University Health Network

UPDATE ON PROSTATE CANCER DIAGNOSIS

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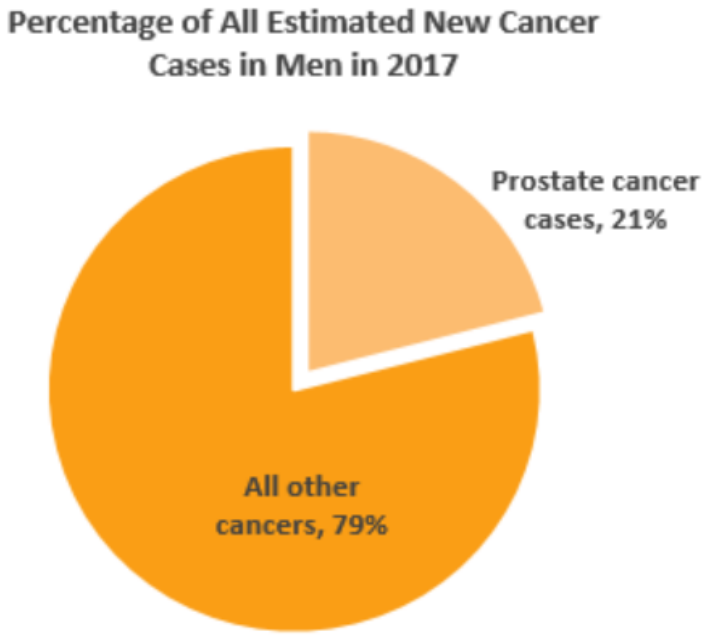
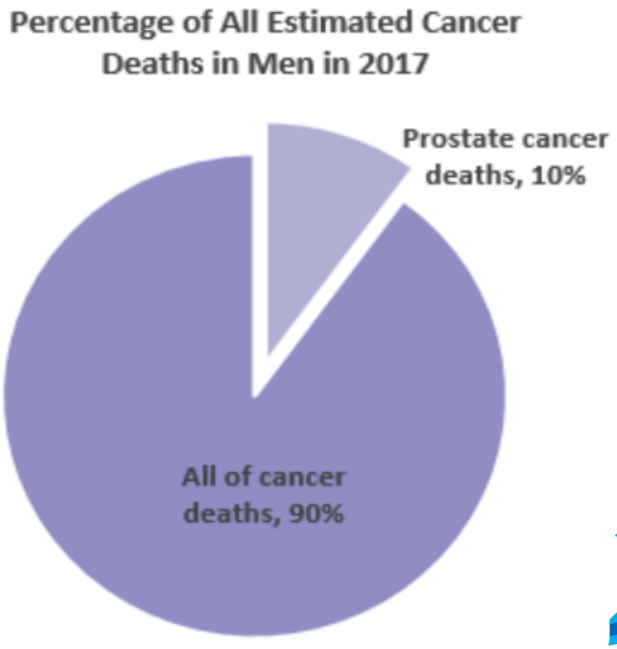
Tuesday May 22, 2018

Prostate cancer statistics

- Excluding skin cancer, prostate cancer (PCa) is the **most common cancer among Canadian and American men.**
- On average, **58 Canadian men will be diagnosed** with PCa every day.
- On average, **11 Canadian men will die** from PCa every day.

