The Christ Hospital Health Network

Prostate Cancer, Screening, Active Surveillance and Surgical Treatment of Prostate Cancer

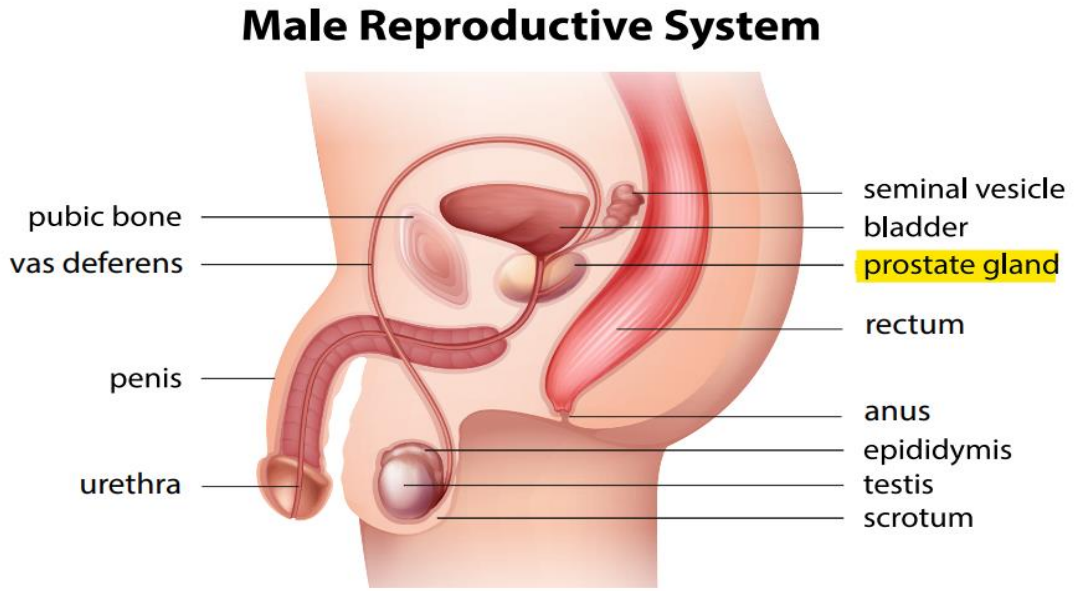
Justin Cox, MD

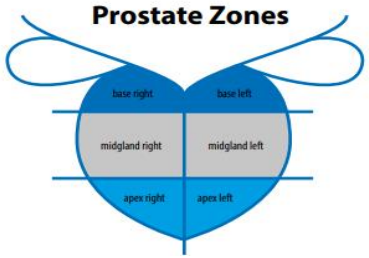
- Prostate Anatomy
- What Is Prostate Cancer?
- Statistics
- Risk Factors
- Signs and Symptoms
- Screening
- Diagnosis
- Gleason Grading System
- Staging/Risk Stratification
- Treatments

ANATOMY

The Prostate:

- A gland in the male reproductive system that makes a liquid that nourishes and helps transmit semen
- Located below the bladder; urine flows through the channel within the prostate
- Size of a walnut (can reach the size of a lemon or orange with age)





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WHAT IS PROSTATE CANCER?

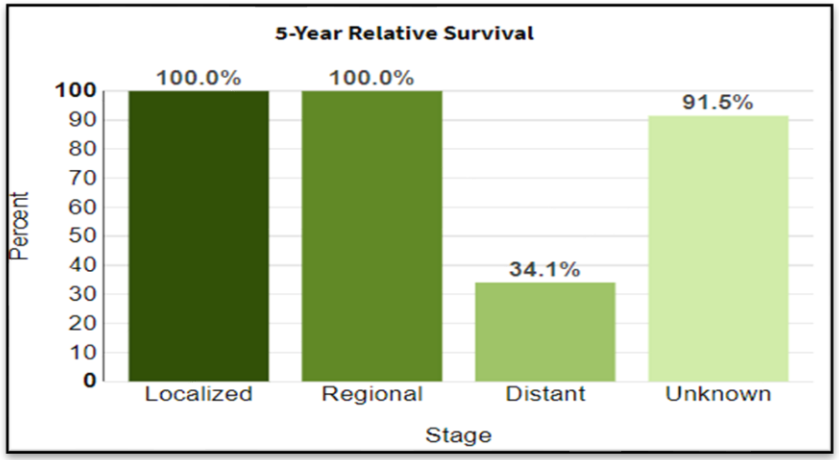
- Most common cancer in American males besides skin cancer
- Early Stage: Contained within the prostate
  - Highly treatable and often curable
- Advanced Stage: Spread beyond the prostate (metastasis)
  - Not curable but treatment can slow growth and reduce symptoms

