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Risk Assessment and Early Detection of Prostate Cancer

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www.prostatecentre.com
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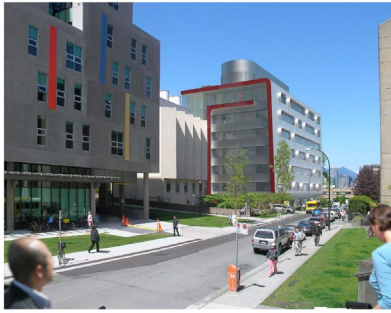

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RESEARCH TREATMENT

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Faculty/Presenter Disclosure

- **Faculty/Presenter:** Martin Gleave

- **Relationships with financial sponsors:**
  - **Grants/Research Support:** TFRI; PCF; DoD; CFI; BCKDF; NIH; Janssen; Astellas; Bayer
  - **Speakers Bureau/Honoraria:** None
  - **Consulting Fees:** Astellas, AZ, Bayer, GDx, Janssen, Sanofi, Pfizer, MDX, AbCellera
  - **Patents**: >200 (OGX-011, OGX-427; ST-CP; ST-POP; SEMA3C; VPC22826)
  - **Founder**: OncoGenex Technologies; Sustained Therapeutics; Sikta Pharma

Mitigating Potential Bias

- I am a urologist who diagnoses and treats men across the spectrum of prostate cancer from biopsy to local and systemic therapies, including surgery, radiotherapy, and systemic AR – targeted drugs, including supportive and end of life care

Learning Objectives

Upon successful completion of this activity participants will be able to:

- Identify men at high risk for developing PCa
- Understand role for PSA in early detection of PCa
- Define use of MRI in biopsy decision-making
- Implement shared decision making for early detection of PCa

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Prostate Cancer Statistics in Canada - 2024

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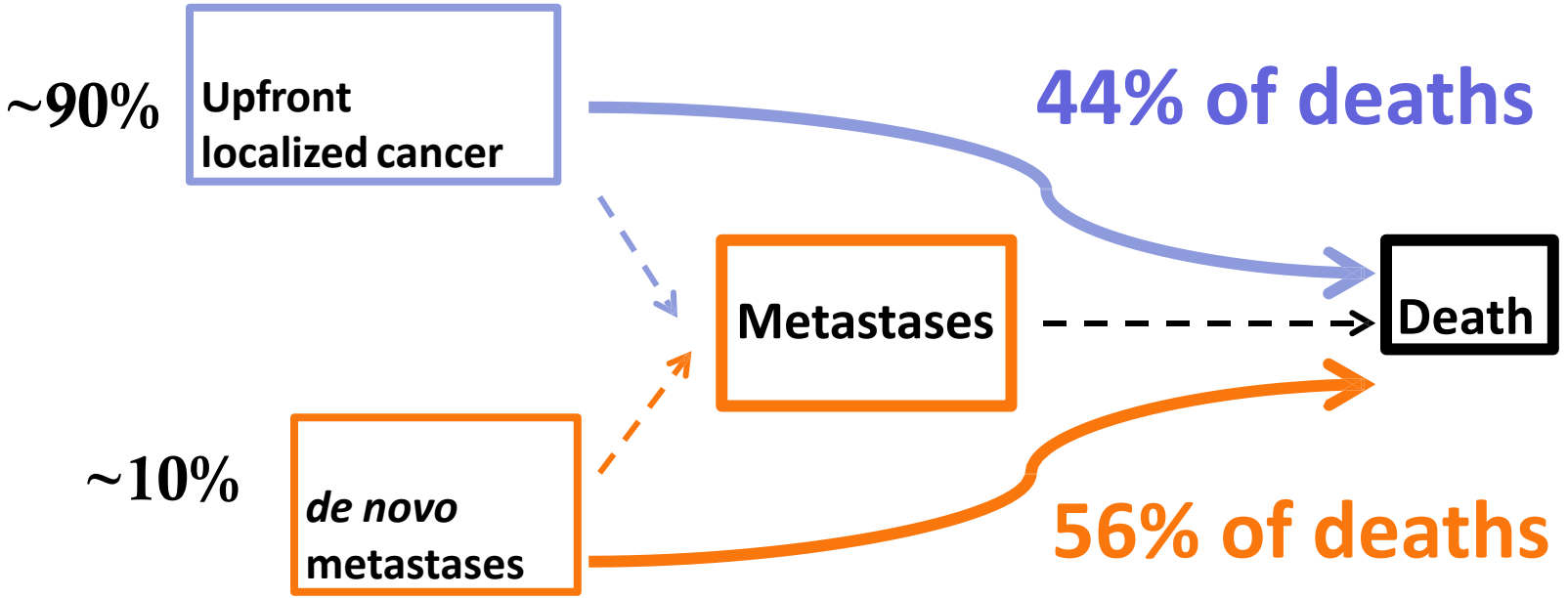
- **27,900 cases, or 22% of all new cancer cases in men.**
- **5,000 deaths, or 11% of all cancer deaths in men.**
- **On average, 76 Canadian men will be diagnosed with, and 14 will die from, prostate cancer every day.**

50% decline in PCa death rate since 1995

- **earlier detection**
- **improved imaging**
- **multimodal local therapies**
- **better systemic therapies**

Who Dies from Prostate Cancer?



~10% of men presenting with metastases account for > 50% of deaths from PCA

Patrikidou A, Prostate Cancer Prostatic Dis. 2014;17(4):348-352.

Prostate Cancer and the Ageing Male

What causes it and how can it be prevented?

- **Risk Factors**
  - »Beyond Your control:
    - »age
    - »Testosterone (AR is a co-oncogene)
    - »Race
    - »Family history (genetic, environmental)
  - »Lifestyle
    - »Geography
    - »Diet

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Prostate Cancer: Why Environment?

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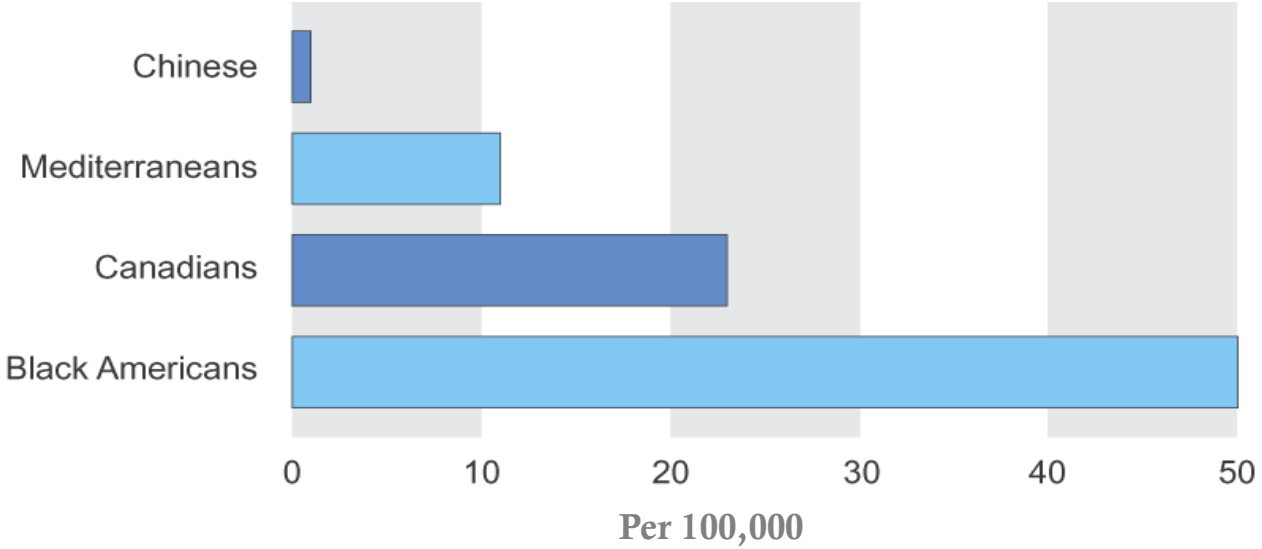
Race and Nationality Mortality Rates



Prostate Cancer Genetics

- Inherited (germline)
  - »DNA repair (DDR):
    - »BRCA 1/2 (HRR)
    - »CHEK2, MUTYH, ATM, FANCA, etc
  - »Mismatch repair – MSH2 (lynch)

- »Acquired (somatic)
  - »GoF AR –enhancing - ETS fusions; FOXA1; SPOP
  - »LoF –TP53, PTEN, CDK12 (and other DDR), RB

Ways to Reduce Prostate Cancer Risk

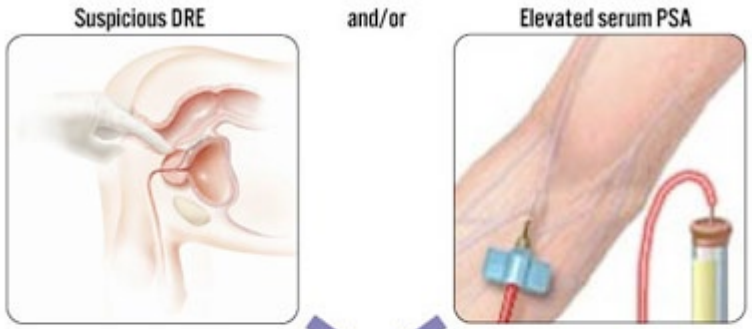
- Evidence of Absence for Benefit – Selenium, metformin, diet

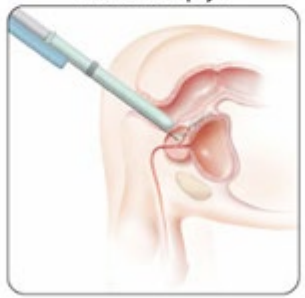
- Rational to recommend a Heart Healthy Life Style:
  - Diet
    - Oxidative stress
      - Caloric restriction/ideal body weight
      - Reduce red meat fats; increase fish, antioxidant food types
- Drugs:
  - 5 ARI (finasteride/dutasteride)
  - PCPT and REDUCE data supportive
    - Finasteride and dutasteride both decrease CaP diagnosis rates by 25%
      - N Engl J Med. 2010 Apr 1;362(13):1192-202)
    - Appropriate to recommend in high risk men, or large BPH, high PSA neg biopsy

Why Screen for Prostate Cancer?

- Most common male cancer.
- No preventable strategies.
- No symptoms until locally advanced or metastatic.
- Multiple effective treatments available to cure early stage PCa.
  - Also: earlier detection and Rx of non curable PCa prolongs survival
- We have an inexpensive and non-invasive test (PSA) that risk stratifies and facilitates early detection.
- Level I evidence that PSA screening reduces PCa specific mortality.

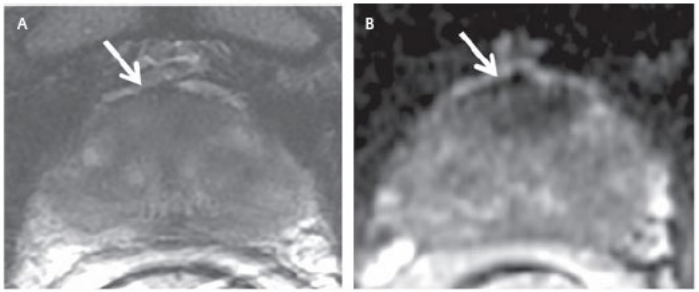
Early Detection of Localized Prostate Cancer
PSA and the Diagnostic Triadd





Transrectal vs transperineal

MRI TRUS Fusion



1) Prostate cancer rarely causes symptoms unless it is advanced and/or metastatic
2) Currently, a majority of prostate cancers are detected because of elevated PSA or abnormal **DRE**

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So Why the Controversy?