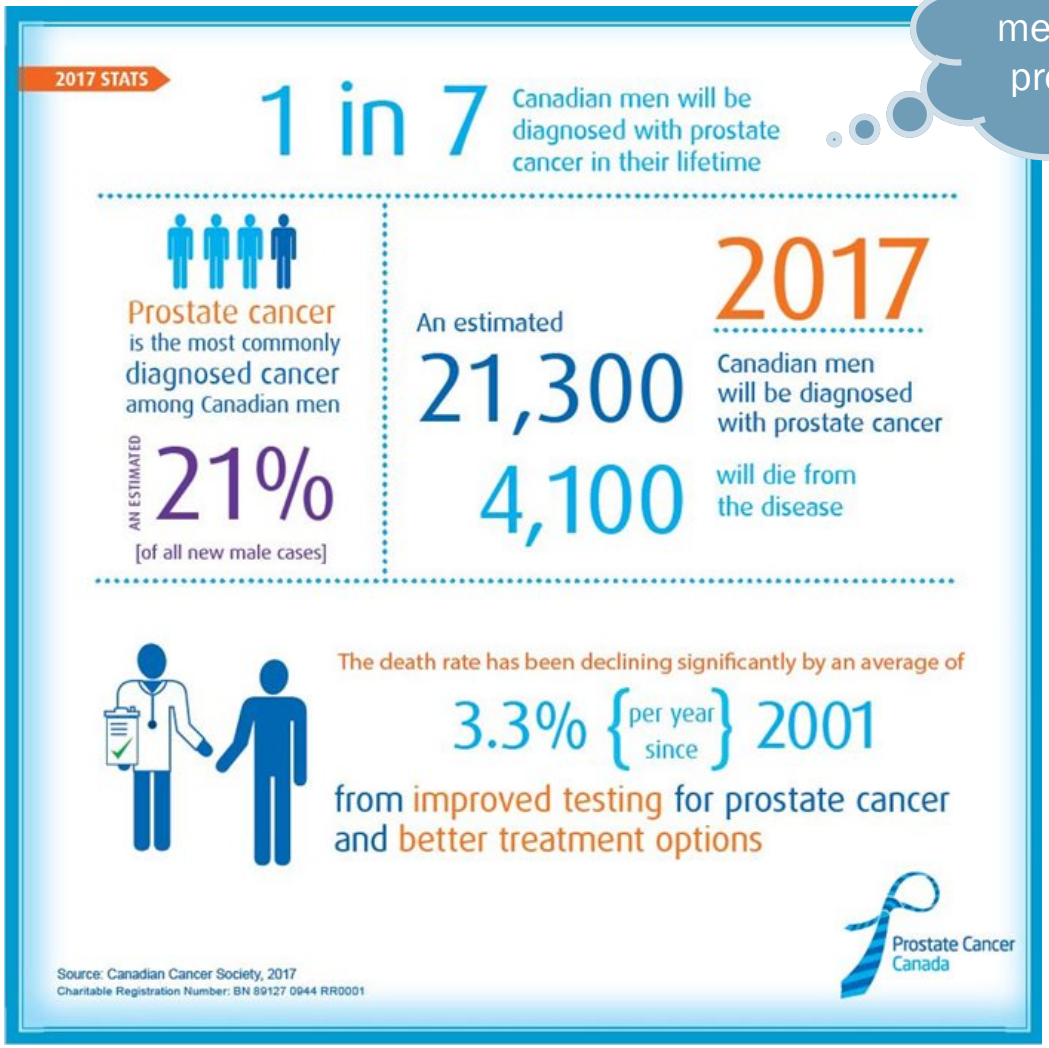




Prostate Cancer Canada

Lifetime risk of prostate cancer

1 in 29 Canadian men will die from prostate cancer

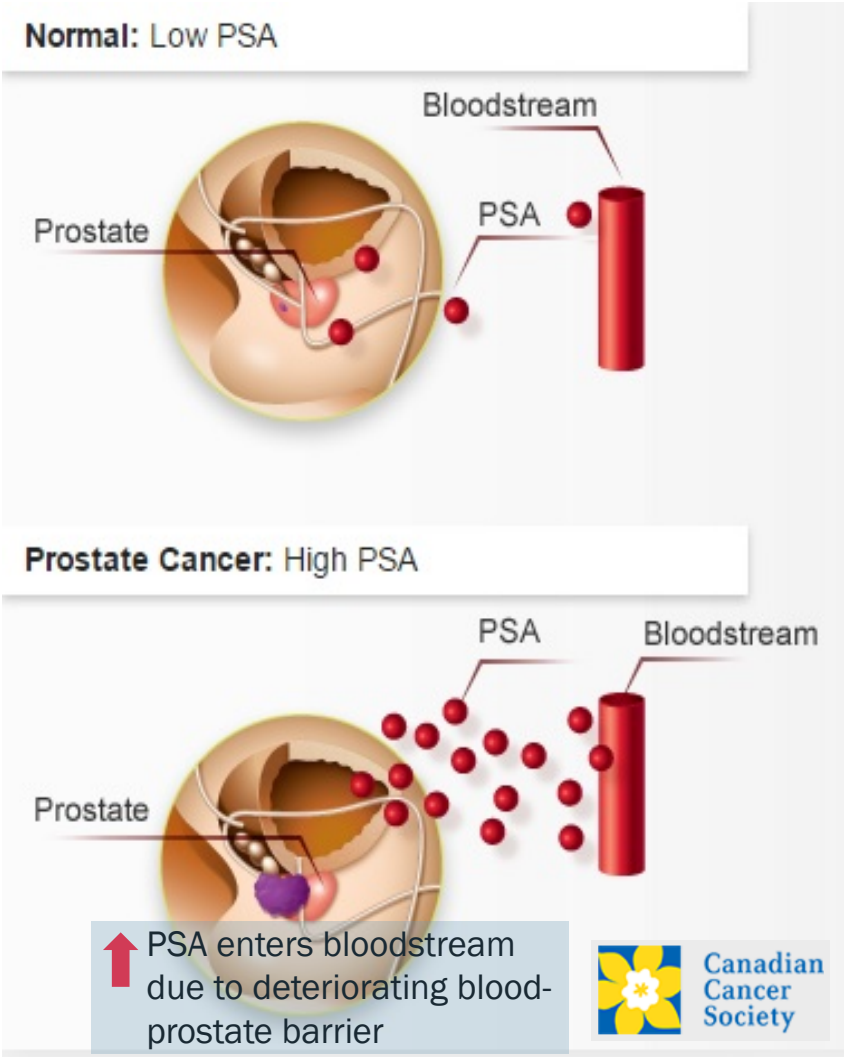


Prostate Cancer Canada

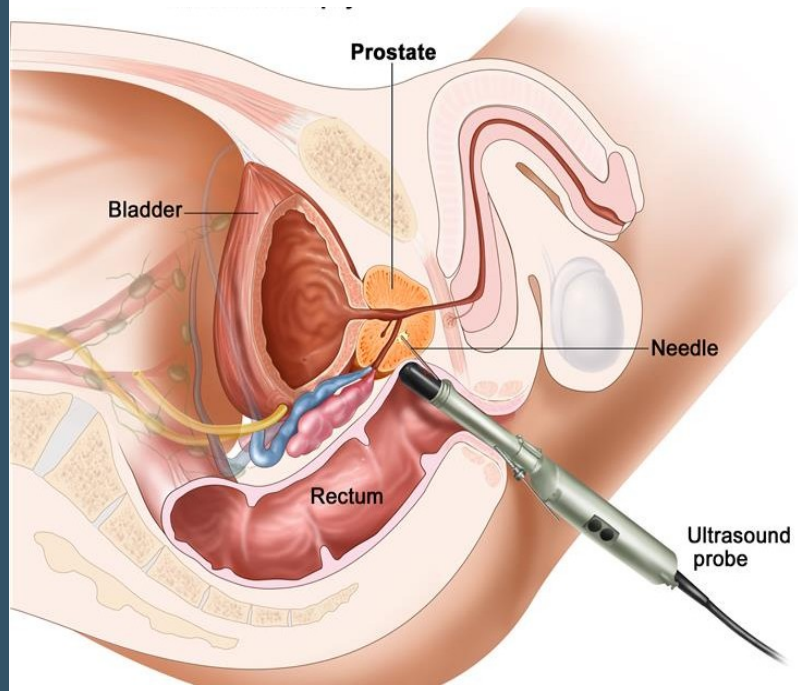
Screening for prostate cancer

- The prostate specific antigen (PSA) is made by prostate cells.
- The PSA test measures the amount of PSA in the blood and is often used with digital rectal exam (DRE) to improve chances of catching PCa early.
- Some may benefit from a PSA test: Men older than 50 years with:
  - *Personal risk of PCa (family history or are of African ancestry)*
  - *Symptoms of PCa (Difficult urinating, burning/pain during urination, blood in urine etc.)*

Blood PSA level of less than 4ng/mL is considered normal



Interpreting results from the PSA test is tricky



Prostate biopsy

- The lack of specificity of PSA test leads to over-diagnosis, over-treatment and the reliance on prostate biopsies.
- About 250,000 men in North America undergo unnecessary prostate biopsies a year.
- Up to 4% of men develop infections that require hospital care after a biopsy. **That is 10,000 men who did not need a biopsy in the first place.**

Indolent PCa → **Active surveillance program**

Yearly biopsies determine progression

Aggressive PCa → **Treatment**

Clinical case discussion

- A sexually active 66 year-old man presenting with the following symptoms:
  - *Mild lower urinary tract symptoms*
  - *Difficulty urination*
  - *Pain during urination*
  - *Frequent urinary infections*
- Family history: Father was diagnosed with intermediate-risk PCa at age 72 and underwent radiation therapy with no recurrence
- Medical comorbidity: Treatment for hypertension (β-blocker). No previous surgeries.