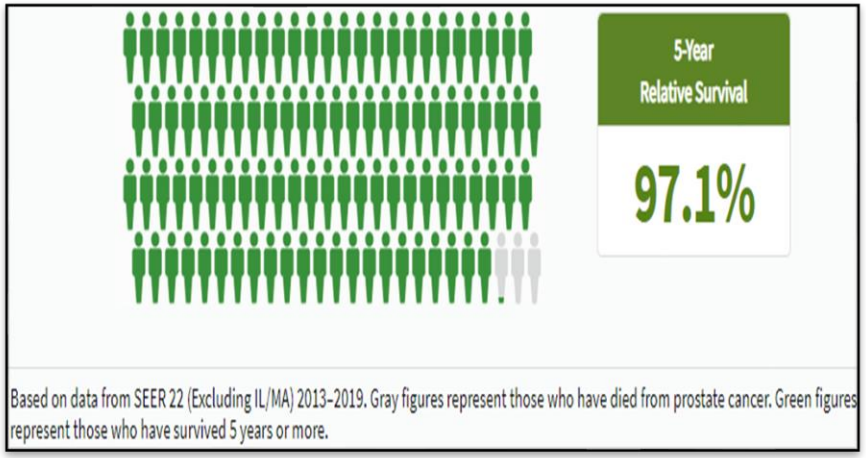
STATISTICS

Estimated New Cases in 2023	288,300
% of All New Cancer Cases	14.7%
Estimated Deaths in 2023	34,700
% of All Cancer Deaths	5.7%

- About 1 in 8 men will be diagnosed with prostate cancer during his lifetime
- Prostate cancer represents 14.7% of all new cancer cases in the U.S.
- Median age at diagnosis: 67
- Median age at death: 79

5 Year Survival Rate



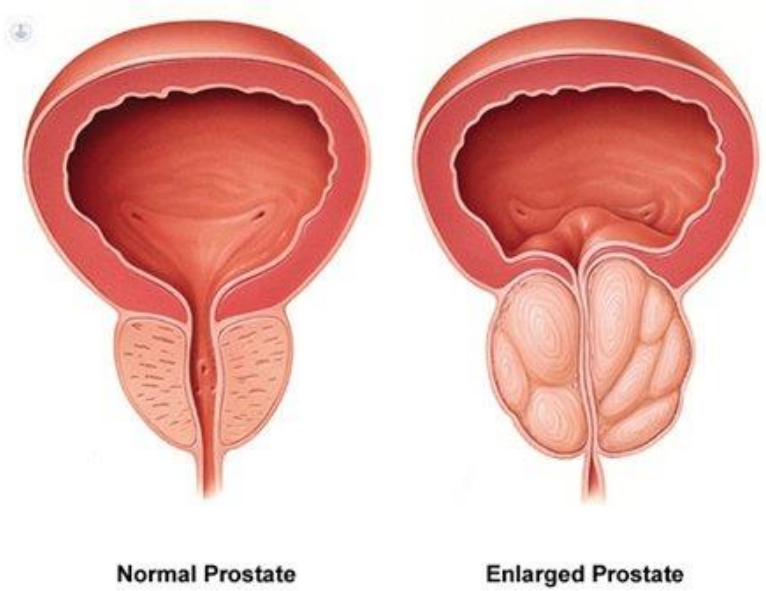


NIH NATIONAL CANCER INSTITUTE
Surveillance, Epidemiology, and End Results Program

RISK FACTORS

- **Age:** Biggest risk factor- Most commonly diagnosed in men 65 and older with increased risk as men get older (risk is higher after 50).
- **Family History:** A close family member (brother or father) with prostate cancer, or other cancers such as breast, ovarian, colon, pancreatic are at higher risk.
- **Genetics:** Inherited genetic abnormality in the BRCA1 and BRCA2 gene likely has a higher risk
- **Race:** Black males are more likely than White males (more likely to occur at an earlier age, and be more aggressive/advanced at diagnosis)
- **Diet:** High fat foods, such as meat and dairy may increase risk, although this has not been proven.
- **Lifestyle:** Smoking and exercise

SIGNS AND SYMPTOMS



Early-stage:

- *Usually does not cause symptoms!*
- Most commonly detected from elevated PSA
- Same symptoms of BPH causing urinary issues-dysuria, weak stream, frequency

Advanced-Stage:

- Same symptoms of BPH causing urinary issues
- Blood in urine or semen
- Trouble getting an erection
- Weakness or numbness in legs or feet, or not being able to control the bowel or bladder, caused by cancer pressing on the spinal cord
- Pain in the hips, spine, ribs caused by bone metastasis.
- Weight loss

Prostate Cancer Screening:
American Urological Association (AUA) Guidelines

- Shared decision-making
- PSA (prostate specific antigen) blood test recommended first screening test
- Screening should be offered to men starting between ages 45 and 50 for **average risk** patient
- Regular prostate cancer screening should be offered every 2 to 4 years to people aged 50 to 69
  - Timing/frequency should be personalized
  - Digital rectal exam (DRE) may be offered alongside PSA
  - Age alone should NOT be a deciding factor

- **Increased risk** patients should be offered to begin screening ages 40-45
  - Black ancestry
  - Germ line mutations (BRCA1 and BRCA 2 gene mutations among others)
  - Strong family history

