cells and healthy cells to a high degree and can kill off some normal cells along the way. So-called targeted therapies, by contrast, are drugs that are specifically designed to interfere with the way cancer cells grow, with the way cancer cells interact with each other, and/or with the way that the immune system interact with the cancer without damaging a man's normal cells.
- Emerging Therapies - In laboratories around the world, researchers are busy identifying new drugs and treatment approaches that might prove beneficial to men with prostate cancer. Most of these investigational agents are being tested in men with advanced prostate cancer: therapy options for men at this stage of disease may not be effective enough to halt progression of the disease, and men are typically affected by side effects from the disease and/or the medications that they're taking. It's therefore the perfect stage at which to test out new drugs because any improvement will likely be rapidly noticed and much appreciated.

Questions that Patients should ask their Health Professional

It is important for health professionals to have honest, open discussions with their patients about prostate cancer. Some questions from patients pertaining to prostate cancer that every health professional should be able respond to:

- What type of prostate cancer do I have?
- What are the chances that the cancer has spread beyond my prostate? If so, is it still curable?
- What further tests (if any) do you recommend, and why?
- Are there other types of doctors I should talk to before deciding on treatment?
- What is the clinical stage and Gleason score (grade) of my cancer? What do those mean to me? Does this make me a low-risk, intermediate-risk or high-risk patient?
- What is my expected survival rate based on clinical stage, grade, and various treatment options?
- Should I consider active surveillance as an option? Why or why not?
- Do you recommend a radical prostatectomy or radiation therapy? Why or why not?
- Should I consider laparoscopic or robot-assisted prostatectomy?
- What types of radiation therapy might work best for me?
- What other treatment(s) might be right for me? Why?
- Will I have to have my testicles removed? If so, why? What will the short and long term effects be?
- What risks or side effects should I expect from my treatment options?
- What are the chances that I will have problems with incontinence or impotence?
- What are the chances that I will have other urinary or rectal problems?
- How quickly do I need to decide on treatment?
- What should I do to be ready for treatment?
- How long will treatment last? What will it be like? Where will it be done?
- How would treatment affect my daily activities?
- What are the chances my cancer will come back with the treatment plans we have discussed? What would be our next step if this happened?
- What type of follow-up will I need after treatment?
- Where can I find more information and support?
- What is my risk of recurrence after surgery or radiation based on my Gleason score, PSA, rate of PSA rise, and stage?

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- What is my risk of progression over time without therapy? Do I need immediate therapy?
- Are you comfortable with me exploring other treatment options and speaking with other specialists (urologists, radiation oncologists, medical oncologists) before deciding upon a final plan of action?
- What are the common side effects of the treatments recommended and when do they occur?
- How many men with prostate cancer do you treat (with surgery, radiation, etc) per year?
- What should I do to keep my body and mind healthy now that I have been diagnosed with prostate cancer?
- Based upon what we know today, what is the chance that my cancer spread beyond the prostate? What is the cure rate for this type of cancer?
- Are there additional tests that we can do to gain the most complete understanding of the stage and aggressiveness of my cancer?
- What are all of the treatment options for this stage of cancer?
- What are the benefits of the type of therapy you are recommending?
- What are the drawbacks/side effects of this type of therapy?
- Will I have problems with sexual function?
- Will I have other urinary or rectal problems?
- What other treatment(s) might be appropriate and why?
- Is my cancer likely to come back based on what you know today?
- What can I do to improve the success of my therapy?
- What kind of follow-up can I expect after treatment?
- Should I join a clinical trial?
- If I am going to be operated, which surgical technique will be used? Open, laparoscopic, robotic?
- Based on your experience, why is this the right approach for me?
- Do you plan to employ a nerve-sparing technique with the aim of conserving my ability to get an erection following surgery?
- What level of success have you had in preserving potency (ability to get an erection) in your patients following surgery?
- What about preserving urinary continence (bladder control)?
- What will you do if you find cancer outside of my prostate during the surgery?
- Will that change my prognosis and future treatment?
- Do I need to be concerned about blood loss during the surgery? Should I store my blood or get my family and friends to donate blood in case it is needed?
- What can I expect following the surgery in terms of recovery time? How long will it be before I can return to my normal activities?
- What are the likely or possible side effects of the surgery, both short-term and long-term?
- What will we do to monitor my prostate cancer following the surgery?
- If I am given radiation therapy, which radiation technique will be used? Seeds, external beam, intensity-modulated radiation therapy (IMRT)?
- Based on your experience, why is this the right approach for me?
- How will this procedure precisely target the cancer tissue but leave the normal tissue unharmed?
- Are there specific radiation therapy approaches that we should discuss or consider, such as IMRT or brachytherapy? What about special markers to help guide the radiation dose in real time to possibly prevent toxicity?
- What dose of radiation will you be using and how/why did you select that dose of radiation?
- How often will I need to come into the clinic for treatments?
- Do you recommend that we initiate androgen deprivation therapy ("hormone therapy") before the radiation treatments? Why or why not?

- What can I expect following the treatments in terms of recovery time? How long will it be before I can return to my normal activities?
- Are there delayed side effects that might appear over time?
- What will we do to monitor my prostate cancer following the radiation?
- What treatment options are there if my cancer progresses?
- How will I be followed? What will be the frequency of PSA tests, rectal examinations, and repeat biopsies?
- When will a repeat biopsy be considered and how will the biopsy information be used to decide on surgery or radiation?
- Who will be the doctor to follow me during this time?
- Are there dietary or lifestyle changes that I can make that can slow prostate cancer growth or that may allow my body to be more healthy to fight this prostate cancer?
- I was told that cannabis oil is effective in treating prostate cancer. Should I consider using cannabis oil? Why or why not?

Medical Disclaimer

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