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# TIME TO RETHINK PROSTATE CANCER SCREENING



### **DISCLOSURES**

### Relationships with financial sponsors/grants:

- Regional Cancer Primary Care Lead- Stipend
- Health Care Unburdened Grant
- Prostate Cancer Canada Foundation Grant
- The Sullivan Urology Foundation Grant
- Breast Cancer Canada Grant
- Consultant-Thrive Health
- Honoraria- Astrazenica

### PROSTATE CANCER

- Most common cancer in Canadian men aside from non-melanoma skin cancers.
- 27,900 cases in Canada in 2024
- 22% of all cancers among males
- 3<sup>rd</sup> leading cause of cancer death in Canadian men, ranking behind lung and colorectal cancers only
- 11% of all cancer deaths in men.



### SHOULD WE SCREEN FOR PROSTATE CANCER?



Prostate cancer screening should focus on those with elevated risks, experts say

### PSA prostate-cancer screening does more harm than good, task force says

KELLY GRANT > HEALTH REPORTER
PUBLISHED OCTOBER 27, 2014



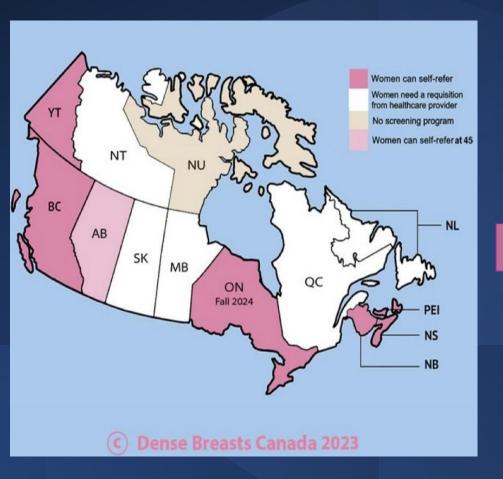
### Trial finds prostate cancer screening for over-50s would save thousands