Life expectancy and general health should be considered with all patients

PSA LEVELS

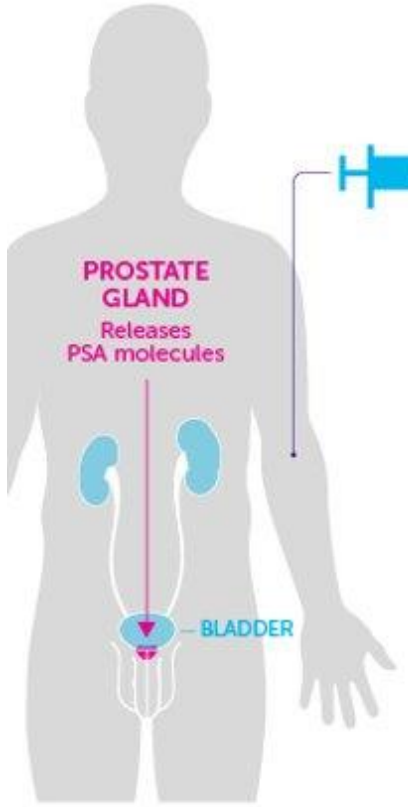
- The chance of having prostate cancer goes up as the PSA level goes up, but there is no set cutoff point that can tell for sure if a man does or does not have prostate cancer

- PSA naturally increases with age

- Most men *without* prostate cancer have PSA levels under 4 ng/mL of blood**.** A level below 4 is not a guarantee that a man doesn't have cancer

AGE-SPECIFIC REFERENCE RANGES FOR SERUM PSA			
Age Range (years)	**Asian Americans**	**African Americans**	**Caucasians**
40 to 49	0 to 2.0 ng/mL	0 to 2.0 ng/mL	0 to 2.5 ng/mL
50 to 59	0 to 3.0 ng/mL	0 to 4.0 ng/mL	0 to 3.5 ng/mL
60 to 69	0 to 4.0 ng/mL	0 to 4.5 ng/mL	0 to 4.5 ng/mL
70 to 79	0 to 5.0 ng/mL	0 to 5.5 ng/mL	0 to 6.5 ng/mL

THE PSA TEST AND WHY ITS RESULTS CAN BE CONFUSING



1 A PSA test measures the amount of PSA molecules in a patient's blood.

2 It's normal for all men to have some PSA in their blood.

3 A high level of PSA can be a sign of prostate cancer, BUT...

4 It can also be raised for lots of other reasons including...


A urinary or urinary tract infection (UTI)


Vigorous exercise


Prostate stimulation, recent ejaculation or anal sex


Certain medications

LET'S BEAT CANCER SOONER
cruk.org

CANCER RESEARCH UK

Diagnosis

- Abnormal PSA (along with another repeat level) or palpable nodule on DRE typically determines further investigation

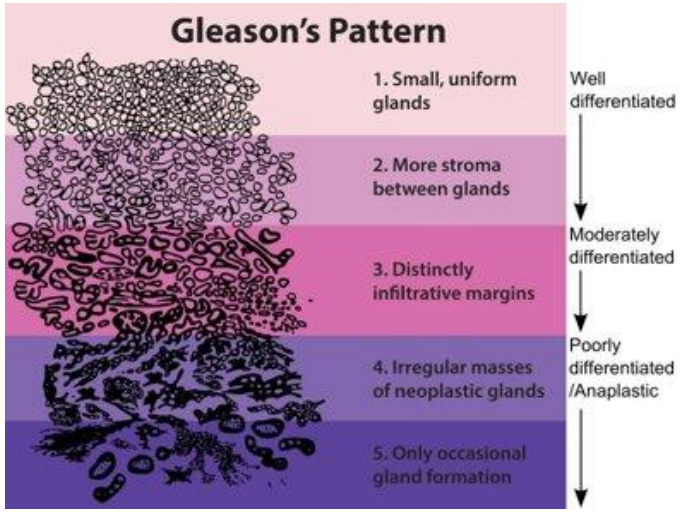
- Prostate MRI
  - PI-RADS scoring system of visible lesions helps determine *risk* of a significant prostate cancer being present
    - PI-RADS 3 = 50% risk
    - PI-RADS 4 = 80% risk
    - PI-RADS 5 = 90-100% risk
- Prostate needle biopsy
  - MRI-fusion biopsy (targeted) vs “standard” 12-core template biopsy
    - Trans-rectal and Trans-perineal
    - I exclusively offer trans-perineal option (significantly less infection risk - sepsis)
    - Tissue from biopsy often sent for additional genetic and/or tumor biology testing
      - Prolaris, Decipher, Oncotype

GLEASON GRADING SYSTEM

- When prostate cancer cells are found in the tissue from biopsy, the pathologist "grades" it (scale of 1 to 5) to measure how quickly the cells are likely to grow and spread (aggressiveness) using the Gleason Grading System

Gleason Score

- Combines the <u>two</u> most common grades found in biopsy samples and develops a **score** which ranges from 6-10
- Looks at how much the cells differ from normal prostate tissue
- A score of grades 3+3=6 suggests a slow growing cancer
- A score of grades 5+5=10 suggests an extremely aggressive cancer



Gleason Score

Risk Groups

- The Gleason score *helps* determine if the cancer is a low, intermediate, or high-risk disease
- Cancers in the lower risk groups have a smaller chance of growing and metastasizing compared to higher risk groups

- Gleason 6: Low risk
- Gleason 7: Intermediate (favorable vs unfavorable) risk
  - 3+4 – favorable
  - 4+3 - unfavorable
- Gleason 8-10: High/very high risk