How would you proceed as a primary care physician?

Check for benign prostate hyperplasia, urinary tract infection, PSA levels?

Alberto Briganti (2005). European Urology Focus. 207-211

Clinical case discussion

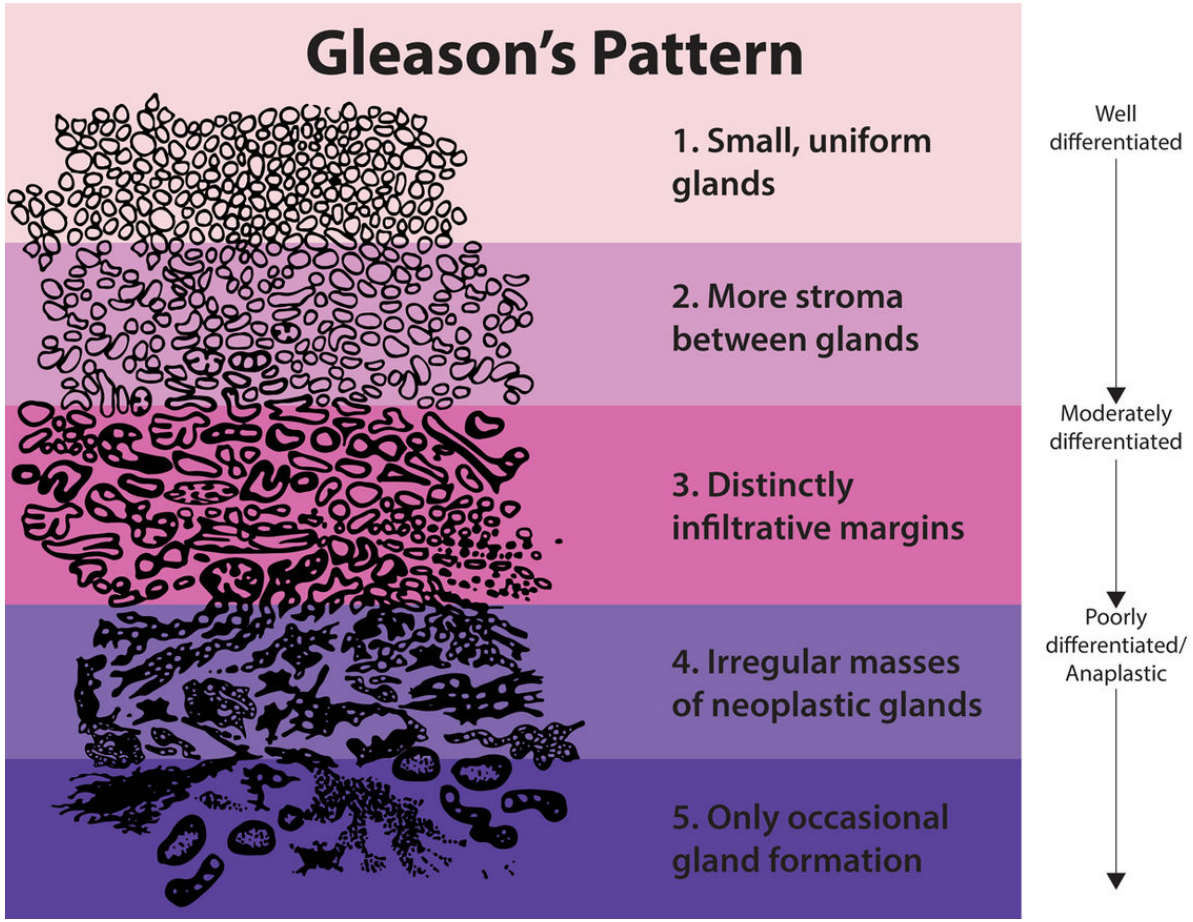
- PSA results: 6.5ng/ml
- DRE revealed no palpable nodules.
- An 18-core transrectal ultrasound (TRUS)-guided prostate biopsy was performed under local anaesthesia.
  - *Presence of adenocarcinoma of the prostate in one core from the right lobe. The tumour was Gleason score (GS) 3 + 4.*

Does this man with low prostate-specific antigen (PSA) density and a single core of GS 3 + 4 PCa require immediate treatment?

Alberto Briganti (2005). European Urology Focus. 207-211

Gleason Score

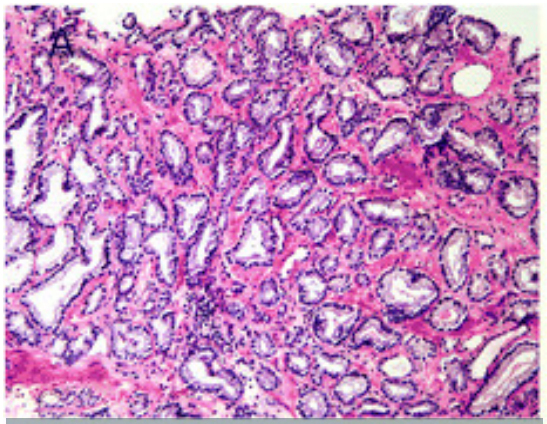
- Gleason Score (GS) is the grading system used to determine the aggressiveness of PCa.
- Describes how much of a biopsy looks like healthy tissue (lower score) or abnormal tissue (higher score).
  - *Most cancers score a grade of 3 or higher.*
- Two grades are assigned for each patient:
  - *Primary grade = cells that make up the largest area of the tumor.*
  - *Secondary grade = cells of the next largest area.*