News

Benefit of early cancer screening proved in trial

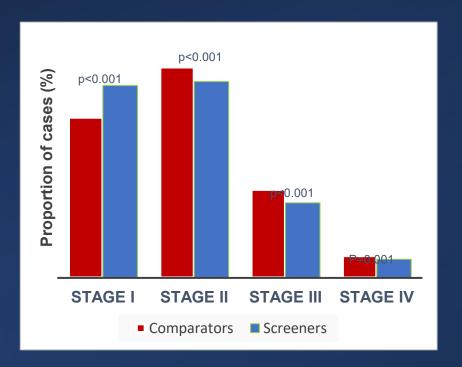


### Screening Debate: Breast Cancer Screening in the 40s

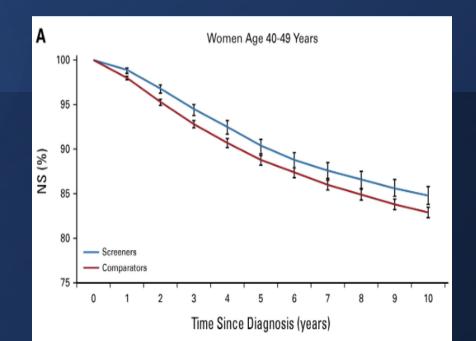




Provincial differences allow assessment of screening outcomes



Earlier stage at diagnosis



Increased Survival

> Wilkinson, A. N. et al. Curr Oncol 29, 5627-5643

### ANOTHER NATURAL EXPERIMENT?

Changing guidelines over time impact uptake and access to PSA screening

#### Recommendation Summary

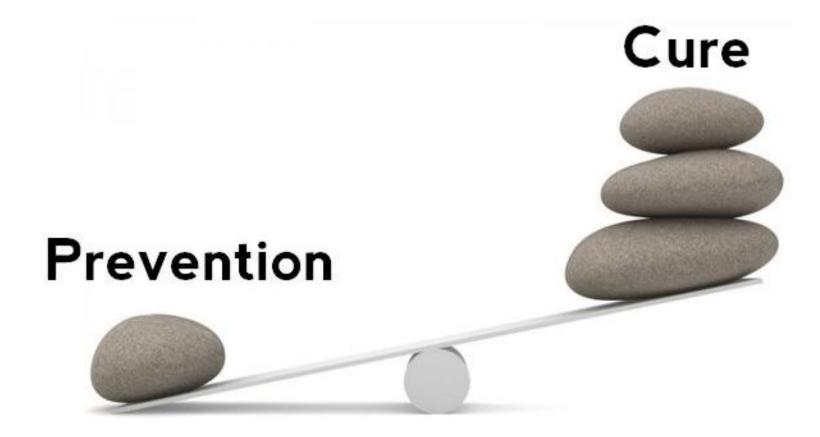
Population	Recommendation	Grade
Men	The U.S. Preventive Services Task Force (US) STF recommends against prostate-specific antigen (PSA)-based screening for prostate cancer.	D

#### Recommendation Summary

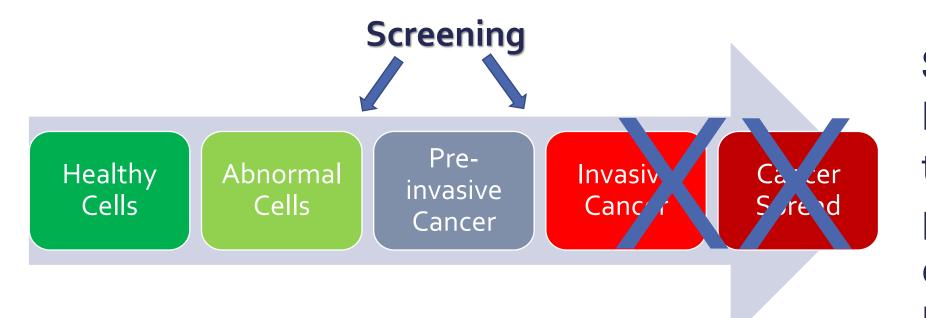
Population	Recommendation	Grade
Men aged 55 to 69 years	For men aged 55 to 69 years, the decision to undergo periodic prostate-specific antigen (PSA)-based screening for prostate cancer should be an individual one. Before deciding whether to be screened, men should have an opportunity to discuss the potential benefits and harms of screening with their clinician and to incorporate their values and prefere less in the decision. Screening offers a small potential benefit of reducing the chance of death from prostate lancer in one men. However, many men will experience potential harms of screening, including fals and sitive results that require additional testing and possible prostate biopsy; overdiagnosis and overtreatment; and treatment complications, such as incontinence and erectile dysfunction. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of family history, race/ethnicity, comorbid medical conditions, patient values about the benefits and harms of screening and treatment-specific outcomes, and other health needs. Clinicians should not screen men who do not express a preference for screening.	C
Men 70 years and older	The USPSTF recommends against PSA-based screening for prostate cancer in men 70 years and older.	D

### CANCER SCREENING

"An Ounce of Prevention is Worth a Pound of Cure"



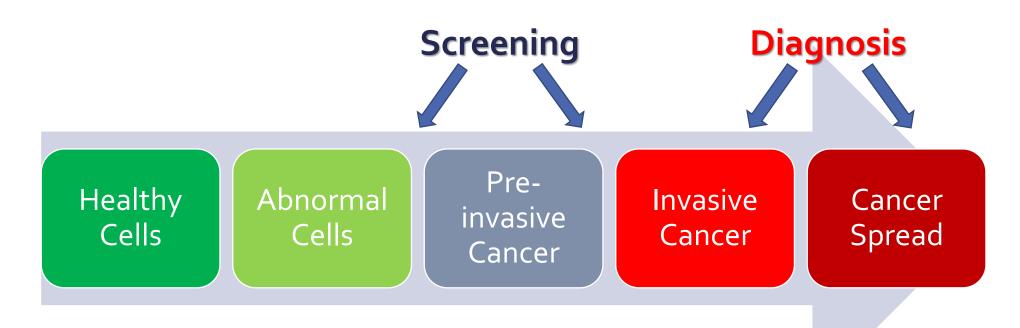
### WHAT IS CANCER SCREENING?