Other factors which influence behavior/decision-making: multiple positive cores, cancer on both sides of prostate, high PSA, family hx

Grade Group

ISUP Prostate Cancer Grade Groups

Grade group	Gleason score	Gleason pattern
1	≤6	≤3+3
2	7	3+4
3	7	4+3
4	8	4+4, 3+5, 5+3
5	9 or 10	4+5, 5+4, or 5+5

INITIAL RISK STRATIFICATION AND STAGING WORKUP FOR CLINICALLY LOCALIZED DISEASE[e]

Risk Group	Clinical/Pathologic Features (See Staging (ST-1))			Additional Evaluation[h,i]	Initial Therapy
Very low[f]	Has all of the following: • cT1c • Grade Group 1 • PSA <10 ng/mL • Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core[g] • PSA density <0.15 ng/mL/g			• Confirmatory testing can be used to assess the appropriateness of active surveillance (See PROS-F 2 of 5)	See PROS-3
Low[f]	Has all of the following but does not qualify for very low risk: • cT1–cT2a • Grade Group 1 • PSA <10 ng/mL			• Confirmatory testing can be used to assess the appropriateness of active surveillance (See PROS-F 2 of 5)	See PROS-4
Intermediate[f]	Has all of the following: • No high-risk group features • No very-high-risk group features • Has one or more intermediate risk factors (IRFs): ▸ cT2b–cT2c ▸ Grade Group 2 or 3 ▸ PSA 10–20 ng/mL	Favorable intermediate	Has all of the following: • 1 IRF • Grade Group 1 or 2 • <50% biopsy cores positive (eg, <6 of 12 cores)[g]	• Confirmatory testing can be used to assess the appropriateness of active surveillance (See PROS-F 2 of 5)	See PROS-5
		Unfavorable intermediate	Has one or more of the following: • 2 or 3 IRFs • Grade Group 3 • ≥ 50% biopsy cores positive (eg, ≥ 6 of 12 cores)[g]	Bone and soft tissue imaging[j,k] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-6
High	Has no very-high-risk features and has exactly one high-risk feature: • cT3a OR • Grade Group 4 or Grade Group 5 OR • PSA >20 ng/mL			Bone and soft tissue imaging[j,k] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-7
Very high	Has at least one of the following: • cT3b–cT4 • Primary Gleason pattern 5 • 2 or 3 high-risk features • >4 cores with Grade Group 4 or 5			Bone and soft tissue imaging[j,k] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-7

See Footnotes for Initial Risk Stratification and Staging Workup for Clinically Localized Disease (PROS-2A).

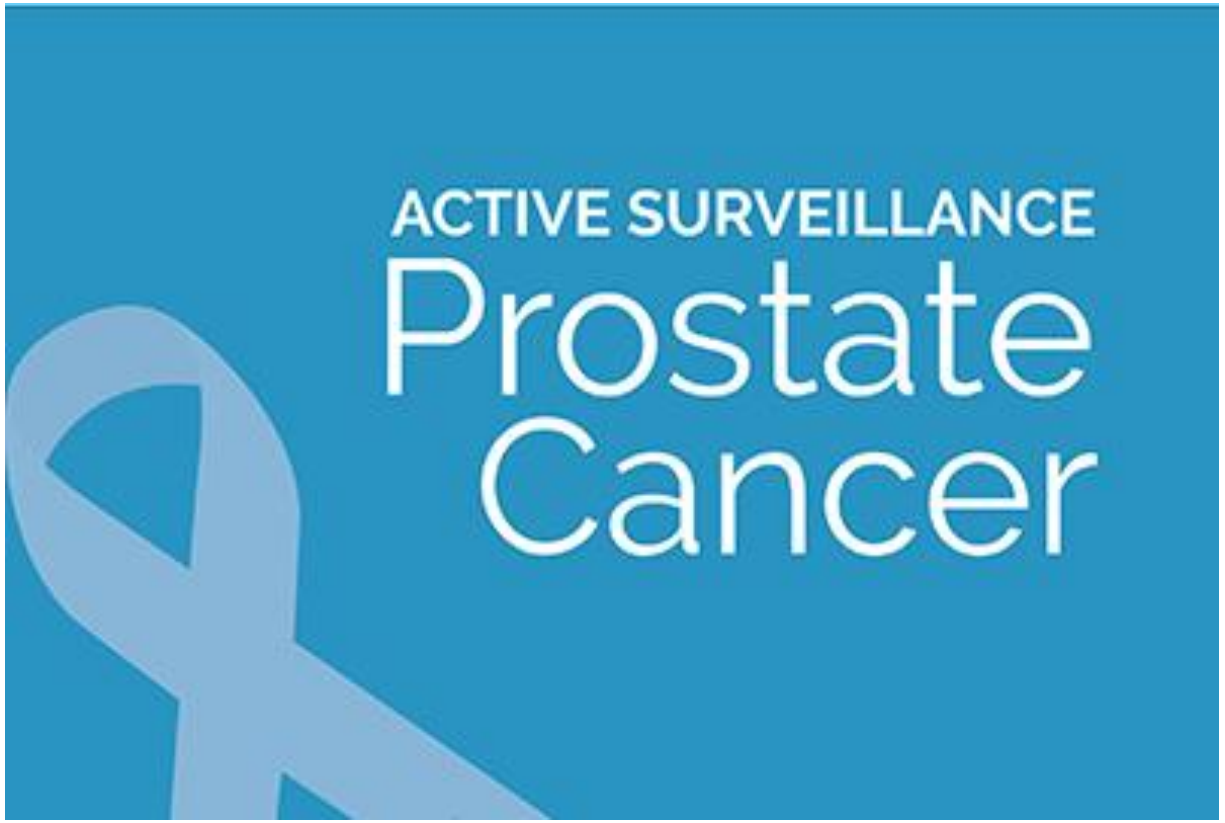
Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Genomic Tests