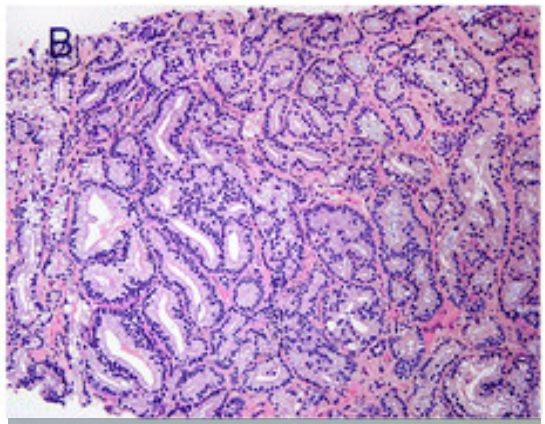
Journal of Imaging

Gleason Score

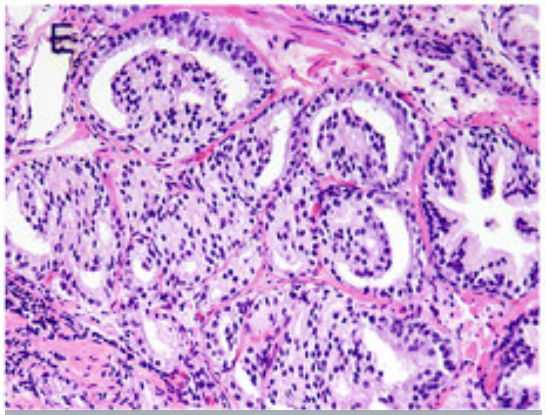
- Higher GS = more likely cancer will grow and spread quickly.
- GS 6 = cancer cells that look similar to normal cells, likely to grow slowly.
- GS 7 = intermediate risk for aggressive cancer. Tumours with 3 + 4 have a fairly good outlook, whereas 4 + 3 are more likely to grow and spread.
- GS $\geq$ 8 = cancer likely to spread more rapidly, often referred to as poorly differentiated or high grade.



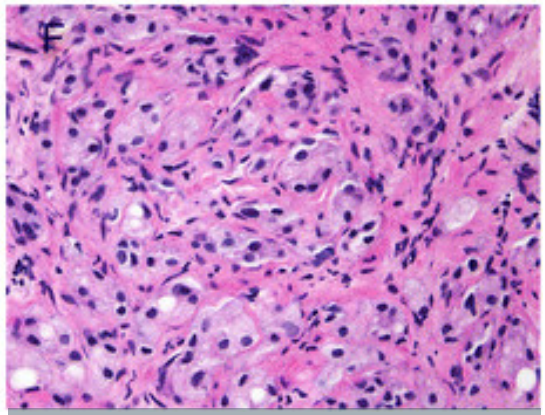
GS 3 + 3 = 6



GS 3 + 4 = 7 (minor component of cribriform glands)



GS 4 + 4 = 8 (glomeruloid glands)

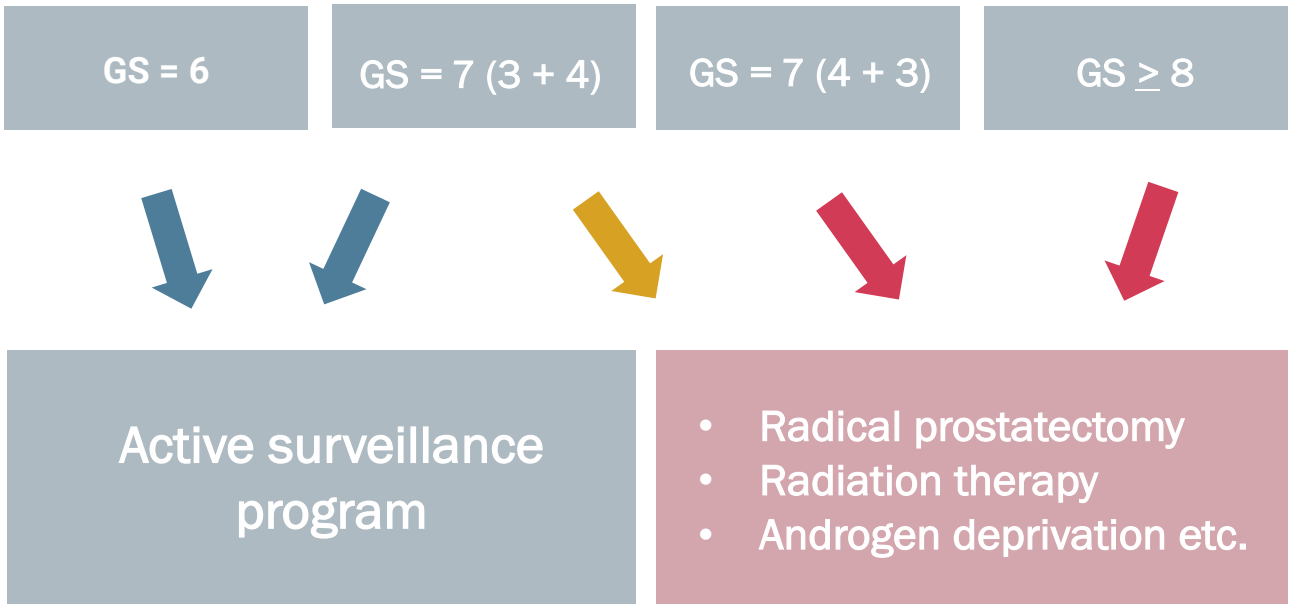


GS 4+ 4 = 8 (poorly-formed glands)

Gordetsky J, and Epstein J (2016). Diagnostic Pathology. 11(1)

Treatment options

- GS grading system can be used to choose appropriate treatment options



Clinical case discussion

Back to the question regarding the patient in our case study:

- PSA results: 6.5ng/ml
- DRE revealed no palpable nodules.
- Presence of adenocarcinoma of the prostate in one core from the right lobe. The tumour was GS 3 + 4.

Does this man with low prostate-specific antigen (PSA) density and a single core of Gleason 3 + 4 PCa require immediate treatment?