Simple test for a healthy population to find a pre-cancer or early-stage cancer before there are symptoms

### SCREENING VS DIAGNOSIS

- Screening is only when there are no symptoms or signs of illness
- Once there are symptoms or signs, it is Diagnosis



### SCREENING- BENEFITS AND HARMS



### SCREENING IS NOT PERFECT

### **HARMS**

- False positives
- False negatives
- Overdiagnosis



### FALSE POSITIVE

PSA can be increased due to reasons other than cancer:

- Infection
- Prostate enlargement (BPH)
- Vigorous activity
- Can lead to unnecessary biopsies

### FALSE NEGATIVE

- Screening test does not pick up a cancer when it is present
- False reassurance
- Delays

### **OVERDIAGNOSIS**

- Cancers diagnosed which wouldn't have caused an issue
- Most relevant in:
  - older men those with medical issues
  - Indolent disease which would not progress

### OVERTREATMENT

- Unnecessary treatment
- Causes unnecessary side effects like erectile dysfunction, bowel/urinary dysfunction
- Important in the setting of indolent disease

Important to **uncouple** screening and treatment



## SCREENING IS NOT PERFECT... BUT IT'S PRETTY GREAT

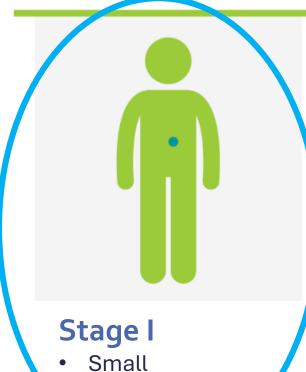
### **BENEFITS**

- Earlier stage at diagnosis
- Decreased morbidity of treatment
- Decreased mortality
- Saves our health system \$\$\$



### BENEFITS OF CANCER SCREENING

Earlier diagnosis= earlier stage



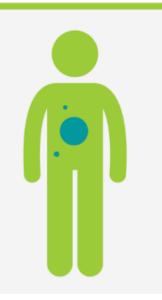
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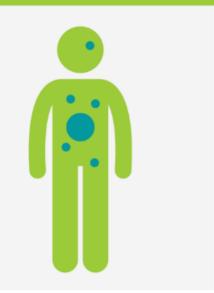
### Stage II