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- False positive tests with of PSA leads to anxiety and interventions (now improved with MRI).
- Evaluation of elevated PSA required invasive transrectal prostate biopsy (now improved with guided transperineal biopsy).
- PCa has a very long natural history, so that only about 1 in 6 men diagnosed with prostate cancer will die of prostate cancer.
  - High risk of overtreatment (mitigated by active surveillance).
  - Treatment associated with bladder, bowel and sexual dysfunction.

Early Detection of Prostate Cancer – Striking a Balance

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Screening reduces the risk of death from prostate cancer.

Harm:
anxiety, infection after biopsy; bladder/bowel/ sexual dysfunction after treatment.

- The key is to find the correct balance between benefit and harm in every individual patient.
- Shared decision making is the foundation of prostate cancer screening.

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Seven criteria of an optimal screening test: Does PSA meet criteria?

1. Disease significantly impacts public health
2. Disease is of adequate prevalence
3. Detection by screening before clinical dx
4. Screening test highly sensitive and specific
5. Screening test tolerated by patient
6. Treatment options available if disease found
7. Earlier treatment leads to improved outcome

PSA: A Central Biomarker in PCa

Gene / protein: KLK3 (kallikrein-related peptidase)/Serine protease, androgen (AR)-regulated

Clinical Roles of PSA:

1. **Diagnosis**: Organ-specific marker enabling early detection
   Best interpreted in context (age, genetic risk, PSA density, MRI)
2. **Prognostic Biomarker**: Reflects disease burden
   Predicts: Risk of treatment failure
   Time to progression; Overall and cancer-specific outcomes

3. **Response Biomarker:** Local therapy: cure vs failure; Earliest indicator of BCR after curative therapy
   Systemic therapy: ADT, ARPI, PSMA Lu,
   -nadir PSA strongly predictive of depth and durability of response
   -emergent resistance to AR-directed and most therapies

Bottom Line

PSA is an imperfect but indispensable biomarker, unique in oncology for its ability to inform diagnosis, prognosis, response, and resistance.

- Value maximized when interpreted dynamically, not as a single threshold

Mammogram vs PSA as Diagnostic Biomarkers

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Mammogram

- **Sensitivity ~75–85% (~65% in dense breasts)**
- **Specificity. ~88–92%**

- **False positive rate. ~7–12% per screening round**
(~50–60% cumulative false-+ve risk over 10 yrs)

- **Positive Predictive Value**
  - **~20–30% for biopsy recommendation**

- **False negative rate**
  - **~15–25% overall**

PSA ≥4.0 ng/mL (better as continuous)

- **Sensitivity ~50–70% (csPCa)**
- **Specificity ~85–90%**

- **False positive rate ~10–15%**

- **PPV ~25–30% for any PCa**
- **~15–20% for csPCa**

- **False negative rate**
- **High for GG1 (which we want)**

PSA vs Mammogram as Diagnostic Biomarkers

PPV for biopsy is remarkably similar between PSA and mammography

- **Mammography's higher sensitivity comes at the cost of:**
  - Repeated recalls
  - Very high cumulative false-positive rates
  - Over detection of DCIS
- **PSA's perceived "poor performance" reflects:**
  - Use as a single-threshold test
  - Detection of biologically indolent disease
  - Historical lack of downstream risk stratification (corrected with MRI, genomics) and overtreatment (corrected with AS)

PSA as a Diagnostic Biomarker

Just as mammography is now:

- Risk-adapted
- Combined with breast density assessment
- Supplemented by MRI in high-risk women

PSA is now:

- Risk-adapted
- Combined with PSA density/kinetics
- Used upstream of mpMRI and targeted biopsy

Additional important considerations for prostate cancer diagnosis in primary care

- PSA testing of men without symptoms or other clinical suspicion of prostate cancer is not an insured benefit in BC under the Medical Services Plan
- Abnormal DRE: refer to urologist regardless of PSA
- For men taking 5-alpha reductase inhibitors (i.e., finasteride & dutasteride): double the measured PSA value for accurate interpretation
- Defer PSA if the patient has signs or symptoms of acute UTI
- Antibiotics should not be used in an attempt to lower PSA
- If PSA is abnormal, check it again in 4-12 weeks before referring

What is a "Normal" PSA?

- Traditional cut-off: 4.0
- "Newer" cut-off: 2.5 (PCPT/NCCN)
- European screening trial: 3.0
- Age-adjusted normal values*:

Utility of DRE is controversial for screening – but every abnormal PSA warrants DRE

Age	PSA Cut-off
40-49	2.5
50-59	3.5
60-69	4.5
70-79	6.5

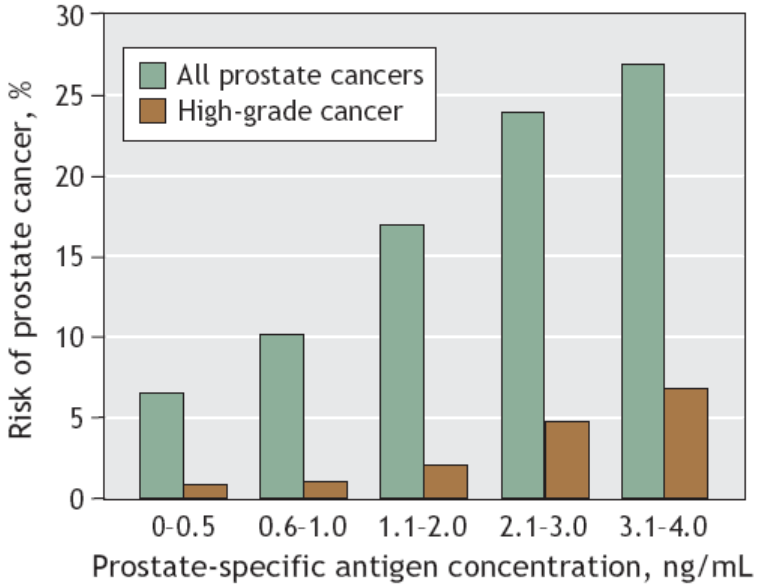
*Oesterling et al. JAMA 1993 Aug 18;270(7):860-4.

Prostate Cancer Prevention Trial

PSA as a Continuum (Key Concept)

There is **no PSA level below which cancer risk is zero**:

PSA (ng/mL)	Cancer on biopsy
<1.0	~5–10%
1–2	~10–15%
2–4	~20–25%
4–10	~25–40%
>10	>50–65%



NEJM. 2013 Aug 15;369(7):603-10

Thompson, CMAJ • June 19, 2007

The Evidence For Screening

Incidence of *de novo* Metastatic Prostate Cancer

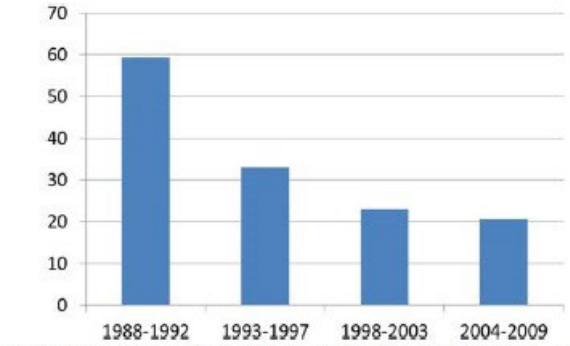


Figure 1. The age-adjusted incidence rates of newly diagnosed metastatic prostate cancer are shown by era of diagnosis.

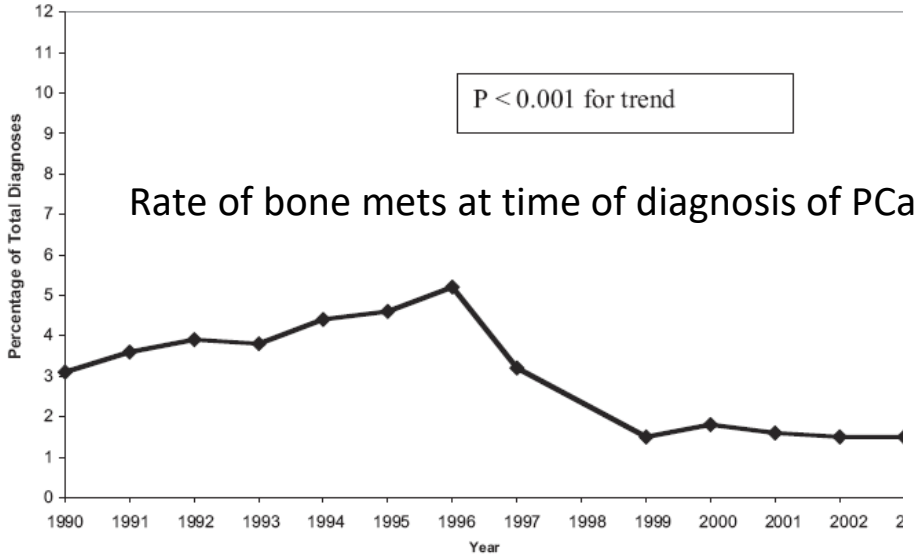
5-30%

<10%

60%

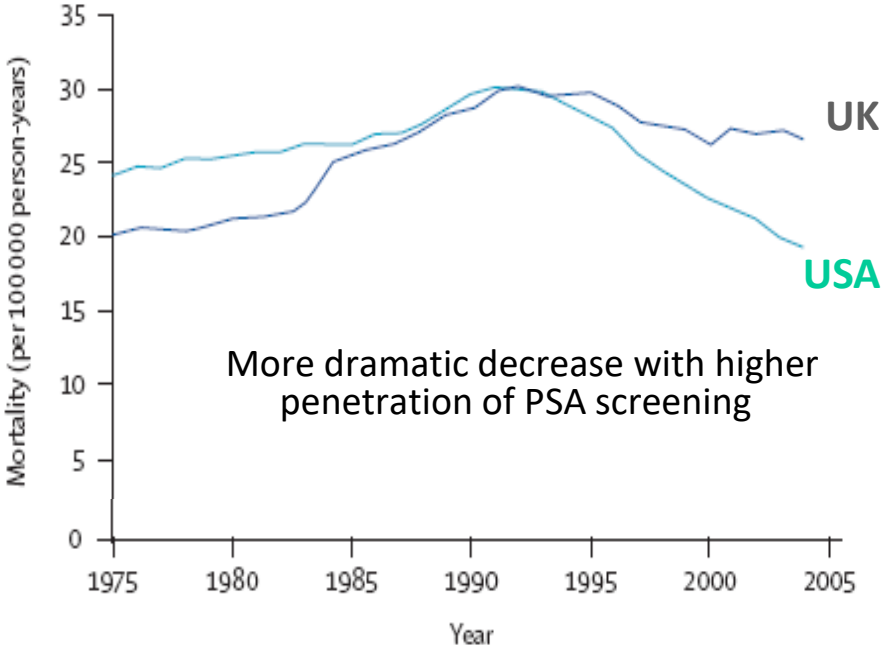
Wu JN, Cancer. 2014;120(6):818-823.

Fewer metastases in PSA era



Ryan CJ et al. Urol Oncol. 2006 Sep-Oct;24(5):396-402.