- Help decision-making – prognostication, guide treatment decisions
  - 10 year prostate CA-specific survival
  - Risk of metastasis at 5 and 10 years

- Prolaris
  - 46 genes
- Decipher
  - 22 genes
- Oncotype
  - 17 genes
  - Candidacy for active surveillance

Active Surveillance



What is it?

Active surveillance as a form of treatment for prostate cancer and it is not the same as having no treatment.

Best candidates?

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2023
Prostate Cancer

1. Preferred in patients with low-risk disease and very low risk disease who are expected to live more than >10 years
    - low risk is heterogeneous and genomic risk is important in addition to a number of cores positive
2. An option for patients with favorable intermediate risk disease with a life expectancy greater than 10 years
    - genomic tests very helpful in these cases

Risk Group	Clinical/Pathologic Features See Staging (ST-1)		
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Low[f]	Has all of the following but does not qualify for very low risk: • cT1–cT2a • Grade Group 1 • PSA <10 ng/mL		
Intermediate[f]	Has all of the following: • No high-risk group features • No very-high-risk group features • Has one or more intermediate risk factors (IRFs): ▸ cT2b–cT2c ▸ Grade Group 2 or 3 ▸ PSA 10–20 ng/mL	Favorable intermediate	Has all of the following: • 1 IRF • Grade Group 1 or 2 • <50% biopsy cores positive (eg, <6 of 12 cores)[g]
		Unfavorable intermediate	Has one or more of the following: • 2 or 3 IRFs • Grade Group 3 • ≥ 50% biopsy cores positive (eg, ≥ 6 of 12 cores)[g]

NCCN Protocol (example)

- **Active Surveillance Program:**
  - **Patients who choose active surveillance should have regular follow-up, and key principles include:**
    - **PSA no more often than every 6 months unless clinically indicated.**
    - **DRE no more often than every 12 months unless clinically indicated.**
    - **Repeat prostate biopsy no more often than every 12 months unless clinically indicated. While the intensity of surveillance may be tailored on an individual basis, most patients should have prostate biopsies incorporated as part of their monitoring.**
    - **Consider repeat mpMRI no more often than every 12 months unless clinically indicated.**
    - **In patients with a suspicious lesion on mpMRI, MRI-ultrasound fusion biopsy improves the detection of higher grade (Grade Group ≥2) cancers.**
    - **Patients should be transitioned to observation when life expectancy is <10 years.**
    - **Repeat molecular tumor analysis is discouraged.**
    - **The intensity of surveillance may be tailored based on patient life expectancy and risk of reclassification.**

- ASCO, ESTRO, AUA, ASTRO all have there own protocols (slight variation)

When to transition to treatment?

1. Patient choice (anxiety)
2. Grade reclassification on biopsy
3. PSA rate of rise or other characteristics
4. Increased tumor volume

ORIGINAL ARTICLE

10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer

F.C. Hamdy, J.L. Donovan, J.A. Lane, M. Mason, C. Metcalfe, P. Holding, M. Davis, T.J. Peters, E.L. Turner, R.M. Martin, J. Oxley, M. Robinson, J. Staffurth, E. Walsh, P. Bollina, J. Catto, A. Doble, A. Doherty, D. Gillatt, R. Kockelbergh, H. Kynaston, A. Paul, P. Powell, S. Prescott, D.J. Rosario, E. Rowe, and D.E. Neal, for the ProtecT Study Group*