Alberto Briganti (2005). European Urology Focus. 207-211

Clinical case discussion

- Discussion with patient that (immediate) radical treatment may affect:
  - *Urinary function (ie, incontinence)*
  - *Sexual function (ie, impotence)*
  - *These conditions reduce quality of life (may be temporary vs lifelong)*
- Low PSA density with a low % of biopsy core involvement associated with lower rates of progression. → May benefit from active surveillance (AS).
- Some AS protocols encourage an early repeat or ‘‘confirmatory’’ biopsy.
  - *Up to 30% of men are found to have higher risk disease features for which immediate treatment may be more appropriate.*

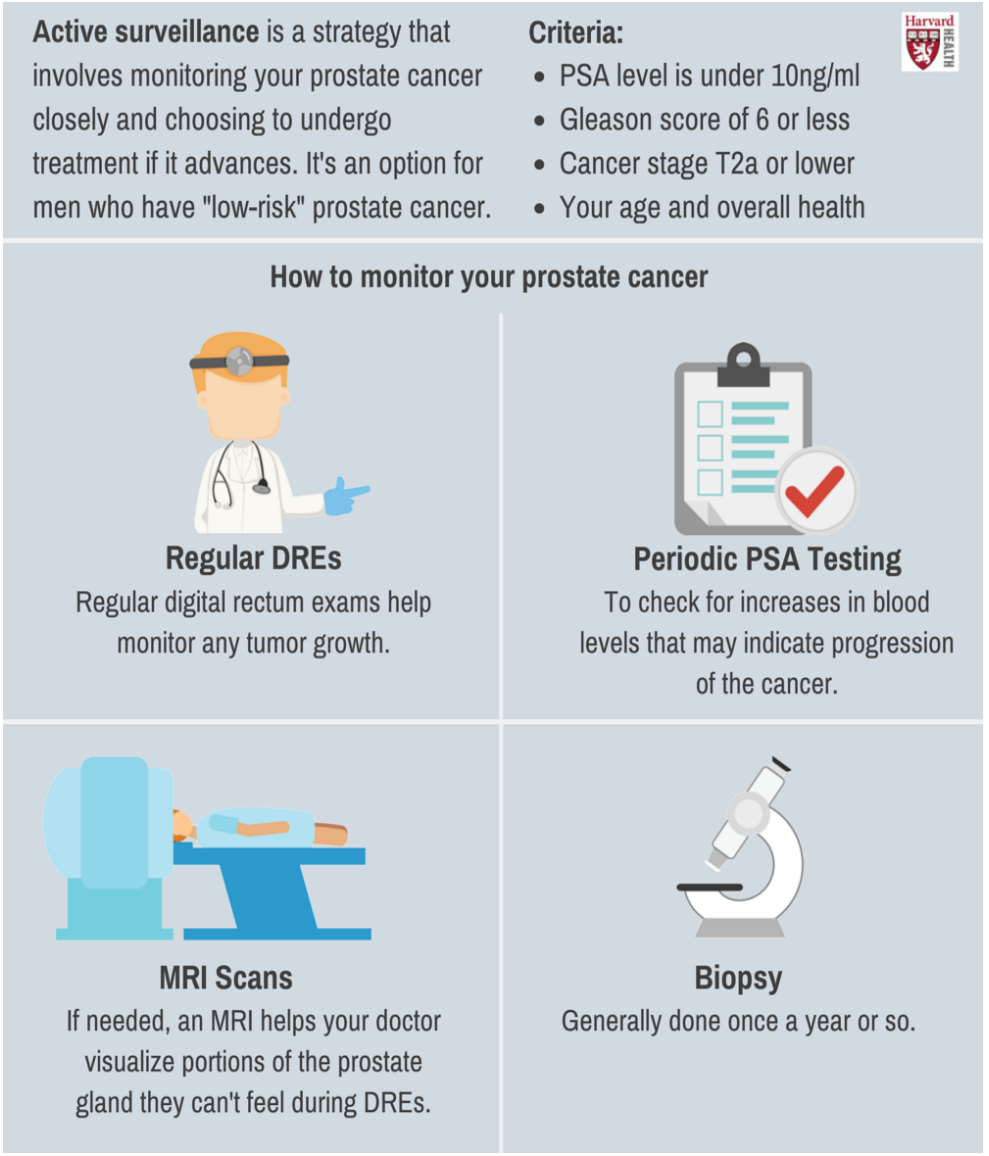
Alberto Briganti (2005). European Urology Focus. 207-211

Active surveillance "Watchful waiting"

- Aggressive PCa (GS = 7 (4+3) or ≥8) must be treated immediately. However, majority of PCa tumors are found to be indolent (slow-growing, low-risk).

Patients enter an AS program

- AS involves close monitoring of slow-growing PCa.
  - *Relies on regular PSA tests, DREs, and yearly biopsies to monitor progression of disease.*