PCa Mortality USA vs. UK



Collin et al. Lancet Oncol 2008; 9: 445–52

Quebec PSA Screening Trial

- Began 1988: men aged **45–80** in Québec City's electoral rolls (~46,486 men) randomized to "invited-to-screen" vs "not-invited."
- PSA cut-off used was **3.0 ng/mL**

- Results – after 11-year follow-up (2004): among those screened, there was a **62% reduction** in PCa–specific mortality compared to controls ($P < 0.002$).

- **Main criticism - Low participation rate ("invite-to-screen" vs "actual screening")** — many men randomized to "invited" never participated;

- thus the comparison is effectively between *those who chose screening* vs *those who did not* (self-selection bias) rather than true "intention-to-screen."

Labrie F et al. *Screening decreases PCa mortality: 11-year follow-up of the 1988 Québec prospective randomized controlled trial.* The Prostate. 2004;59(3):311–318

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Level 1 Evidence

European Randomized Study of Screening for Prostate Cancer (ERSPC)

- also Göteborg Swedish Update 2010

Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO)

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	ERSPC	PLCO
Trial	1993 - 2005 182,000 men in 8 European countries Age 50-74 years Screening q 2-4 yrs vs. no screening PSA (DRE only for elevated PSA) 16 years follow-up	**1993 - 2001** **76,693 men in 10 U.S. Centers** **Age 55 – 74 years** **Annual screening vs. "usual care"** **DRE for 4 years, PSA for 6 years** **13 years follow-up**
Results	**Incidence of prostate cancer increased 1.32x** • **Screened: 11.5% (=8444)** • **Control: 8.7% (=7732)** **Risk of death from prostate cancer:** • **20% reduction in screened group (520 vs. 793)** • **Absolute risk reduction 1.75 death per 1000 men, therefore number needed to screen 570** • **Number needed to diagnose to save 1 life: 18**	**Incidence of prostate cancer increased 1.12x** • **Screened: 11.1% (=4250)** • **Control: 9.9% (=3815)** **Risk of death due to prostate cancer:** • **9% increase in screened group (158 vs 145) (difference not statistically significant)** **High rate of screening in "usual care" arm:** • **40% had PSA within 3 years of entering trial** • **90% had PSA on trial (contamination)**

Schroeder et al. NEJM 2009;360(13):1320-1328
Schroeder et al. Lancet 2014;384(9959):2027-35
Schroeder et al. Eur Urol 2019; 76(1): 43–51

Andriole et al, NEJM 2009 360(13):1310-1319
Andriole et al, JNCI 2012 104:125-132
JE Shoag et al, NEJM 2016 374;18

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Reevaluating PSA Testing Rates in the PLCO Trial

90% of patients in control arm had PSA test during trial; 70% within 2 years; 50% within last year

men in the control group had more cumulative PSA testing than men in the intervention group

JE Shoag et al, NEJM 374;18 (2016)

PSA Screening:

Göteborg Update 2010

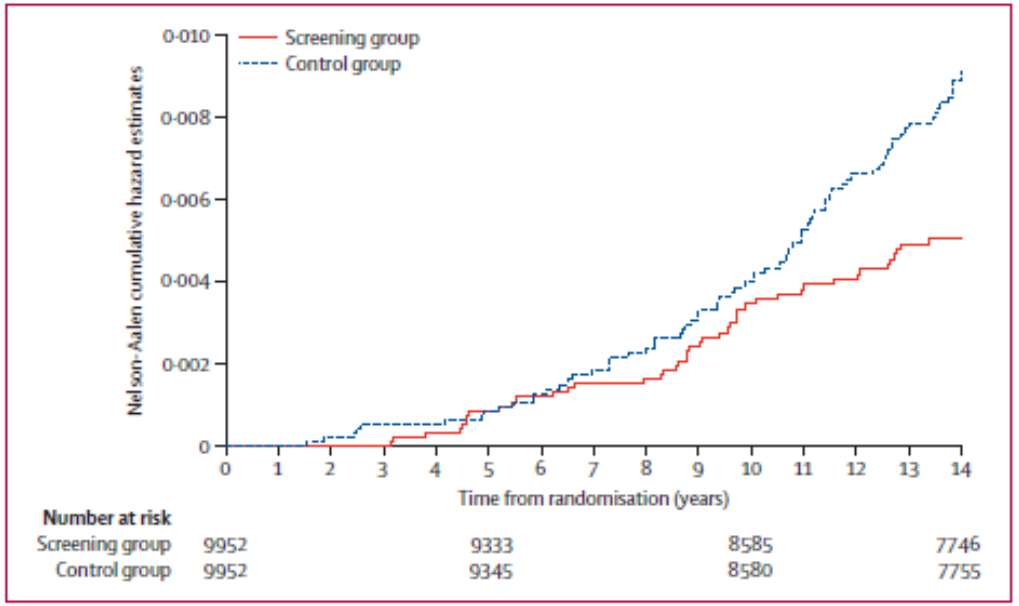
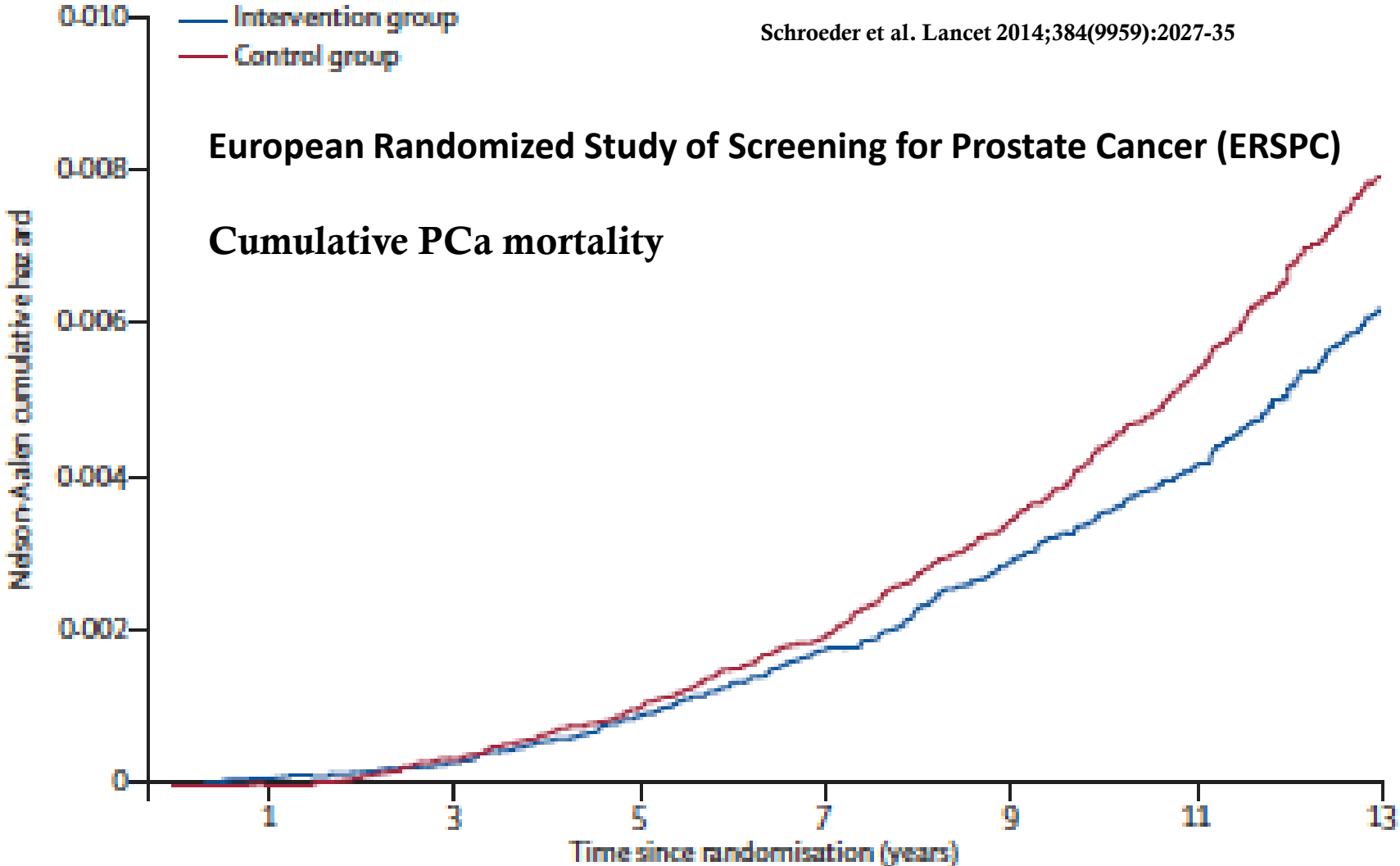


Figure 3: Cumulative risk of death from prostate cancer using Nelson-Aalen cumulative hazard estimates

- 10,000 men, mean follow-up 14 years
- 44% reduction in rate of death from prostate cancer in screened group compared to control
- to save one death from prostate cancer:
  - number needed to screen: 273
  - number needed to diagnose: 12

Hugosson, The Lancet, 2010


Intervention group
Control group
Schroeder et al. Lancet 2014;384(9959):2027-35
European Randomized Study of Screening for Prostate Cancer (ERSPC)
Cumulative PCa mortality
Nelson-Aalen cumulative hazard
0·010
0·008
0·006
0·004
0·002
0
1
3
5
7
9
11
13
Time since randomisation (years)

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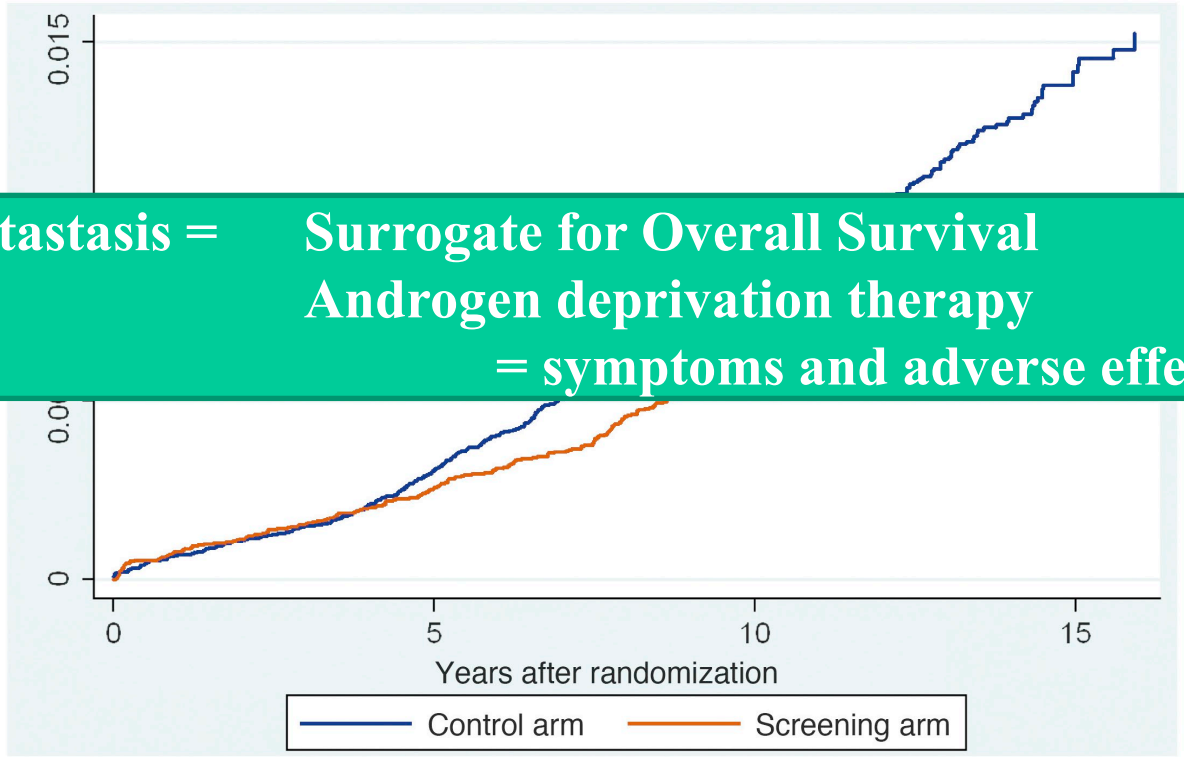
The relative benefit increases over time

	number needed to screen	number needed to diagnose
9 years	1410	48

Screening Reduces Risk of Metastasis



Metastasis = Surrogate for Overall Survival
Androgen deprivation therapy
= symptoms and adverse effects