- Larger
- Localised



### Stage III

- Larger
- Regional
- Lymph nodes



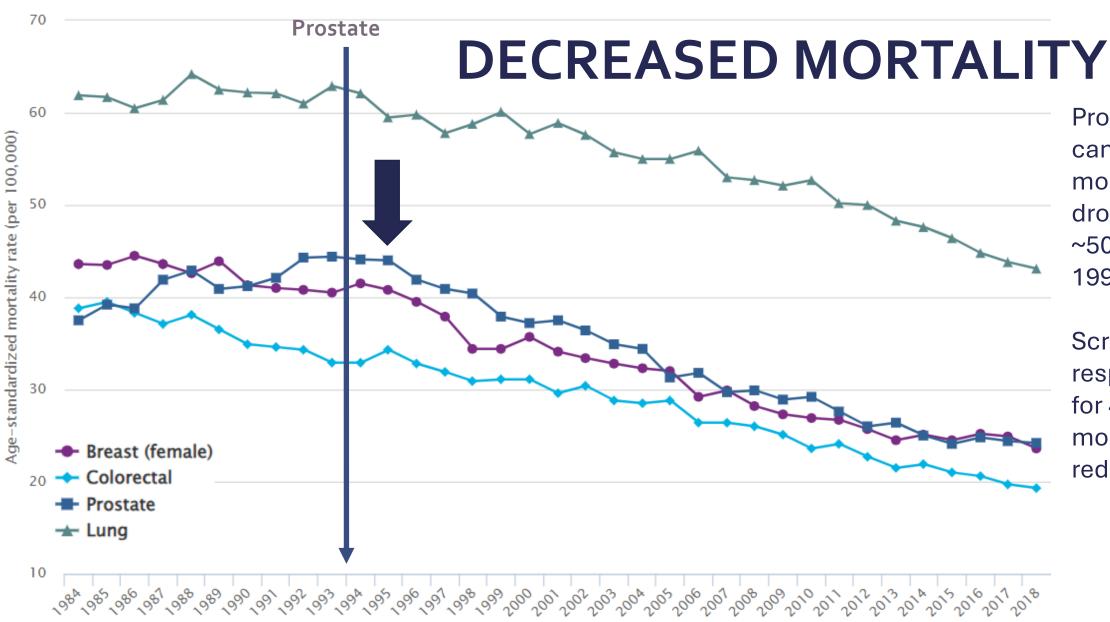
### Stage IV

- Spread to other organs or area of body
- Typically not curable

### BENEFITS: IMPROVED SURVIVAL

5-year survival for prostate cancer by stage:





Prostate cancer mortality has dropped by ~50% since 1993

Screening responsible for 40-70% of mortality reduction

### DCIS ■ Stage I Stage II ■ Stage III ■ Stage IV \$300,000 \$200,000 \$100,000 HR+ HR+/HER2+ HER2+ Breast Cancer Subtype

## DECREASED TREATMENT COSTS

**Breast Cancer Costs** 

\$15K for pre-cancer (DCIS)

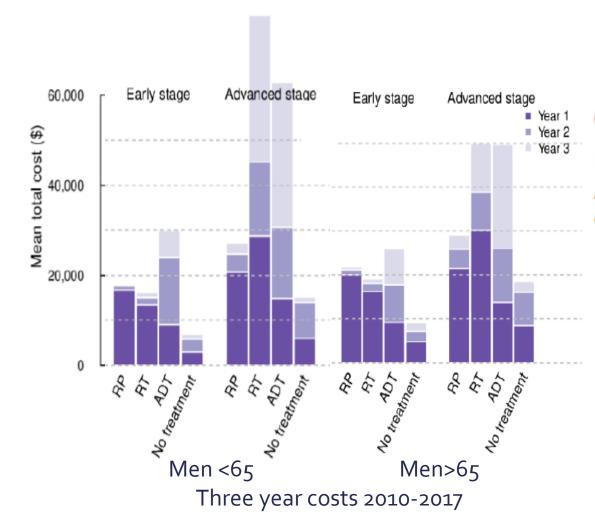
\$30K for Stage I

\$500K for Stage IV

Screening for breast cancer at age 40 SAVES ~\$500 million yearly

What is the Prostate Cancer Equivalent?

### DECREASED TREATMENT COSTS





For some prostate cancer patients, new treatment option ...

Apr 17, 2025 — A radioactive drug delivered by IV that would target his cancer and spare cells, unlike chemotherapy.

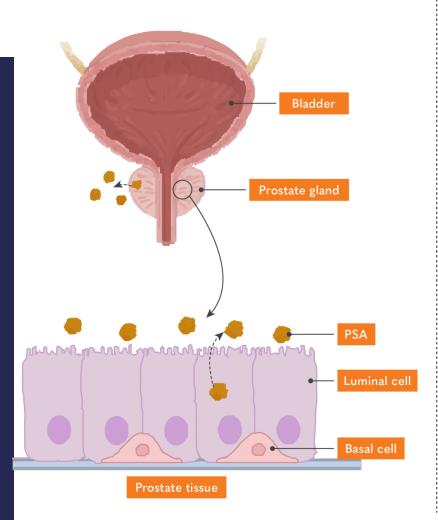
"The list price for Pluvicto is \$27,000 a dose. Patients receive up to six doses, six weeks apart, for a total as high as \$162,000."