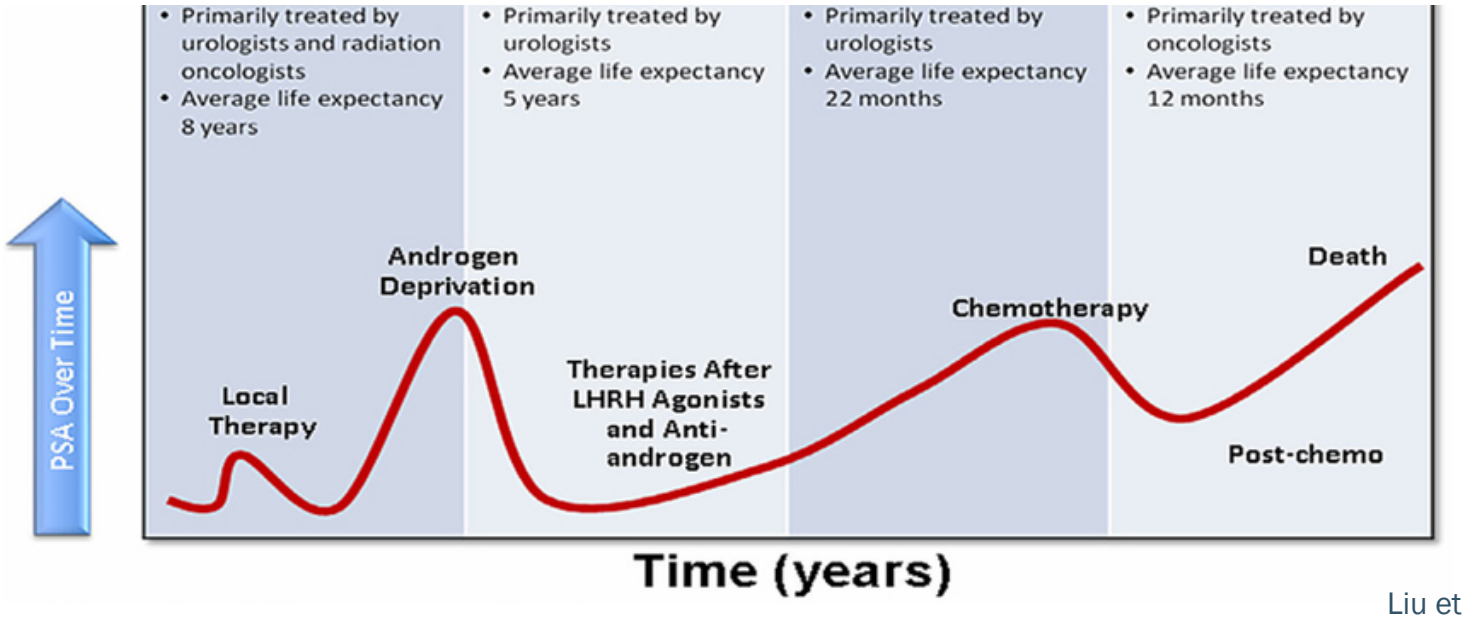


Treatment options

- Aggressive PCa (GS = 7 (4+3) or ≥8) must be treated immediately. However, majority of PCa tumors are found to be indolent (slow-growing, low-risk).

→

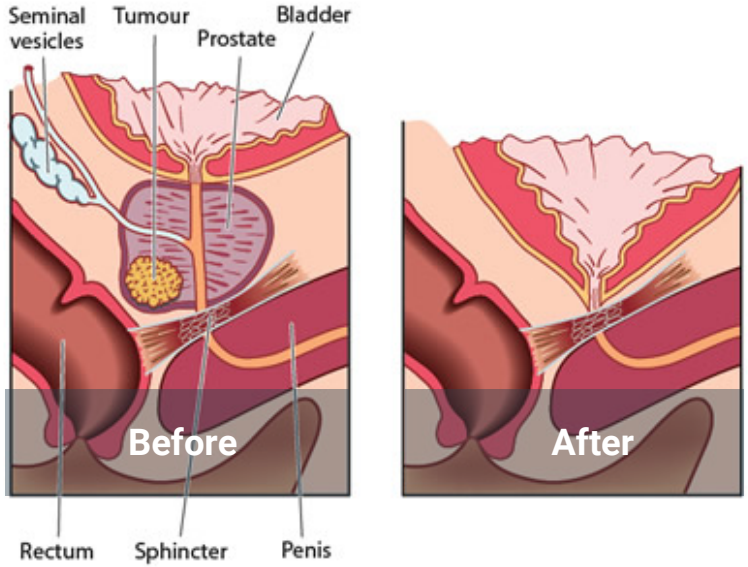
- Radical prostatectomy
- Radiation therapy
- Androgen deprivation
- Chemotherapy

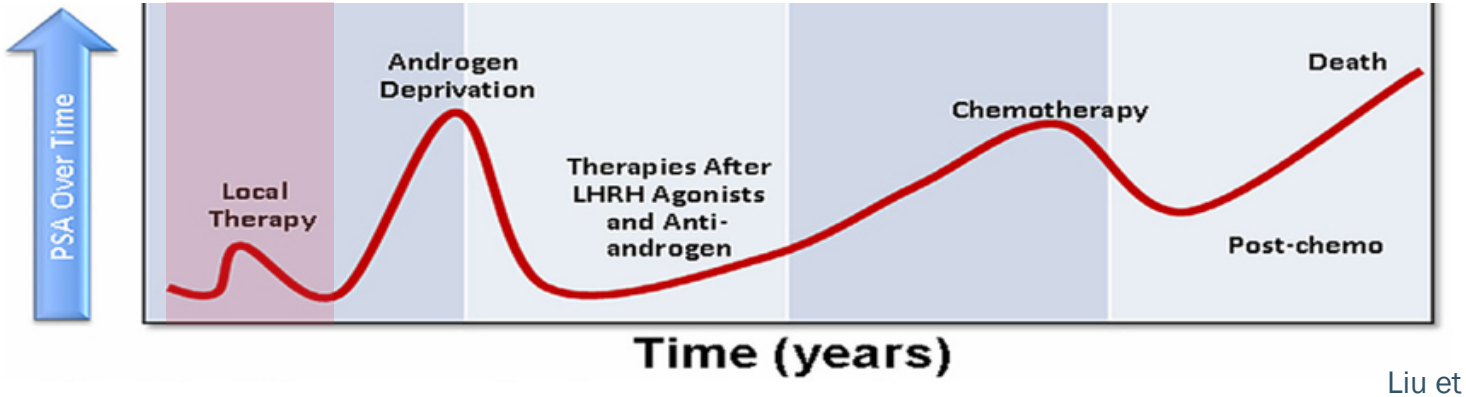


Liu et al. (2014). Biomedicine.

Radical prostatectomy

- Surgery that completely removes the prostate gland, as well as the seminal vesicles and part of the urethra within the prostate.
- Potentially removes all cancer cells.
- Recommended if cancer has not spread outside the prostate.
- May be used in combination with other treatments like radiation.





Nick Brook Urology

Liu et al. (2014). Biomedicine.