PSA-Based Early Detection

- appears to be doing what it's supposed to do:
  - Finding tumors early, tumors that *can be cured* and some tumors that need to be cured
  - men who choose to have regular PSA ⇒ cancers diagnosed earlier and a lower risk of dying of PCa
  - Level 1 evidence - >20% reduction in PCa deaths, increasing over time
  - **BC Cancer, VPC, CUA, AUA, EAU, ASCO, NCCN recommended**

- **But….**
  - **Anxiety, Leads to more biopsies ⇒ risk of over diagnosis & treatment**
  - **Task Force Recommendations (failure to uncouple Dx from Rx in USA)**

US Preventive Services Task Force 2012

Prostate cancer screening “downgraded”:

Prior to 2012:
Grade C: not enough evidence to recommend or discourage PSA screening (i.e. shared decision making)

After 2012:
Grade D: PSA screening causes more harm than benefit (i.e. do not screen)

- Presents population level benefit vs harm
- Reflects concern for over-treatment (failure to uncouple Dx from Rx)

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Canadian Task Force 2014

CMAJ Oct 27, 2014

RECOMMENDATIONS

- For men aged less than 55 years, we recommend not screening for prostate cancer with the prostate-specific antigen test.

  (*Strong recommendation; low quality evidence*) **DO NOT SCREEN**

- For men aged 55–69 years, we recommend not screening for prostate cancer with the prostate-specific antigen test.

  (*Weak recommendation; moderate quality evidence*) **DO NOT SCREEN**

- For men 70 years of age and older, we recommend not screening for prostate cancer with the prostate-specific antigen test.

  (*Strong recommendation; low quality evidence*) **DO NOT SCREEN**

➢ **no content experts; targets an over-Rx problem that does not exist in Canada**

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Criticisms of the USPSTF Grade D Report

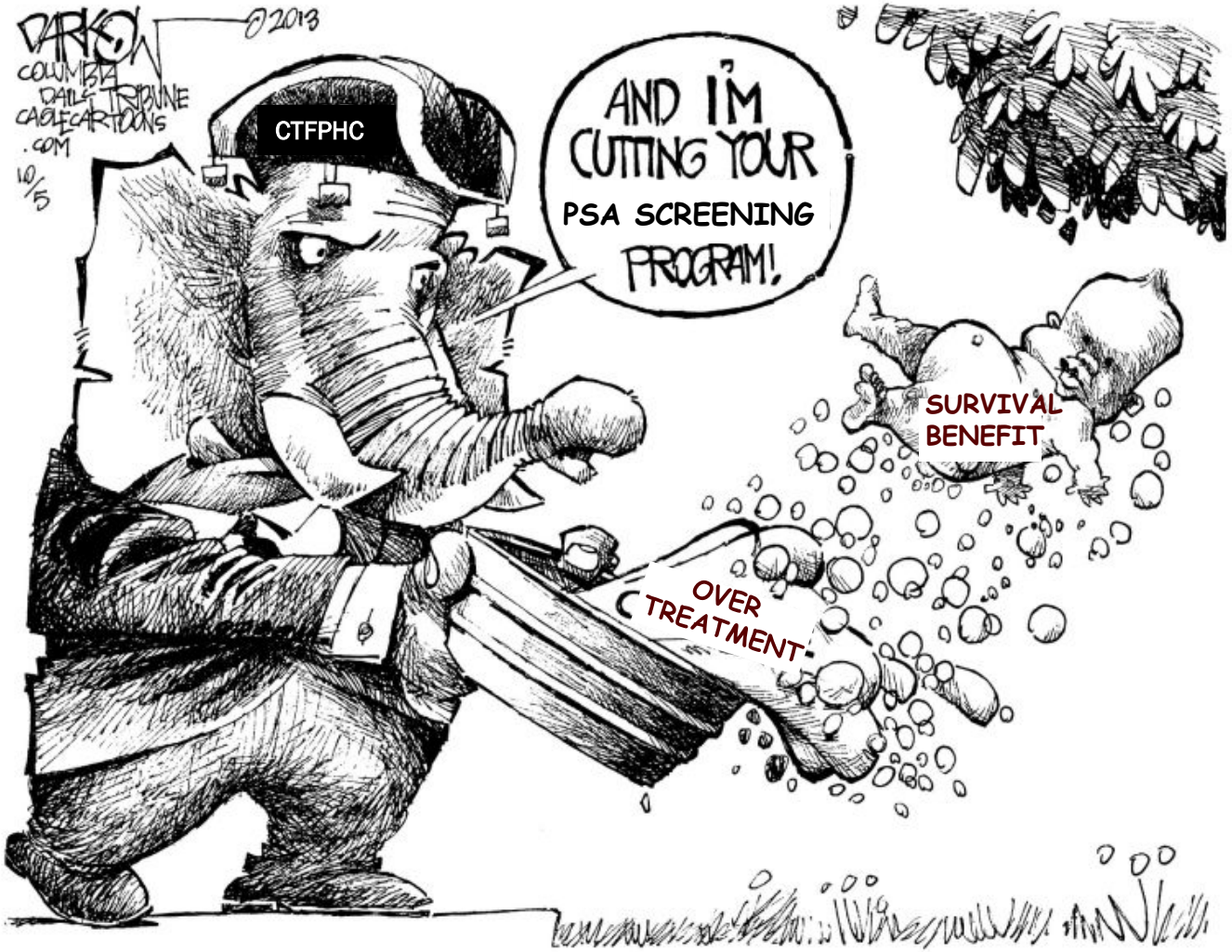

CLINICAL GUIDELINE | Annals of Internal Medicine

Screening for Prostate Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, PhD, on behalf of the U.S. Preventive Services Task Force*

- Underestimated benefits and overstated harms
- Overlooked contamination flaws of PLCO trial
- Ignored short f/u of ERSPC trials (2009 reports)
- Placed little weight on longer-term Göteberg (Swedish) trial
- Focused almost solely on mortality data (id not consider morbidity of PCa)
- Did not account for increased use of active surveillance for low-risk PCa
- Under-emphasized emerging risk-adapted screening tools

Moyer VA, on behalf of the US Preventive Services Task Force. Ann Intern Med 2012;157:120-34; Andriole GL, et al. New Engl J Med 2009;360:1310-9; Schröder FH, et al. N Engl J Med 2009;360:1320-8; Hugosson J, et al. Lancet Oncol 2010; 11:725-32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CAGLECARTOONS.COM
10/5
CTFPHC
AND I'M CUTTING YOUR PSA SCREENING PROGRAM!
SURVIVAL BENEFIT
OVER TREATMENT

Convergent Advances in Imaging, Biopsy, Risk Assessment Improve "Early" Dx of Prostate Cancer

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- False positive tests with of PSA leads to anxiety and interventions (now improved with MRI).
- Evaluation of elevated PSA required invasive transrectal prostate biopsy (now improved with guided transperineal biopsy).
- PCa has a very long natural history, so that only about 1 in 6 men diagnosed with prostate cancer will die of prostate cancer.
  - High risk of overtreatment (mitigated by active surveillance).
  - Treatment associated with bladder, bowel and sexual dysfunction (reduced with improved therapies).

Early Detection of Localized PCa - MRI Imaging

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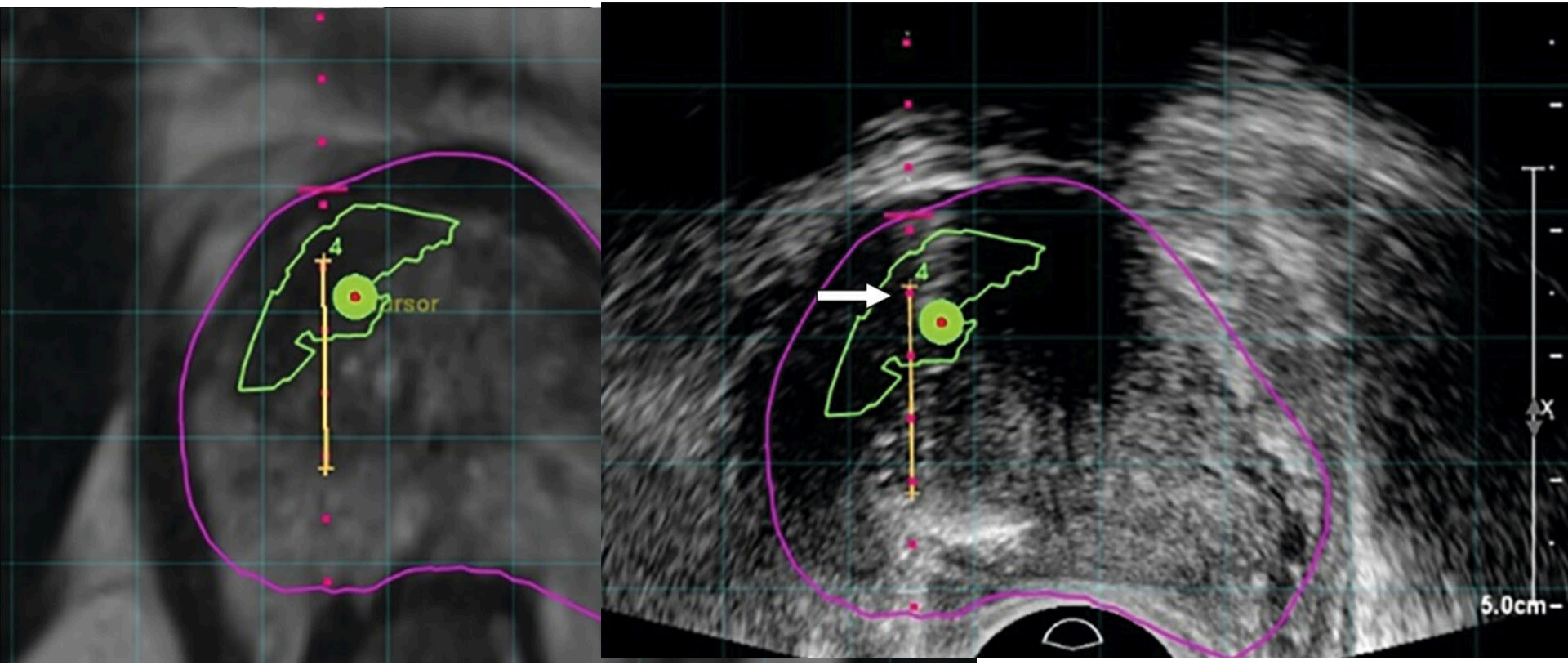
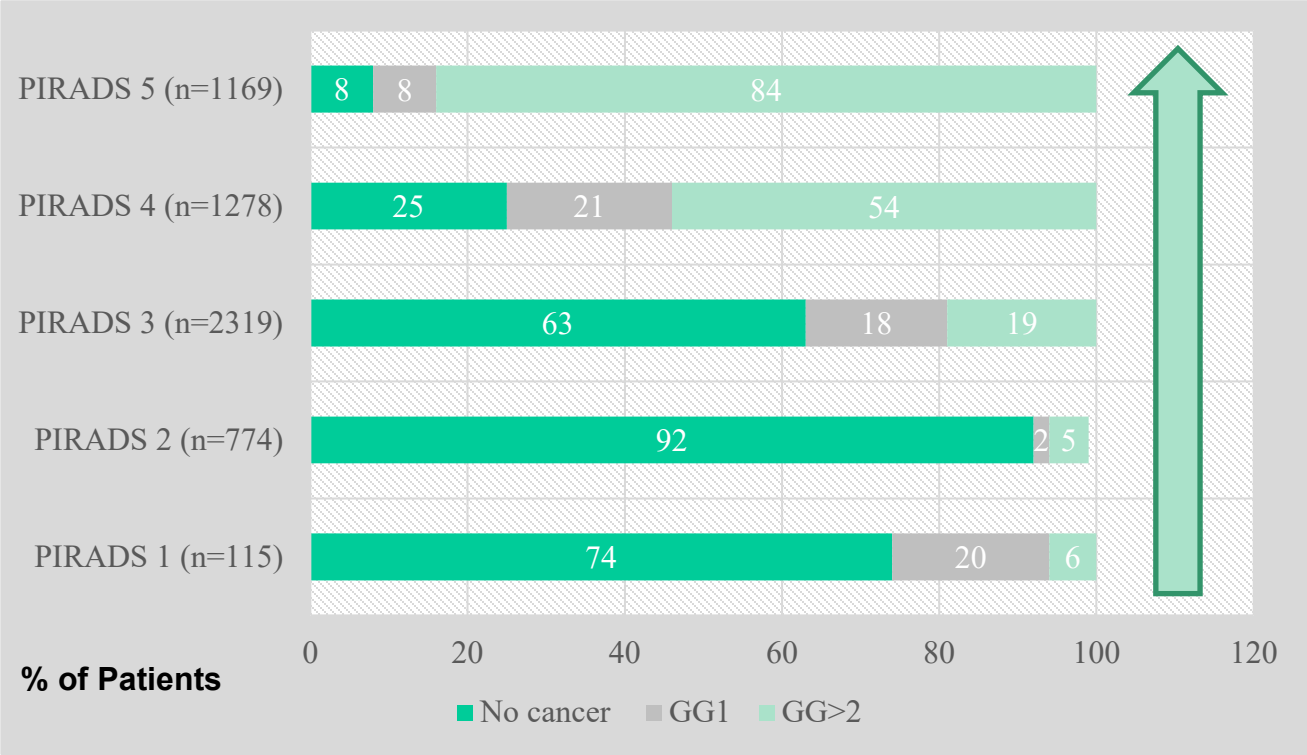