Zhang, W., Guh, D. P., Mohammadi, T., Pataky, R. E., Tam, A. C. T., Lynd, L. D., & Conklin, A. I. (2023). Health Care Costs Attributable to Prostate Cancer in British Columbia, Canada: A Population-Based Cohort Study. *Current oncology (Toronto, Ont.)*, 30(3), 3176–3188. https://doi.org/10.3390/curroncol30030240

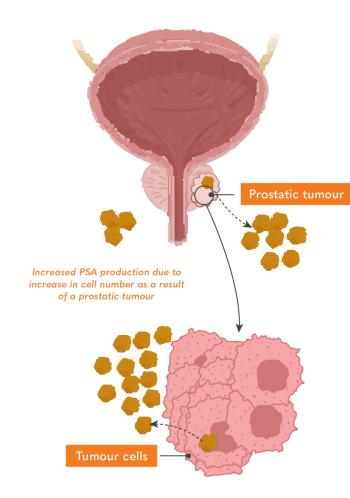
## WHAT IS PSA SCREENING?

- PSA is a protein made by prostate cells
- When there is a prostate cancer, PSA production is increased
- PSA levels in the blood can be used as a screen for prostate cancer

Healthy prostate facilitating normal PSA production



Prostatic tumour resulting in the overproduction of PSA



### THE EVIDENCE BEHIND PSA SCREENING

- ·Prostate Lung Colorectal Ovarian
  - No significant reduction in prostate cancer mortality
  - •BUT! 90% of men in the control arm had PSA testing
- European Randomized Study of Screening for Prostate Cancer
  - •PSA every 4 years
  - •21% prostate cancer relative mortality reduction at 13 years
- Göteborg
  - 44% prostate cancer relative mortality reduction at 14 years
- Kaiser Permanente (retrospective cohort study)
  - •64% reduction in prostate cancer mortality over 16 years
- •Number of men needed to screen to *prevent one death* from prostate cancer
  - -1,410 after 9 years; 570 after 16 years; modelled to be 385 after 25 years
- Participation in major prostate cancer trials has been 96% White men

Compare with breast:
RCT mortality reduction: 15%
Observational trials: ~50%
Number needed to screen:
1333 (50s)

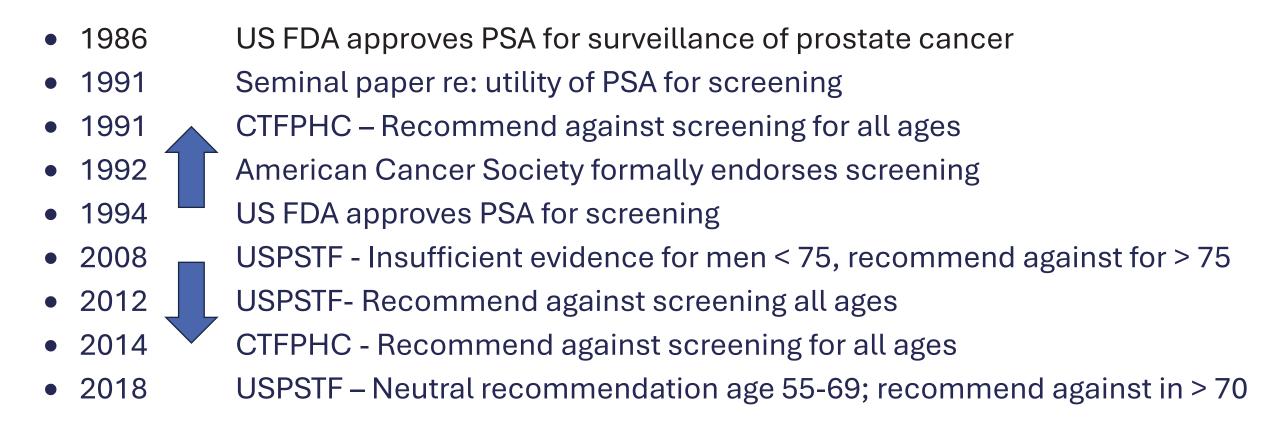
Tsodikov et al., "Reconciling the Effects of Screening on Prostate Cancer Mortality in the ERSPC and PLCO Trials," Ann. Intern. Med., vol. 167, no. 7, pp. 449–455, Oct. 2017, doi: 10.736/m16-2586

F. H. Schröder *et al.*, "Screening and prostate cancer mortality: results of the Europear Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow-up," *The Lancet*, vol. 384, no. 9959, pp. 2027–2035, Dec. 2014, doi: 10.1016/s0140-

Alpert, "New Evidence for the Benefit of Prostate-specific Antigen Screening: Data From 400,887 Kaiser Permanente Patients," *Urology*, vol. 118, pp. 119–126, Aug. 2018, doi: 10.1016/j.urology.2018.02.049.