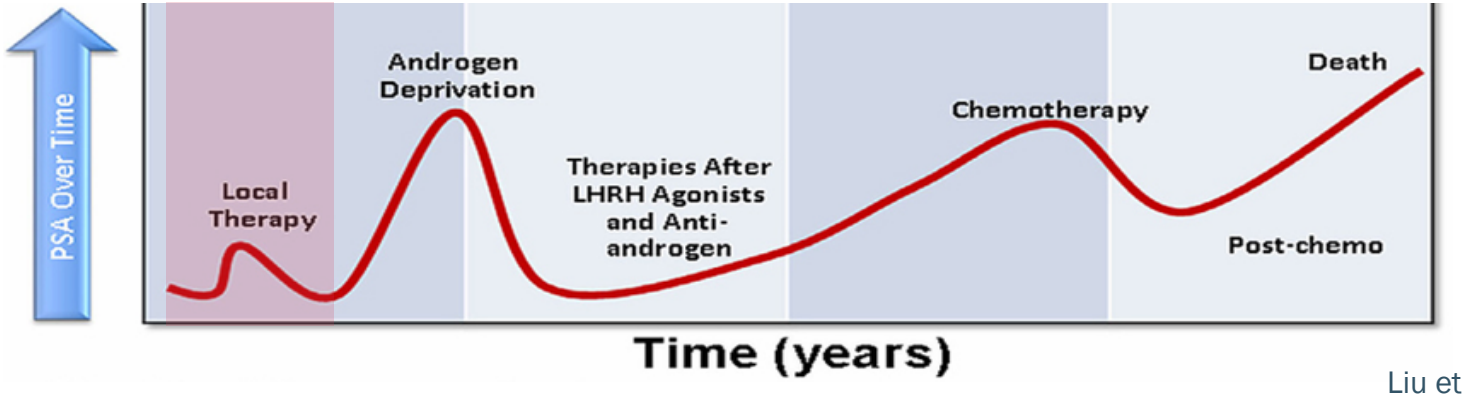
Radiation therapy

1. External Beam Radiation

- Delivers therapeutic x-rays to a localized area in order to kill cancer cells.
- May be a good option if age or general health makes surgery too risky.

2. Brachytherapy

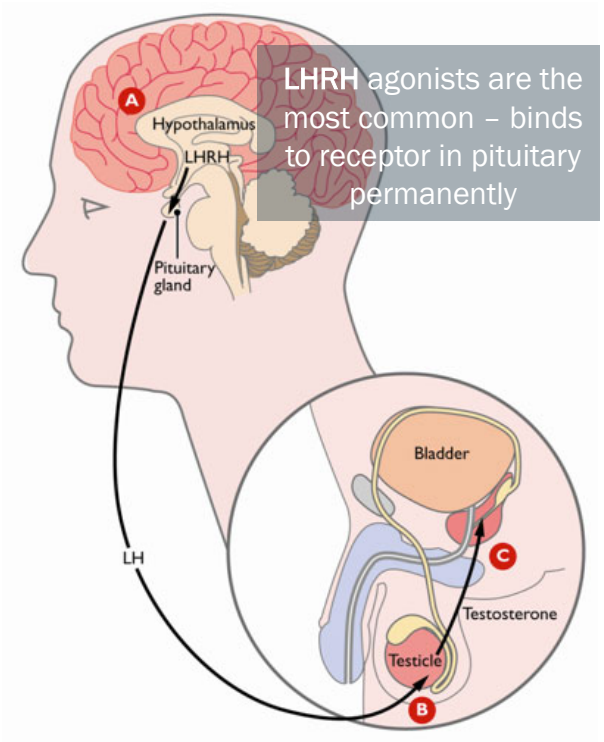
- Delivers radiation internally with either:
  - *Radioactive seeds, the size of a grain of rice, implanted directly into the prostate.*
  - *<u>For more advanced PCa:</u> Around 15 needles in the prostate, concentrating on the cancerous areas.*



Liu et al. (2014). Biomedicine.

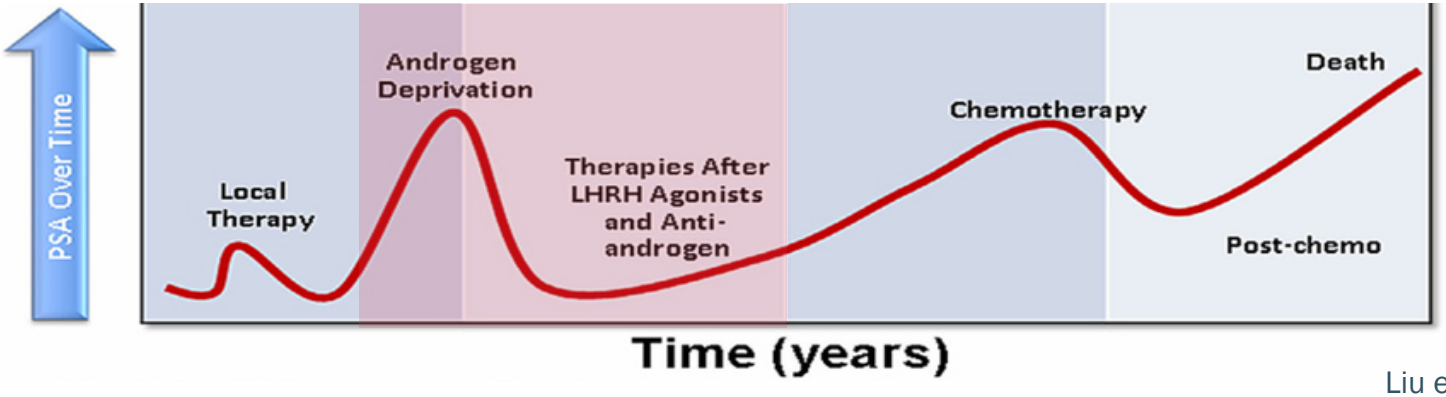
Androgen deprivation therapy (ADT)

- ADT blocks the production or effects of testosterone and other male hormones.
- ADT is most often used to treat:
  - *Cancer that has spread outside the prostate*
  - *Recurrence of PCa*
  - *Men at high risk of experiencing cancer recurrence after surgery or radiation therapy*