Chang et al. ARJ. 2023

Cancer detection rates according to PI-RADS v2.1 score



- **70 studies → 13,300 pts (early detection)**
- **11,686 lesions on MRI**
- **PSA: 9.8 (6–35) ng/mL**
- **cancer prevalence: 43%**

B Oerther **et al.**, *Radiology*, 2024 Aug;312(2)

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Prostate MRI Pearls

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When available, most men should have MRI before biopsy
(exceptions – locally advanced, PSA> 20; co-morbidities)

MRI findings determine need for biopsy
and guide biopsy strategy

PSA density can be used to stratify risk of cancer
and refine indication for biopsy (cut-off 0.15)

Most patients with normal MRI do not need biopsy but
~10% of clinically significant cancer is missed on MRI

Four Years of Screening for Prostate Cancer with PSA and MRI

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 26, 2024 VOL. 391 NO. 12

Results after Four Years of Screening for Prostate Cancer with PSA and MRI

Jonas Hugosson, M.D., Ph.D., Rebecka Arnsrud Godtman, M.D., Ph.D., Jonas Wallstrom, M.D., Ph.D., Ulrika Axcrona, M.D., Ph.D., Anders Bergh, M.D., Ph.D., Lars Egevad, M.D., Ph.D., Kjell Geterud, M.D., Ph.D., Ali Khatami, M.D., Ph.D., Andreas Socratous, M.D., Vasiliki Spyratou, M.D., Linda Svensson, R.N., Johan Stranne, M.D., Ph.D., Marianne Månsson, Ph.D., and Mikael Hellstrom, M.D., Ph.D.

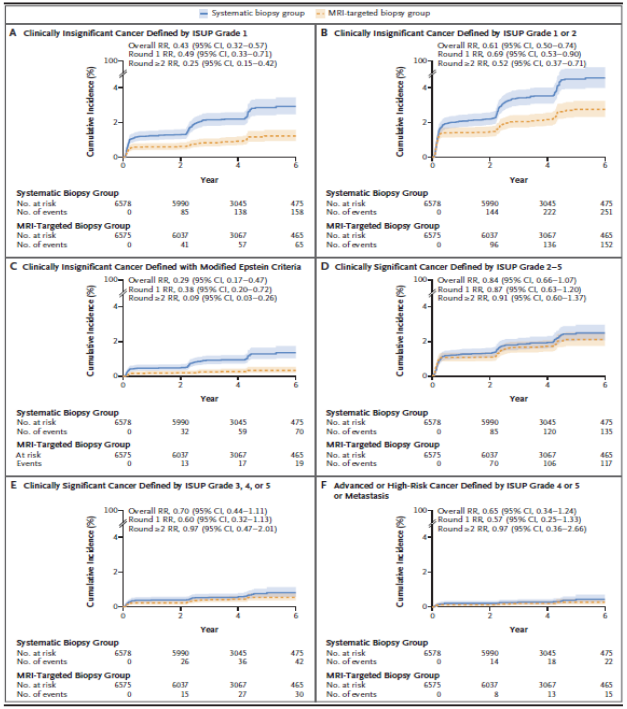
- >13000 men with PSA >1.8ng/ml randomized to systematic biopsy or MRI-targeted biopsy
- Repeat screening for 2, 4 or 8 years
- Primary outcome: detection of clinically insignificant PCa

Conclusions:

-omitting biopsy in men with negative MRI eliminated > 50% of clinically insignificant PCa

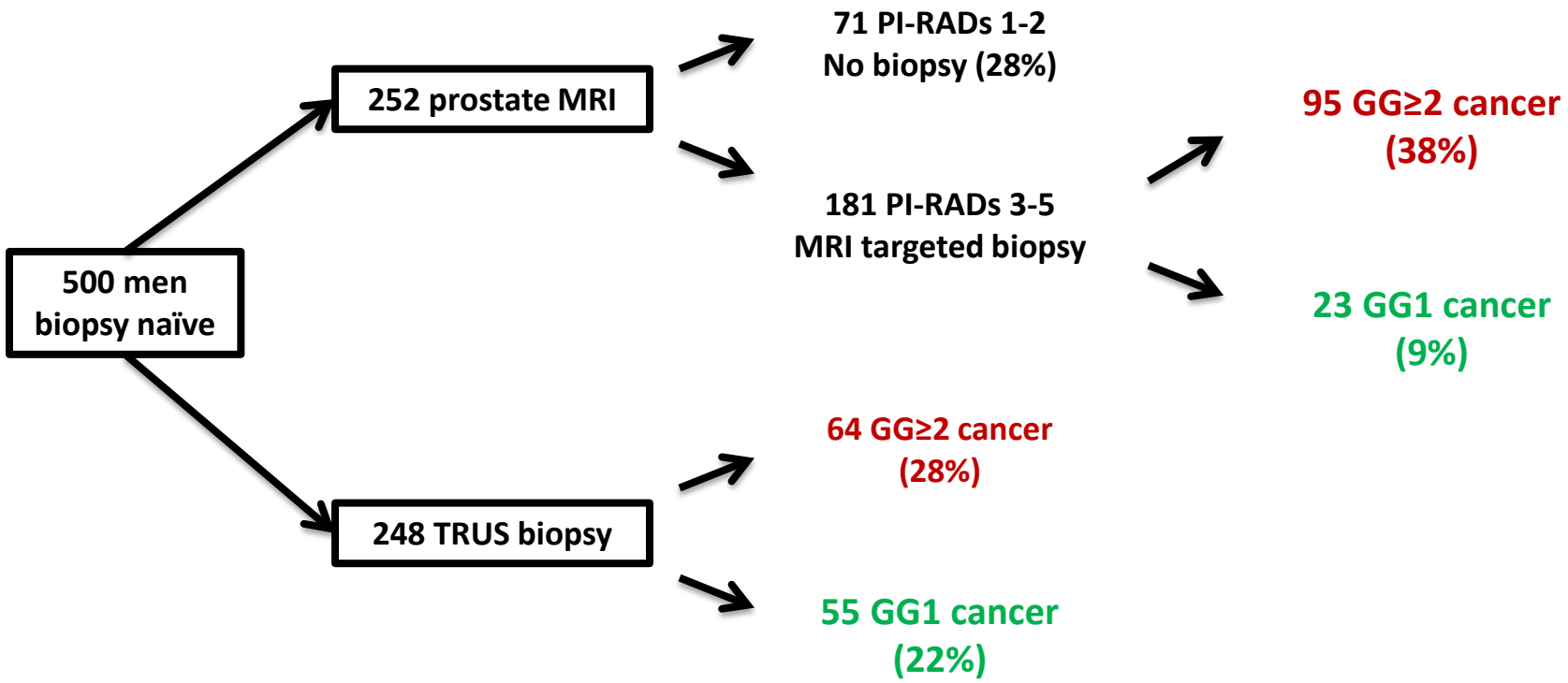
-risk of having incurable cancer diagnosed at screening or as interval cancer was very low.

Cumulative Incidence of Detection of Clinically Insignificant Prostate Cancer, and Advanced or High-Risk Prostate Cancer



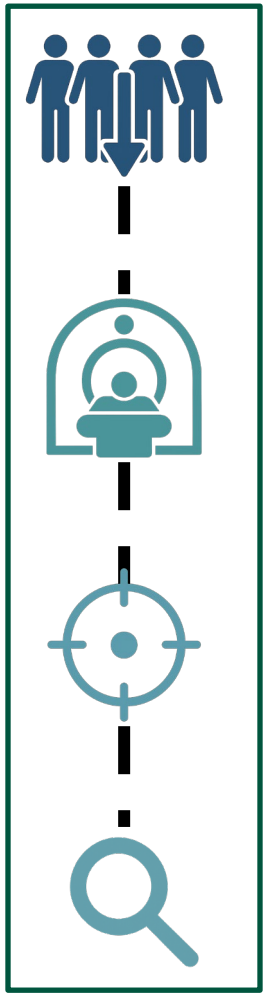
Hugosson J, et al. N Engl J Med. 2024 Sep 26;391(12):1083-1095. doi: 10.1056/NEJMoa2406050. PMID: 39321360.