ABSTRACT

Prostate cancer-specific deaths

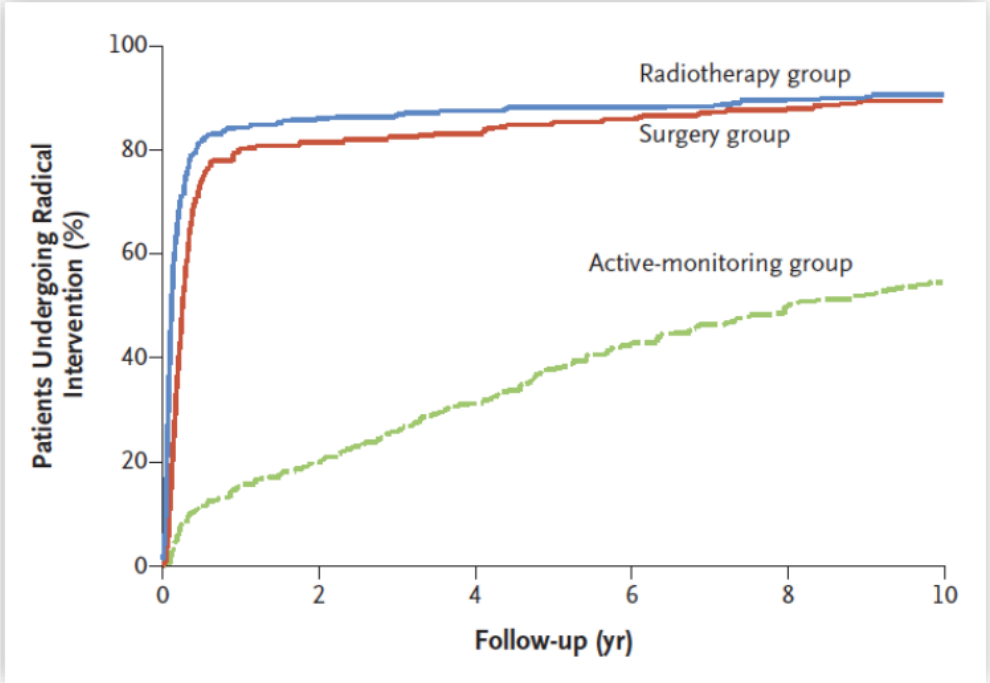
NHS National Institute for Health Research

Variable	Active Monitoring N=545	Surgery N=553	Radiotherapy N=545	P value
PCa mortality	8	5	4	
Pca survival % (95% CI)				
At 5 years	99.4 (98.3-99.8)	100	100	
At 10 years	98.8 (97.4-99.5)	99.0 (97.2-99.6)	99.6 (98.4-99.9)	
Pca deaths per 1000 person-yr (95% CI)	1.5 (0.7-3.0)	0.9 (0.4-2.2)	0.7 (0.3-2.0)	0.48

Patients receiving treatments

NHS National Institute for Health Research

Hamdy et al, N Eng J Med 2016



- Approximately 80% of men on active monitoring had no sign of progression
- More than half had received treatment by 10 years
- 44% of men on active monitoring avoided treatment

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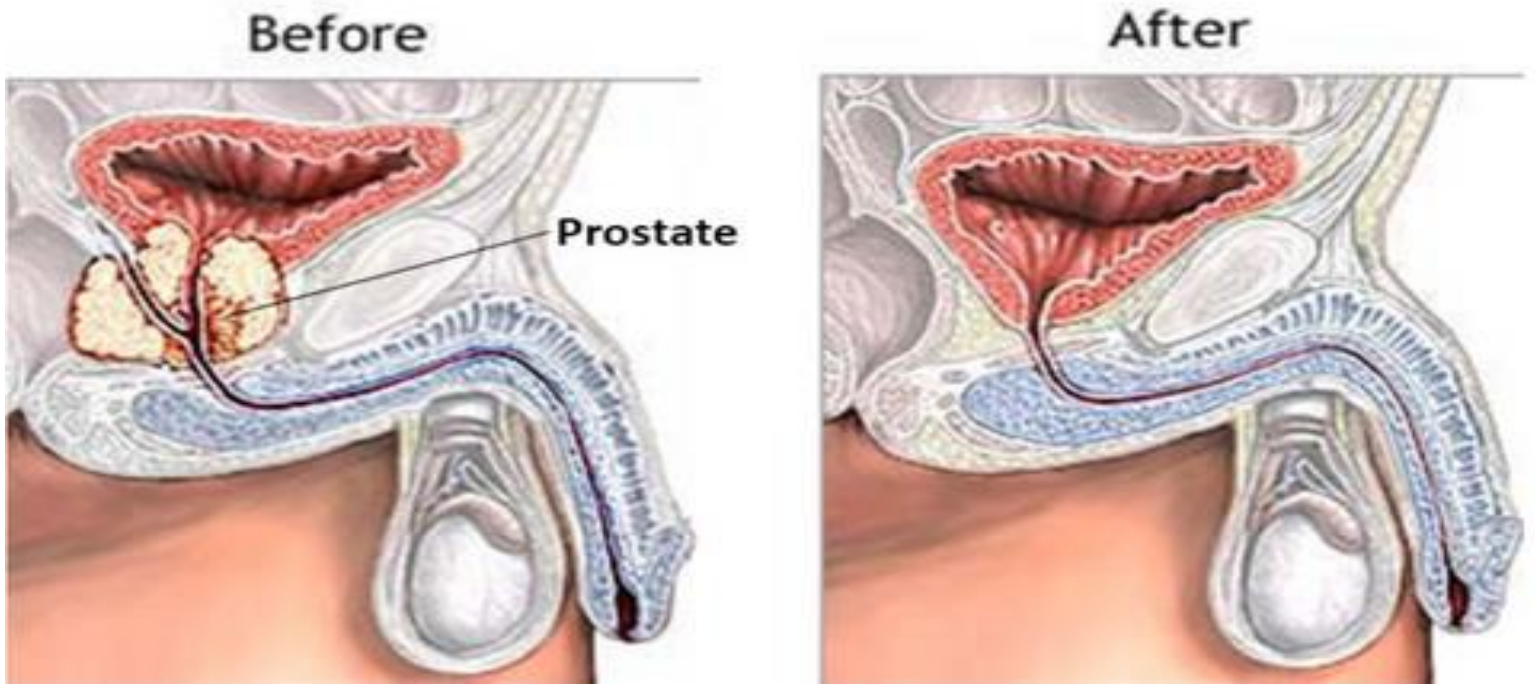
Surgical Management of Prostate Cancer