J. Hugosson *et al.*, "Mortality results from the Göteborg randomised population-based prostate-cancer screening trial," *Lancet Oncol.*, vol. 11, no. 8, pp. 725–732, Aug. 2010, doi: 10.1016/s1470-2045(10)70146-7.

### THE EVOLUTION OF PSA SCREENING



## WHY DID THE US CHANGE THEIR SCREENING RECOMMENDATIONS IN 2018?

- Increasing incidence of prostate cancer in US since 2014
- Increasing rates of aggressive Gleason disease since 2012
- 36.9% Increase in stage IV since 2012
- Stagnating mortality after 2013, with recent increase
- Mortality increases more pronounced in Black men, and those over age 60

J. Presti, S. Alexeeff, B. Horton, S. Prausnitz, and A. L. Avins, "Changes in Prostate Cancer Presentation Following the 2012 USPSTF Screening Statement: Observational Study in a Multispecialty Group Practice," J. Gen. Intern. Med., vol. 35, no. 5, pp. 1368–1374, May 2020, doi: 10.1007/s11606-019-05561-y.

J. C. Hu et al., "Increase in Prostate Cancer Distant Metastases at Diagnosis in the United States," JAMA Oncol., vol. 3, no. 5, p. 705, May 2017, doi: 10.1001/jamaoncol.2016.5465.

<sup>70]</sup> S. S. Butler et al., "Prostate cancer incidence across stage, NCCN risk groups, and age before and after USPSTF Grade D recommendations against prostate-specific antigen screening in 2012," Cancer, vol. 126, no. 4, pp. 717–724, Feb. 2020, doi: 0.1002/cncr.32604.

### WHAT ABOUT CANADA?

- PSA screening never recommended in Canada
- Proximity to US impacts screening activity
- Variable access
  - Publicly funded in many provinces if ordered by a primary care provider
  - Self-pay in Ontario, British Columbia and Quebec.
- Screening is happening!
  - >50% of men have had at least one PSA in their life
- Screening has decreased in recent years
  - 56% relative reduction in PSA in one Ontario health region from 2011 to 2015
  - In US, 18% reduction between 2010 and 2013, and 23.4% decrease between 2010 and 2015.

### CANADIAN GUIDELINES

Guidelines made by the Canadian Task Force on Preventive Health Care

- Drive provincial screening practices
- Inform family doctor recommendations for care

October 2024: Minister Holland calls for External Expert Review (EER) of CTFPHC due to concerns regarding existing guidelines, especially breast cancer screening

Spring 2025: Minister Holland called a temporary pause of the work of the CTFPHC

**June 2025**: EER report: CTFPHC needs to modernisation to ensure equitable, responsive, and adaptable guidelines

**Spring 2026**: Renewed Task Force to be launched

### WHAT ABOUT CANADA?

### Canadian Prostate Cancer Screening Guidelines not revisited since 2014

- Prioritize RCTs
- Include RCT found to have significant contamination
- Strong focus on harms of screening, especially overdiagnosis

"I can tell you a story from my own practice... I screened a man in his 60s, and we found a cancer. He went on to have surgery, and he developed incontinence and impotence.... He probably didn't need the surgery in the first place and then he suffered these complications which really affected his quality of life." (Globe and Mail, July 2025)

 Do not reflect recent advances in screening, diagnosis and treatment which have improved overdiagnosis and overtreatment