MRI for Diagnosis of PCa : PRECISION Trial



Kasivisvanathan et al., *NEJM*, 2018

PSA and MRI Imaging to Guide Biopsy for Dx of PCa



Reduce the # of patients undergoing biopsy

32% of men avoid a biopsy

Reduce diagnosis of indolent cancer (GG1)

12% lower GG=1 detection

Increase detection of clinically significant cancer (GG≥2)

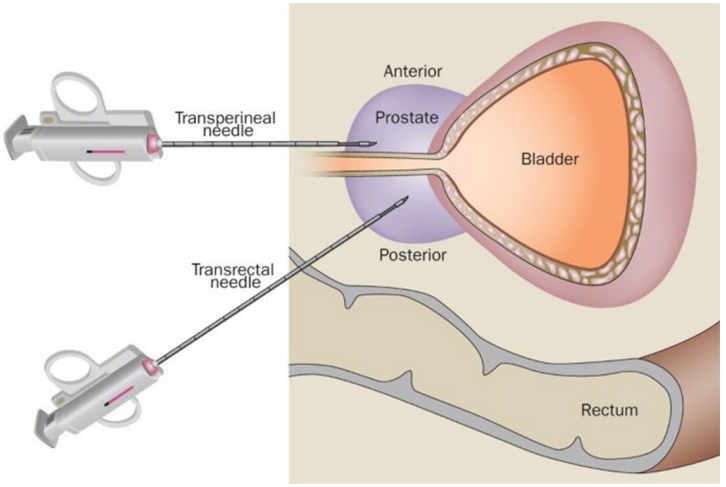
9% more GG≧2 cancers detected

More accurate targeted biopsy cores

29% more positive biopsy cores

Kasivisvanathan et al., *Eur Urol* 2025

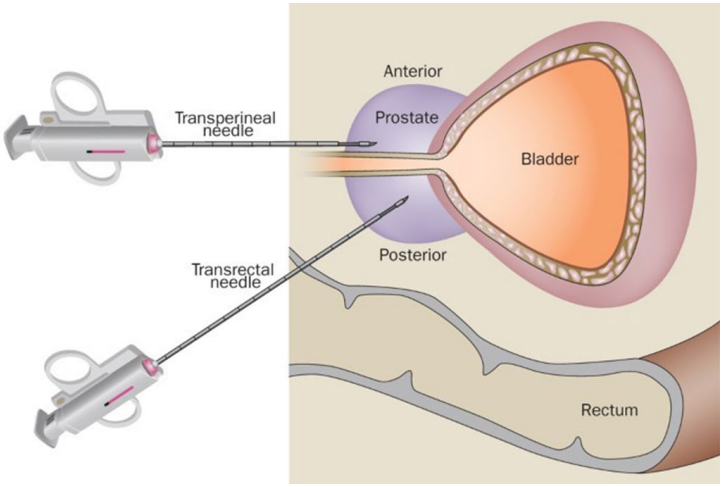
Case #1



- 64-year old male
- frankly malignant DRE
- PSA 257

➢ Does not need to wait for MRI – proceed directly to prostate biopsy

Case #2



- 64-year old male
- frankly malignant DRE
- PSA 45

➢ Does not need to wait for MRI – proceed directly to prostate biopsy

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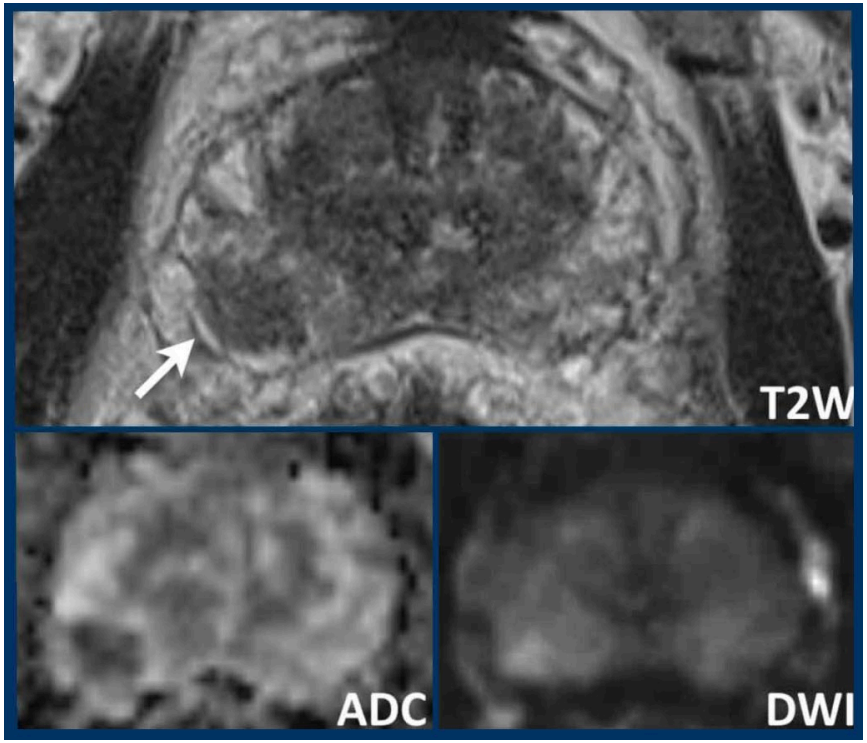
Case #3

- 69-year old male
- normal DRE
- PSA 6.5 & 7.1

- MRI: 16 mm PIRADS 5

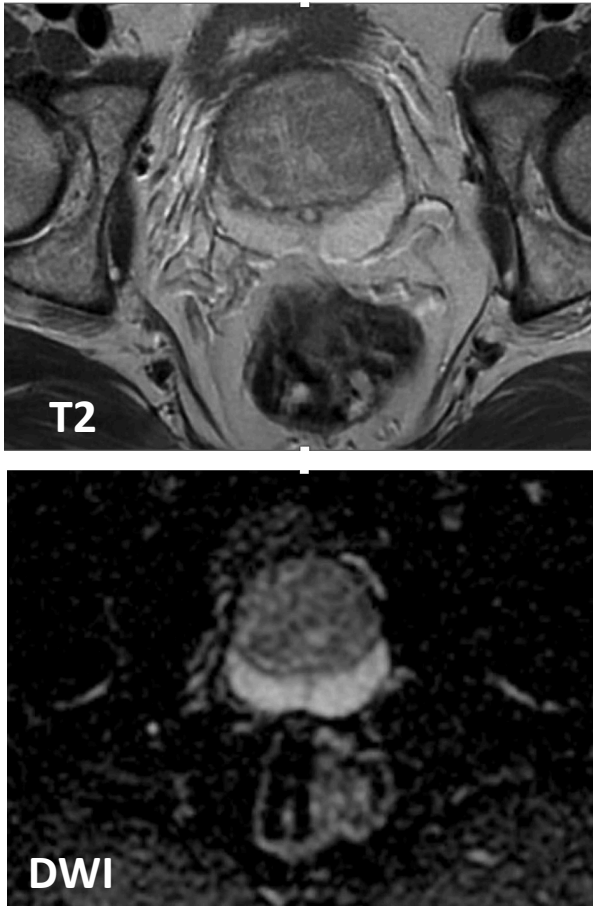
➢ Biopsy with cognitive fusion



Case #4

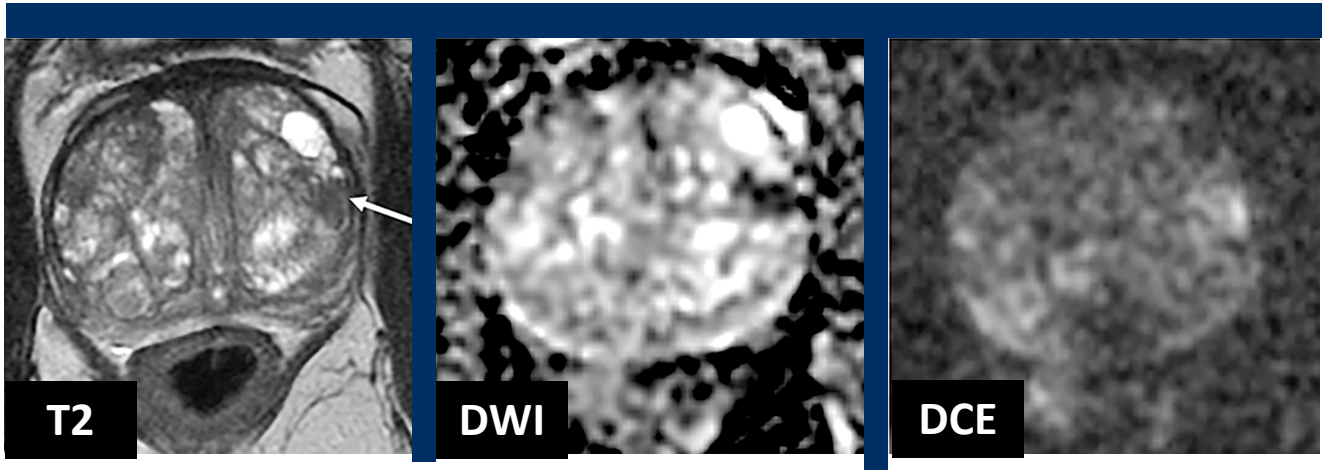
- 57-year old male
- normal DRE
- PSA 5.3 & 5.6
- MRI: normal; volume 52 ml

➢ No biopsy, PSA surveillance



Case #5

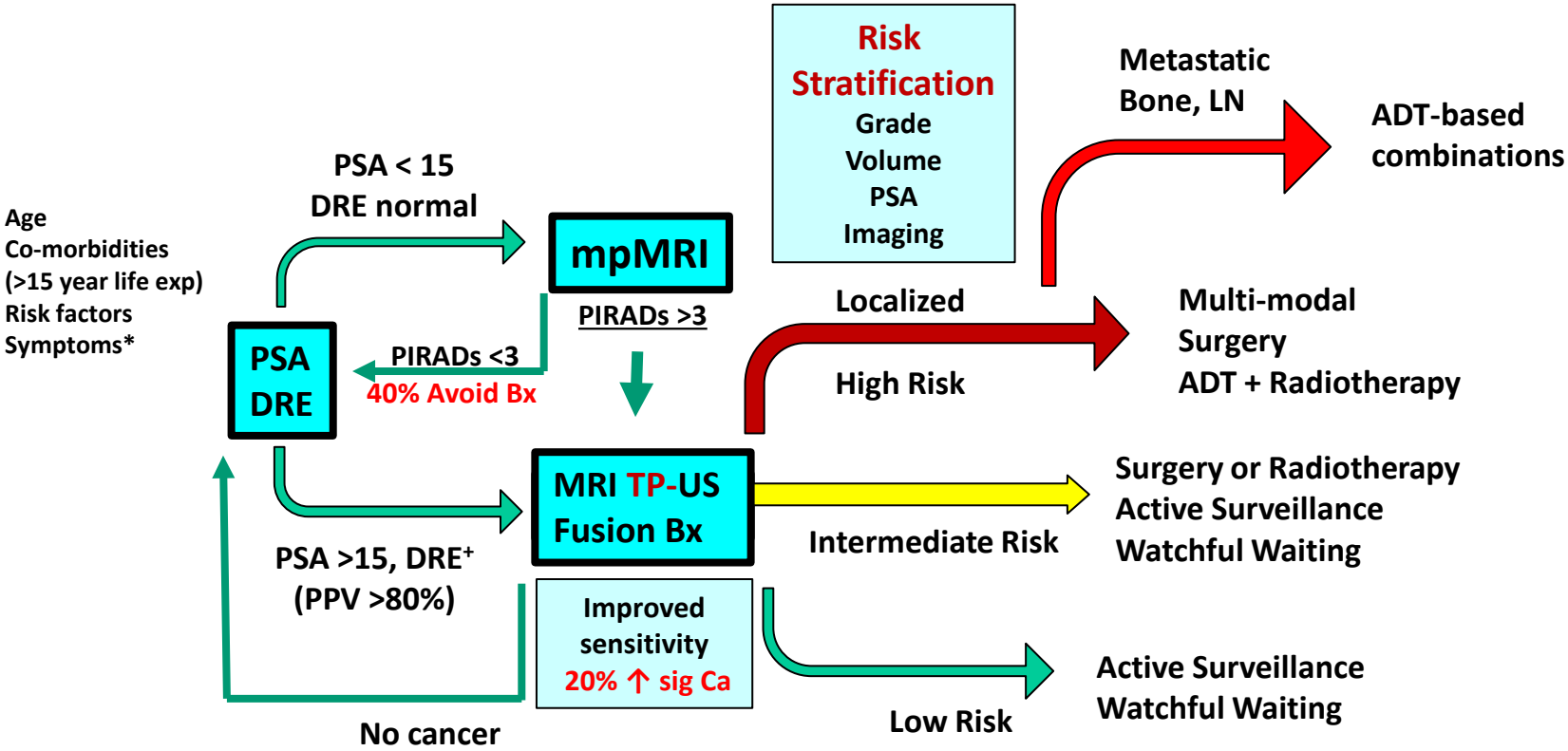
- 62 years
- PSA 8
- nl DRE



- MRI: 12 mm PIRADS 3; Vol 95 (PSAD 0.08)
- No prior PSA, no family history, Asian