LHRH agonists are the most common – binds to receptor in pituitary permanently

Anti-androgen blocks binding of testosterone to receptor

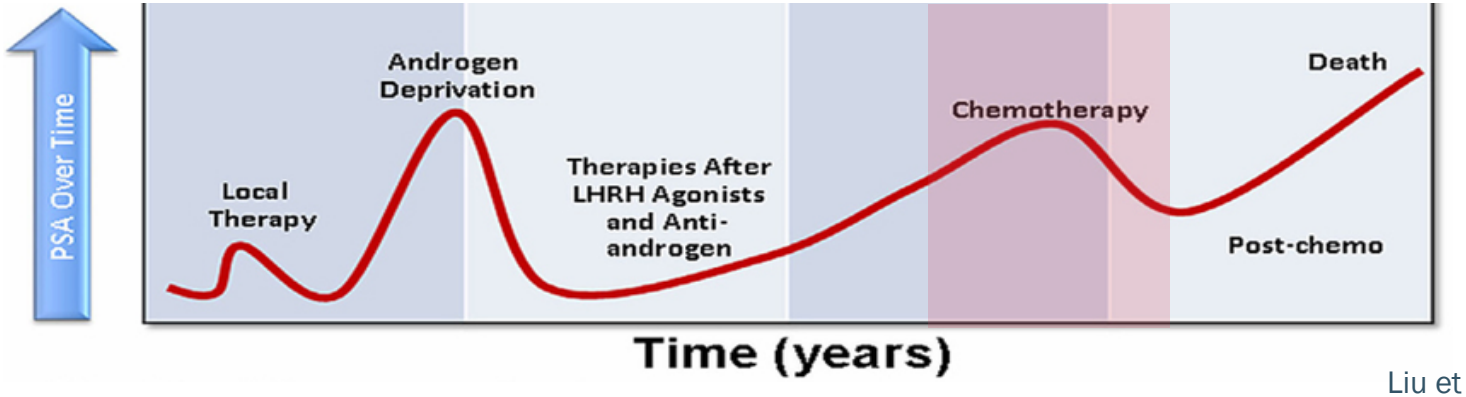


Urology WAIKATO

Liu et al. (2014). Biomedicine.

Chemotherapy

- Use of specific drugs to treat cancer.
  - *Docetaxol is usually given as an injection once every 3 weeks. It is moderately effective and shows moderate toxicity.*
- Treats recurring or metastatic PCa if hormone therapy no longer works.
- Affects both cancer cells and healthy cells.
  - *Side effects: Gastrointestinal problems, anemia, hair loss, osteoporosis, vulnerability to infection etc.*



Liu et al. (2014). Biomedicine.

Latest on prostate cancer screening

JAMA Network

Editorial

March 6, 2018

Screening for Prostate Cancer
Is the Third Trial the Charm?

Michael J. Barry, MD[1,2]

With **419, 582** men, this is by far the largest, randomized trial of PSA screening for PCa

Men diagnosed with PCa were offered randomization to radical prostatectomy, external beam radiotherapy, or AS.

At a median follow-up of 10 years, # of men diagnosed with PCa was higher in the intervention group (n = 8054; **4.3%**) than the control group (n = 7853; **3.6%**), which is about 0.65 new diagnoses per 1000 person-years

CONCLUSIONS

The results of the CAP trial[1] reported in this issue of *JAMA* do not provide compelling support for PSA screening.

Can prostate cancer screening strategies be modified to provide a better balance of benefits and risks from an individual perspective, and greater efficiency from a societal perspective? Efforts to uncouple the risk of overtreatment from the higher risk of diagnosis may help mitigate the harms of PSA screening for men who decide to be screened.

Latest on prostate cancer diagnosis

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

March 19, 2018
DOI: 10.1056/NEJMoa1801993

MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis

Veeru Kasivisvanathan, M.R.C.S., Antti S. Rannikko, Ph.D., Marcelo Borghi, M.D., Valeria Panebianco, M.D., Lance A. Mynderse, M.D., Markku H.

Undergo MRI, with or without targeted biopsy:

- 71 of 252 men (28%) had negative MRI results and did not undergo biopsy.
- PCa was detected in 95 men (38%) in the MRI-targeted biopsy group.

Multicenter, randomized trial of 500 men with suspicion of PCa

Standard transrectal ultrasonography–guided biopsy:

- 64 of 248 men (26%) found to have PCa after biopsy.

CONCLUSIONS

The use of risk assessment with MRI before biopsy and MRI-targeted biopsy was superior to standard transrectal ultrasonography–guided biopsy in men at clinical risk for prostate cancer who had not undergone biopsy previously.

Latest on prostate cancer treatment

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

April 12, 2018
N Engl J Med 2018; 378:1408-1418
DOI: 10.1056/NEJMoa1715546

Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer

Matthew R. Smith, M.D., Ph.D., Fred Saad, M.D., Simon Chowdhury, M.B., B.S., Ph.D., Stéphane Oudard, M.D., Ph.D., Boris A. Hadaschik, M.D., Julie

806 men in the apalutamide (competitive inhibitor of androgen receptor) group:
- 240 mg per day
- Continued ADT
- Median metastasis-free survival (detection of distant metastasis on imaging or death): **40.5 months**

Double-blind, placebo-controlled, phase 3 trial with **1207** men with nonmetastatic castration-resistant PCa and a PSA doubling time of ≤10 months

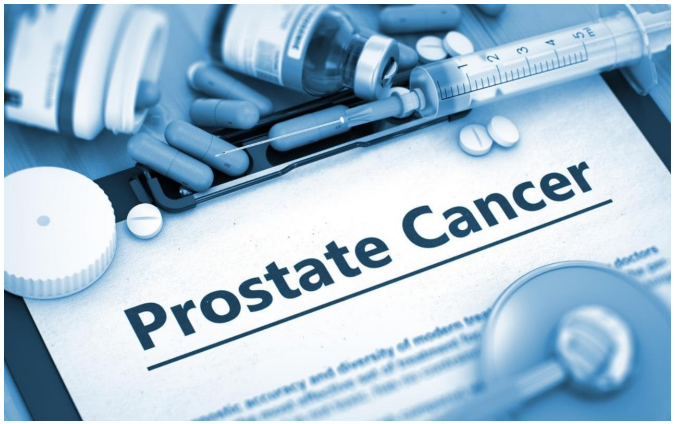
401 men in the placebo group:
- Continued ADT
- Median metastasis-free survival: **16.2 months**

CONCLUSIONS

Among men with nonmetastatic castration-resistant prostate cancer, metastasis-free survival and time to symptomatic progression were significantly longer with apalutamide than with placebo.

Conclusion

- The PSA test aids in detecting prostate cancer early. However, screening in the asymptomatic population may cause more harm than good
  - Increases anxiety and decreases quality of life without significantly improving diagnostic/survival rate.
- New diagnostic methods, such as MRI-targeted biopsy, may reduce overdiagnosis and overtreatment associated with the use of PSA tests alone.
- Active surveillance is a huge part of PCa care. Biomarkers that can detect progression to aggressive PCa as early as possible are needed to allow for prompt treatment.
  - New treatments are in the works that could offer superior effectiveness compared to existing drugs.



Acknowledgements

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