Meanwhile, in clinic →

### 2025: NOTYOUR FATHER'S SCREENING...

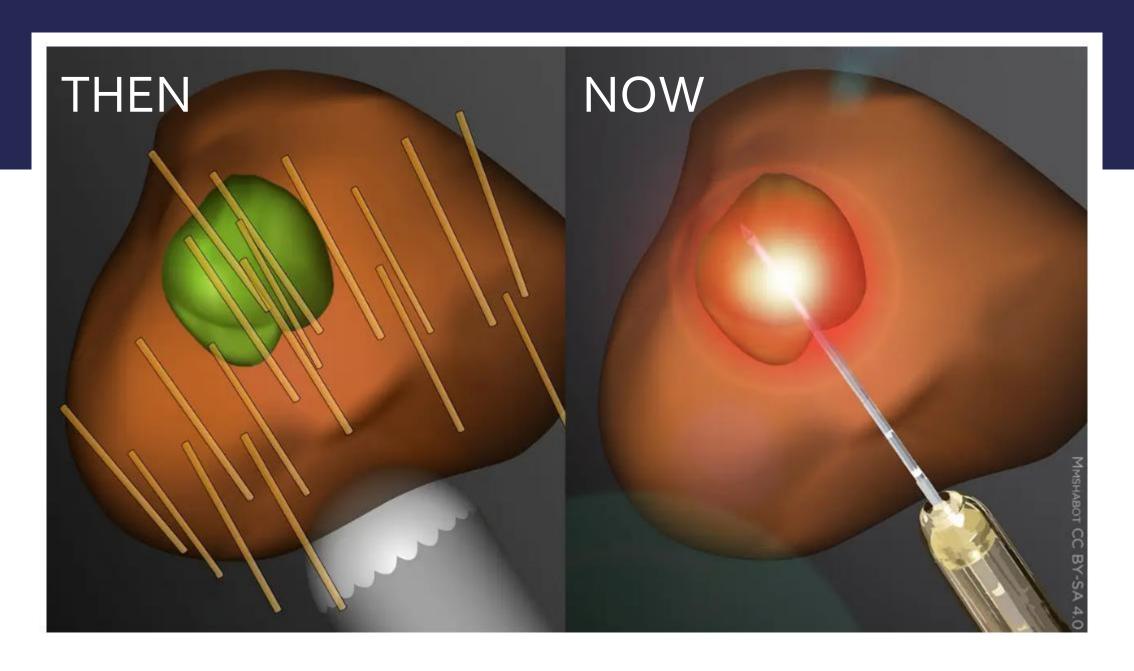
#### - 1990s

If PSA >4 → biopsy → treatment for all

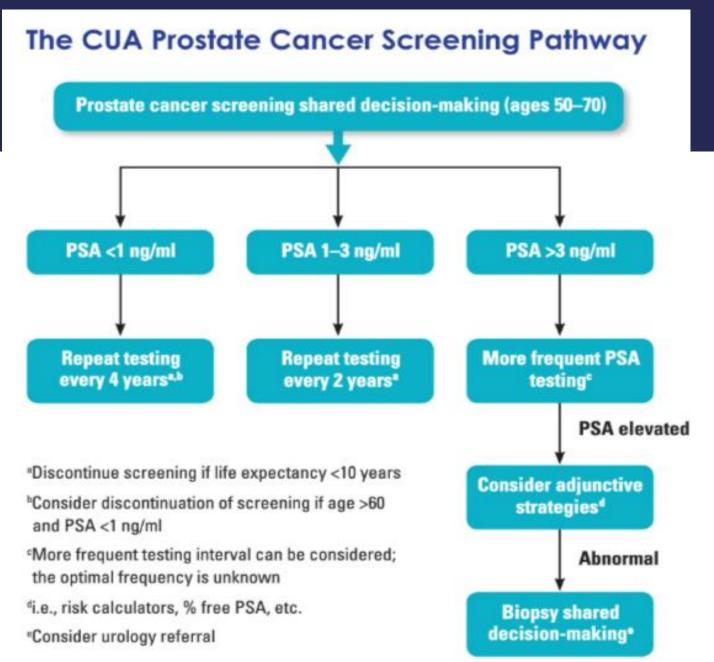
### - 2025

- PSA testing only if life expectancy greater than 10 years
- Longer screening interval
- Repeat PSA (decreases biopsy by 25%)
- Risk assessment with MRI (decreases biopsy by 33%)
- Targeted biopsy
- Trans-perineal biopsy instead of trans-rectal
- Active surveillance- uncoupling diagnosis and treatment