➢Shared decision making: no biopsy

Convergent Advances in Imaging, Biopsy, Risk Assessment Improve "Early" Dx of Prostate Cancer



Ahmed HU et al (PROMIS). The Lancet. 2017 Feb 25;389(10071):815–22
Kasivisvanathan V et al. N Engl J Med. 2018 May 10;378(19):1767–77

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Convergent Advances in Imaging, Biopsy, Risk Assessment Improve "Early" Dx of Prostate Cancer

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The Future of Prostate MRI

Prevalence of MRI lesions in men responding to a GP-led invitation for a prostate health check: a prospective cohort study

BMJ Oncology 2023

Caroline M Moore ,[1,2] Elena Frangou,[3] Neil McCartan,[1,4] Aida Santaolalla,[5] Douglas Kopcke,[6,7] Giorgio Brembilla,[6] Joanna Hadley,[2,6] Francesco Giganti,[1,7] Teresa Marsden,[1,2] Mieke Van Hemelrijck,[5] Fiona Gong,[6] Alex Freeman,[8] Aiman Haider,[8] Steve Tuck,[9] Nora Pashayan,[10] Thomas Callender,[11] Saran Green,[5] Louise C Brown,[3] Shonit Punwani,[6,7] Mark Emberton,[2,12] on behalf of the Re-Imagine Study group

Artificial intelligence and radiologists in prostate cancer detection on MRI (PI-CAI): an international, paired, non-inferiority, confirmatory study

Lancet Oncol 2024

Anindo Saha, Joeran S Bosma*, Jasper J Twilt*, Bram van Ginneken, Anders Bjartell, Anwar R Padhani, David Bonekamp, Geert Villeirs, Georg Salomon, Gianluca Giannarini, Jayashree Kalpathy-Cramer, Jelle Barentsz, Klaus H Maier-Hein, Mirabela Rusu, Olivier Rouvière, Roderick van den Bergh, Valeria Panebianco, Veeru Kasivisvanathan, Nancy A Obuchowski, Derya Yakar, Mattijs Elschot, Jeroen Veltman, Jurgen J Fütterer, Maarten de Rooij†, Henkjan Huisman†, on behalf of the PI-CAI consortium‡*

➜ Screening with MRI ("Manogram"/"Prostagram")

➜ AI aids for interpretation

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PSA and PCa Detection - why the controversy?

- Performance characteristics of PSA are not great (now improved with MRI).
- Evaluation of elevated PSA required invasive transrectal prostate biopsy (now improved with guided transperineal biopsy).
- PCa has a very long natural history, so that only about 1 in 6 men diagnosed with prostate cancer will die of prostate cancer.
  - High risk of overtreatment (mitigated by active surveillance).
  - Treatment associated with bladder, bowel and sexual dysfunction.

Early Detection of Localized Prostate Cancer
PSA and the Diagnostic Triadd

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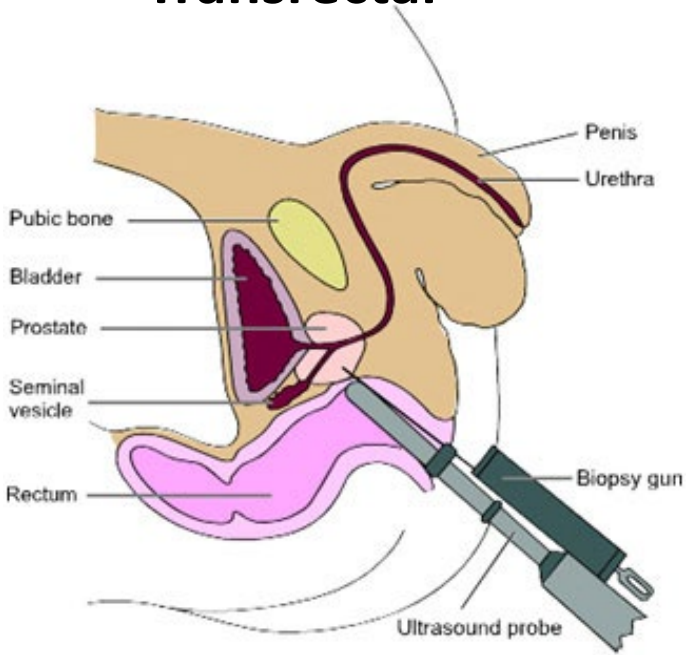
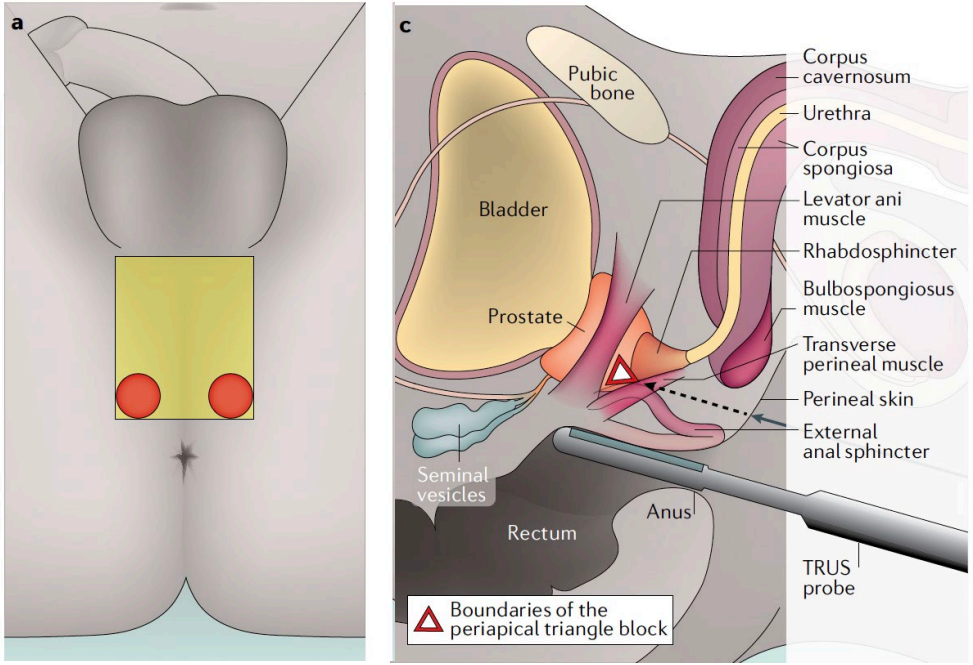
Transrectal



Transperineal



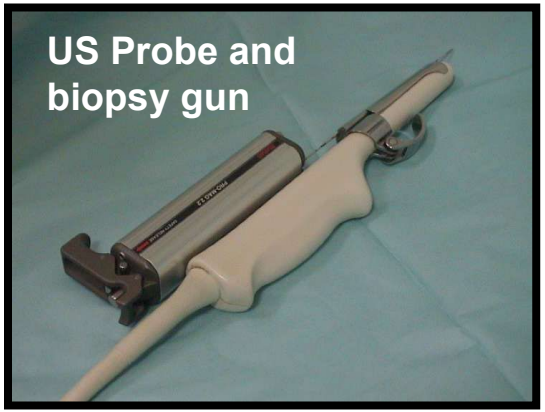
https://qprostate.com.au/prostate-cancer/diagnosis/transrectal-ultrasound-guided-prostatic-biopsy-trus/

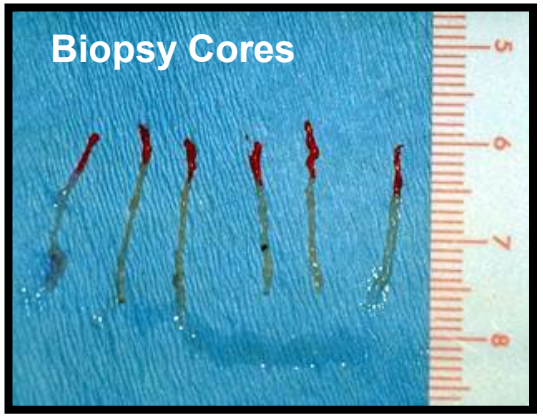
Basourakos et al. Nat Rev Urol. 2021

Early Detection of Localized Prostate Cancer PSA, MRI, and TP Biopsy

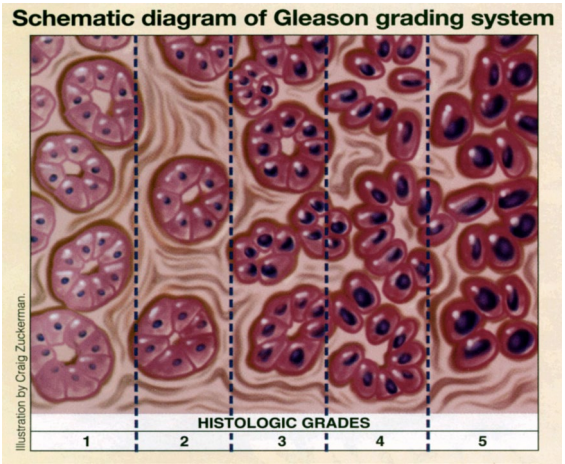
- TP Bx maximize detection of clinically significant prostate cancer
- TP minimize complications
- TP leads to responsible use of antibiotics
- Cognitive biopsy is cost efficient, time efficient, and effective
- Micro-ultrasound reduces time, improves access and detection of clinically significant prostate cancer

Prostate Biopsy and Risk Stratification





- Gleason score low vs grade
- Quantify amount of PCa in biopsy
  - Number (%) of +ve cores
  - Linear extent/% of cancer in core(s)
  - Extracapsular disease
  - Aggressive patterns



Diagnosis

Risk Stratification Localised PCA

Risk	Low	Intermediate	High
PSA	0-10	10.1-20	>20
Stage	T1C, T2a	T2b	T3
Gleason	6	7	8-10
		Volume of pattern 4 or 5	