- Goal: Curative intent
- Removal of the entire prostate gland with overlying fat, seminal vesicles, and +/- pelvic lymph nodes
- Indications
  - Localized Cancer
  - Life expectancy of 10 or more years (age alone not a determinant)
  - No other serious health conditions
- Open vs minimally invasive
  - Minimally invasive, robotic-assisted has become standard
  - Incisions on the abdomen
- Overnight hospital stay
- Catheter for 7-10 days
- Routine follow up w/ PSA checks
  - PSA expected to go to 0 post-surgery

Surgical Management of Prostate Cancer: Radical Prostatectomy

- Removal of the entire prostate with attached seminal vesicles
  - Nerve-sparing and non-nerve sparing approaches
- Suturing the bladder opening back to the urethra
- Regional lymph nodes may also be removed



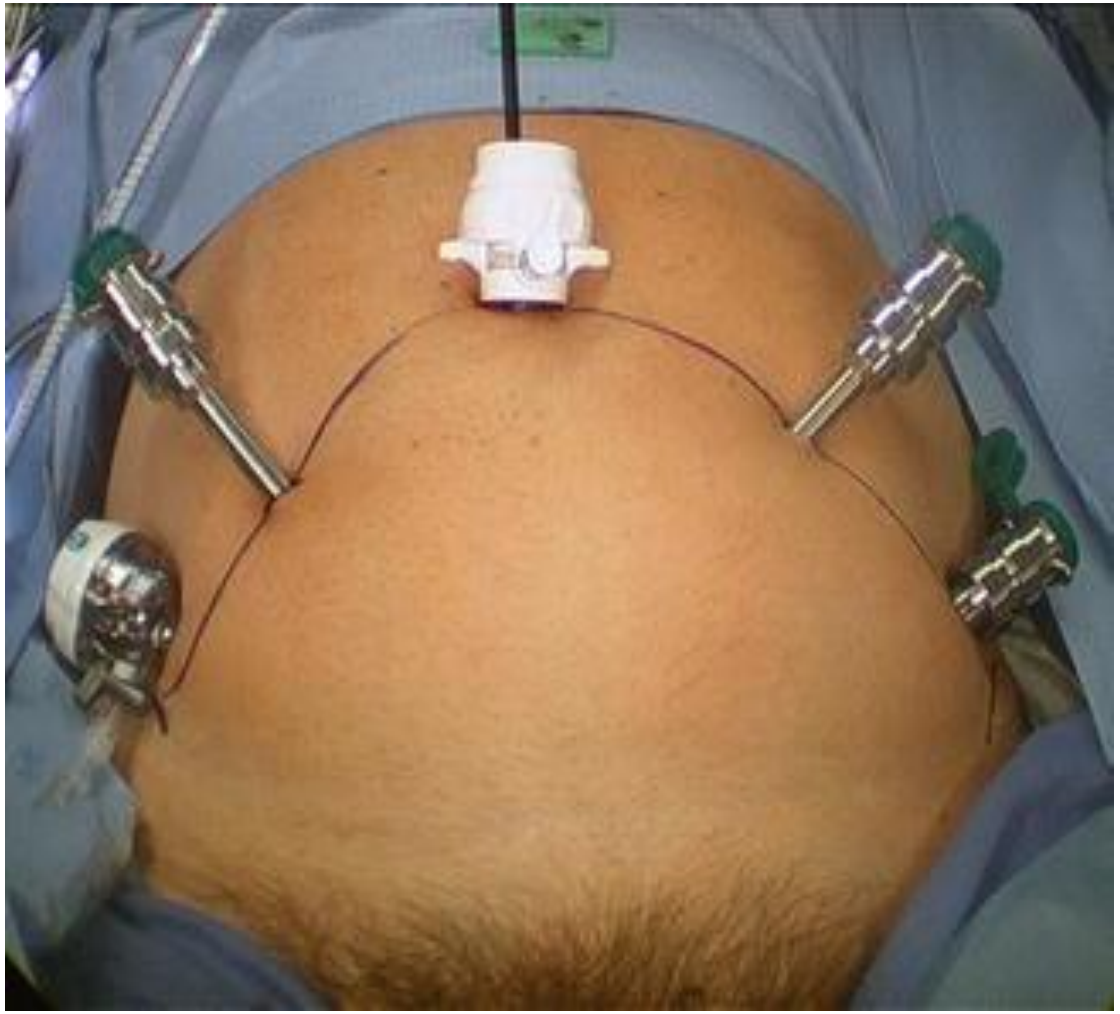
Robotic-Assisted Laparoscopic Radical Prostatectomy (RALRP)