Active Surveillance

Surgery or Radiation ADT with RT

D'Amico, J Urol, 1998

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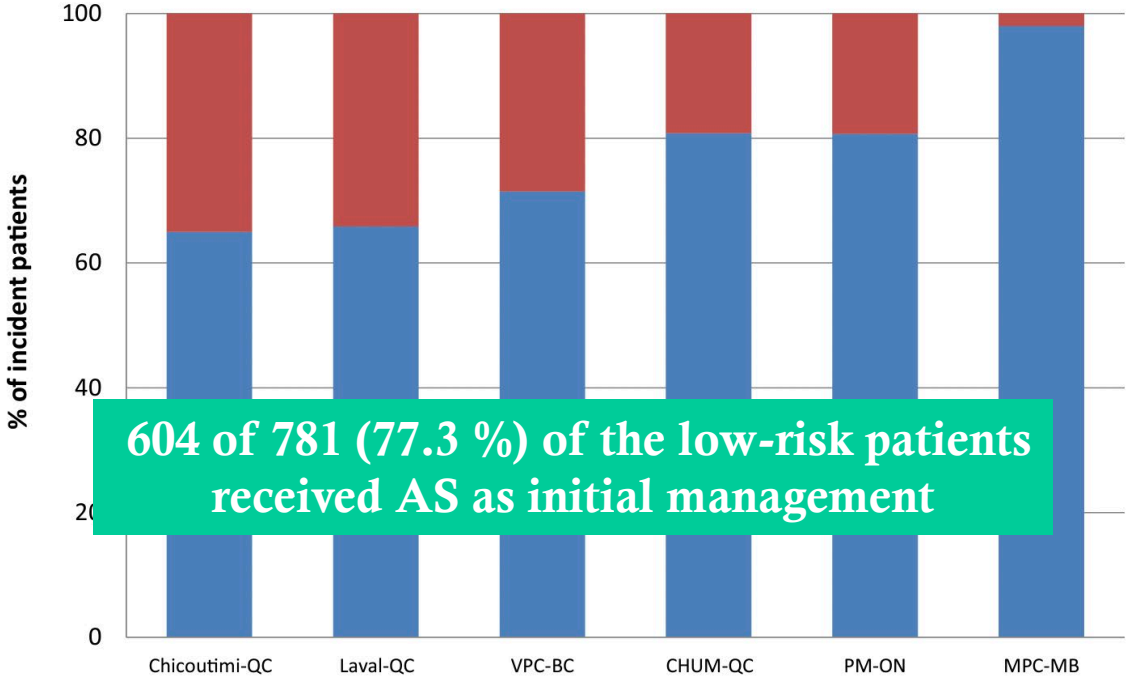
Active Surveillance Across Canada

All men diagnosed in 2010



604 of 781 (77.3 %) of the low-risk patients received AS as initial management

Upfront therapy, n (%)	21 (35)	32 (34)	37 (28)	60 (19)	26 (19)	1 (2)
Chose initial AS, n (%)	39 (65)	62 (66)	93 (72)	252 (81)	109 (81)	49 (98)

N Timilshina et al., World J Urol (2017) 35:595–603

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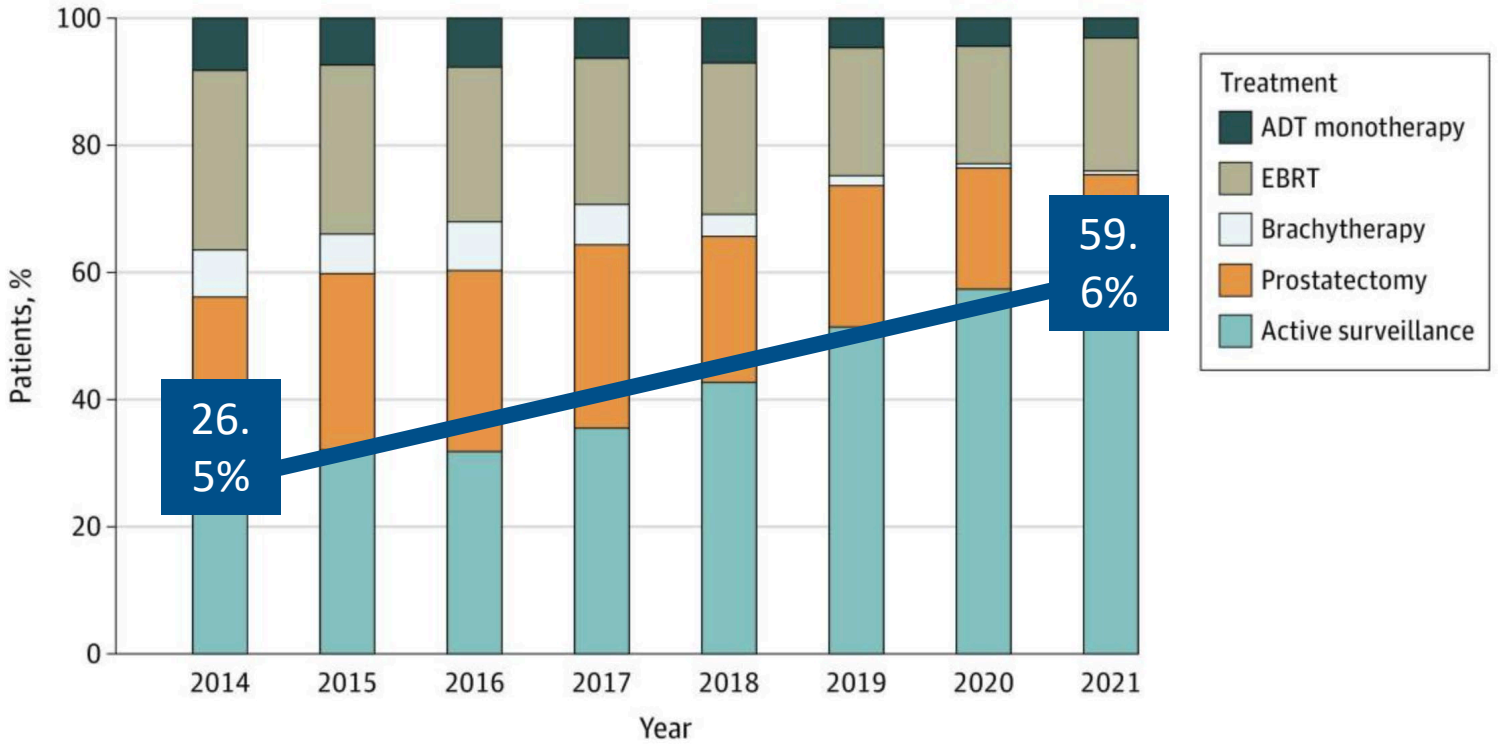
Trends in U.S.



BC GU Tumour Group and VPC

- The Genitourinary Cancer Tumour Group of the BC Cancer Agency and the Vancouver Prostate Centre recommends that asymptomatic men 50 years of age or older, with an estimated life expectancy of more than 10 years, who are informed about the risks of over-diagnosis and over-treatment, consider PSA testing for the early diagnosis of prostate cancer.
- There is evidence from randomized controlled trials that mortality decreases with PSA screening for the early detection of prostate cancer and its treatment.
- Early detection of prostate cancer should be linked to a treatment algorithm that includes discussion and prioritization of active surveillance for men with low-risk prostate cancer.

- Similar Guidelines – CUA, AUA, EAU, ASCO, ACS, PCF, NCCN, NCI

Summary – PSA in Early Detection of PCa

- PSA screening reduces mortality but risks overdiagnosis and overtreatment.
  - MRI reduces biopsy rate and overDx, improves detection of csPCa
  - Image-guided TP biopsies improve tolerability and accuracy
- Risk-stratified screening enhances precision and minimizes harm.
- PSA screening must link to active surveillance to reduce overtreatment
- Future strategies will integrate genomics and AI for personalized screening
- Emerging trials (eg, PROBASE, Göteborg-2, STHLM3) support tailored approaches

Early Detection of PCa – Risk Adjusted Guidelines

- Shared informed decision-making key. PSA is neither mandatory nor inappropriate, depends on patient values, health, and risk factors
- Baseline PSA early 40's (refer if > 2.5)*
    - annual testing thereafter if PSA ≥ 0.6 at baseline; and/or high risk group (Black, family history, or hereditary genetic anomaly (BRCA 1/2)
- Repeat PSA at age 45 & 50 if PSA < 0.6
- Risk adjusted annual or bi-annual testing in men over 50
    - monitor PSAdt (normal > 4 years)
- MRI guides need for, and improves accuracy of, TP Bx
- Cease PSA testing if stable and < 10 yrs life expectancy

* Baltimore Longitudinal Study of Aging

Key NCI & Guideline Recommendations

- **Shared Decision-Making (SDM):** Essential for men over 45 to discuss pros/cons before testing.
- **Individualized Approach:** No one-size-fits-all; consider personal/family history, race (higher risk for Black men), and overall health.
- **Risk vs. Benefit:** Screening offers small benefit in reducing death but risks include false positives, biopsies, and overtreatment for slow-growing cancers (overdiagnosis).
- **Screening Frequency:** Varies; some suggest every 2 years if PSA is low (<2.5), annually if higher, stopping if life expectancy is <10 years, but consult your doctor

PSA and Risk of PCa

- BLSA remains among the strongest evidence that a single midlife PSA predicts long-term risk of future prostate cancer.
- Malmö Preventive Project: Single PSA at age ~44–50 predicted advanced PCa up to 25 years later. Men with higher early PSA had much greater long-term risk.

- supports a **risk-stratified screening paradigm**: men with low baseline PSA need less frequent surveillance; men with higher baseline PSA may benefit from closer follow-up.
- PSA is **not just a snapshot for current diagnosis**, but a **long-term risk biomarker**

- Implication: Early midlife PSA can identify a relatively small high-risk subgroup who might benefit from more intensive surveillance

PMID: 11549490
PMID: 17264339

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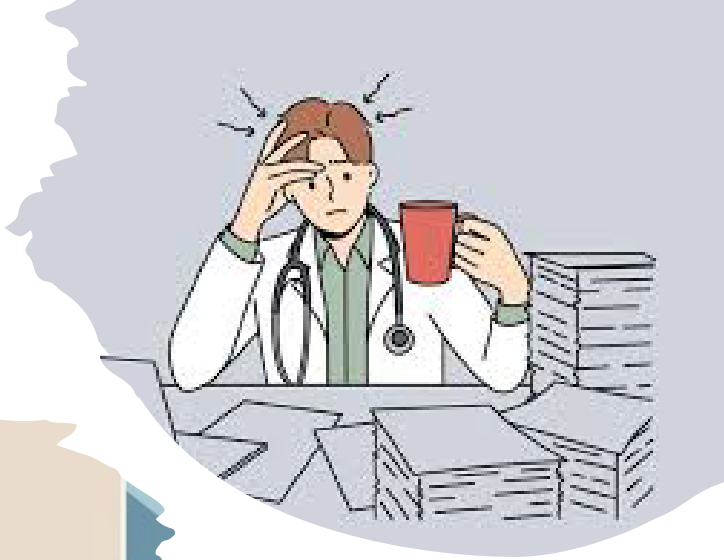
Shared Decision Making for Family Doctors



- Ask ChatCPT for a one-page, patient-facing decision aid adapted to Canadian guidance, reflecting CCS, CUA, AUA–aligned principles to support informed decision-making.

RESEARCH TREATMENT
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