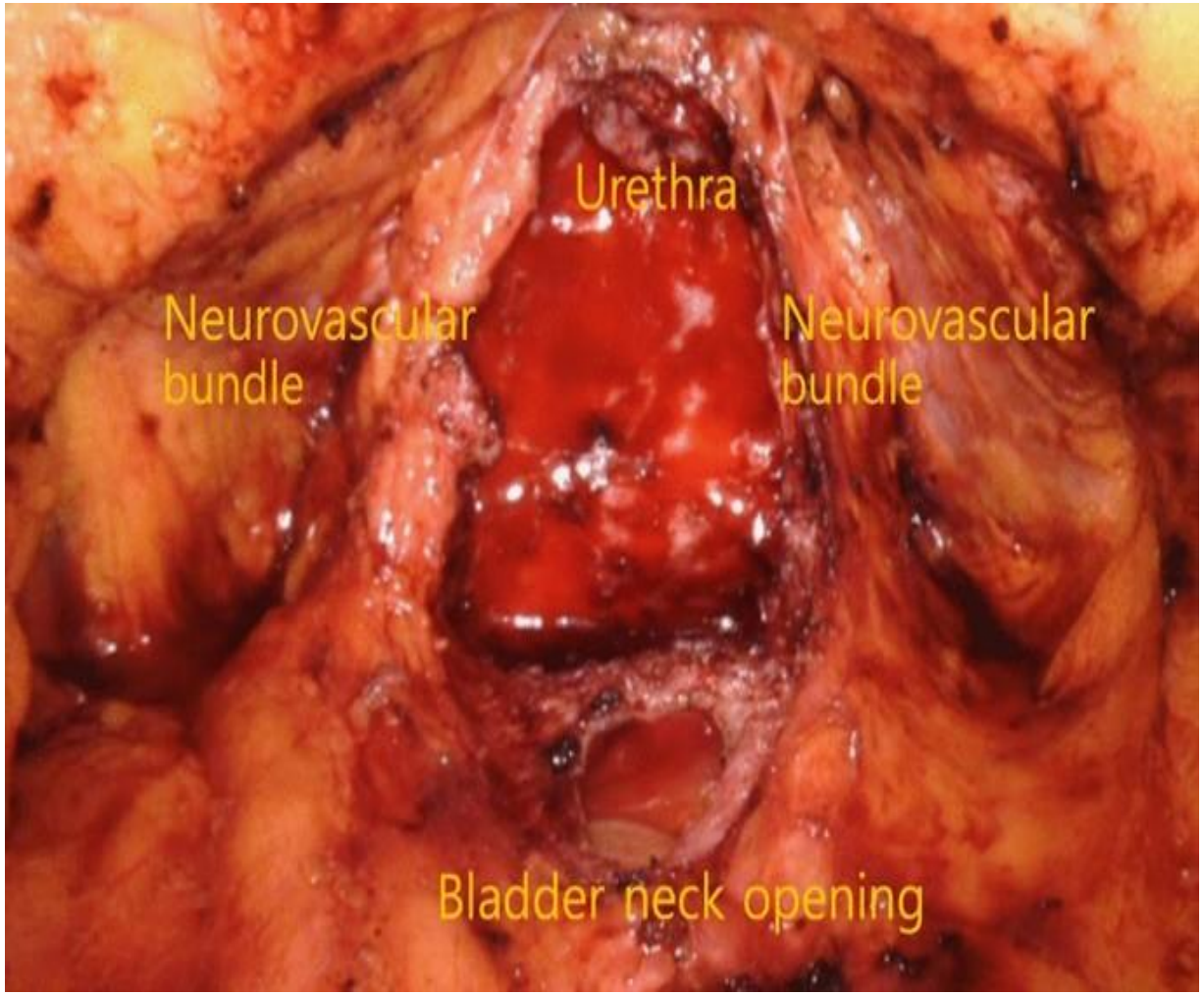
- Da Vinci surgical system (Intuitive Surgical)

Advantages of Robotic-Assisted Surgery

- Significant reductions in:
  - Pain and narcotic use
    - Many patients do not use anything more than Tylenol and Ibuprofen
  - Hospital stay
  - Bleeding
  - Time off work

- Improved control of urine leakage and return of sexual function




Urethra
Neurovascular bundle
Neurovascular bundle
Bladder neck opening

Side Effects of Radical Prostatectomy

All men will have these side effects initially

Stress Urinary Incontinence

- Leaking urine with activity: cough, laugh, sneeze, lifting
  - Requires adult diapers and pads
- Usually improves within a few months.
- **<u><5% still have significant beyond one year</u>**
- KEGEL exercises:
  - Begin prior to surgery and resume once catheter removed
- Pelvic Floor PT/OT pre and post op
- Options for the minority of men who are unable to get dry: clamps, surgery

Erectile Dysfunction

- Recovery depends on multiple factors:
  - Baseline erectile function (poor function prior to surgery will not improve post-surgery)
  - Age and underlying health issues: diabetes, high blood pressure, cardiac disease
  - Nerve-sparing vs Non-nerve-sparing
- Start Cialis post-op to improve blood and oxygen to penis to help restore nerve function and prevent scarring
- Can take up to 2-2.5 years for full recovery
- Oral medications, Injections, Vacuum Erectile Device (VED), prosthetics
- Important to have discussions with partner ahead of time to be prepared

Post-Radical Prostatectomy

- Return to work 2-6 weeks post-surgery depending upon job
- PSA 6 weeks after surgery (expected to be 0)
  - Every 3 months for 1st year
  - Every 6 months 2nd year
  - Annually