https://www.medpagetoday.com/hematologyoncology/prostatecancer/102117



## CANADIAN PROSTATE CANCER TRENDS IN THE CONTEXT OF PSA SCREENING GUIDELINE CHANGES

- 40 years of Canadian Cancer Registry data
- 543,545 prostate cancer cases, 148,475 prostate cancer deaths
- Total population 50-74, 5 year age bands
- Incidence
- Mortality
- Stage
- Net survival (Cancer-specific survival, in absence of other causes of death)
- No PSA/Gleason data
- Multidisciplinary team: Statistical and Clinical expertise
   (Statistics Canada, Dr. Michael Ong, Dr. Scott Morgan, Dr. Chris Morash, Dr. Rodney Breau, Dr. Larry Goldberg, Dr. Anna Wilkinson)

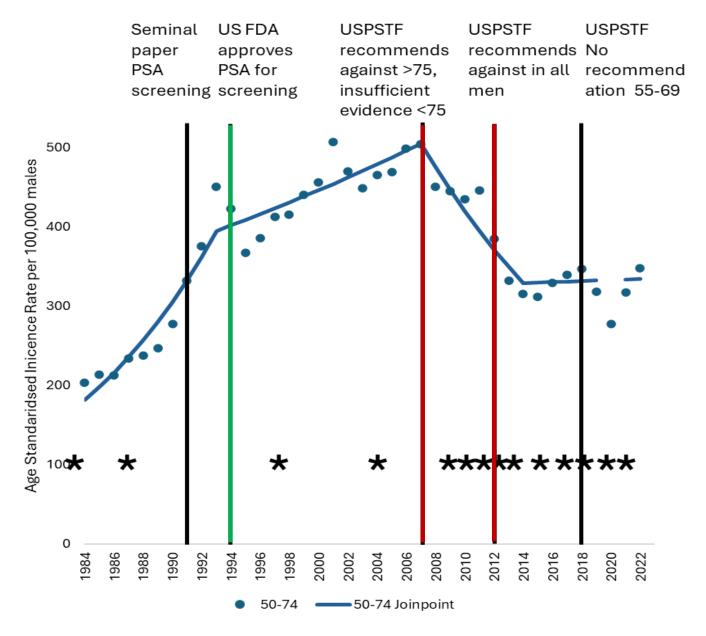


#### Incidence rate (per 100,000 men) <del>-</del>2007 **-**2014 <del>--</del>2022 60 to 75 to 80 to 85+ Age Group

### IMPACTS OF PSA SCREENING

## 750 Age specific Mortality rate (per 100,000 men) 150 50 to 54 55 to 59 60 to 64 65 to 69 70 to 74 75 to 79 80 to 84 Age Group **—** 1993 **—** 2007 **—** 2014 **—** 2023

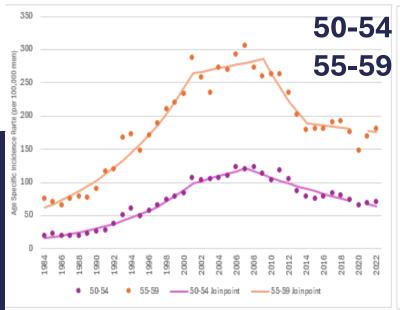
### IMPACTS OF PSA SCREENING

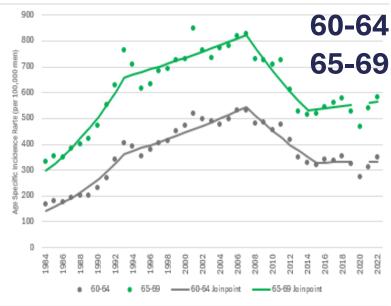


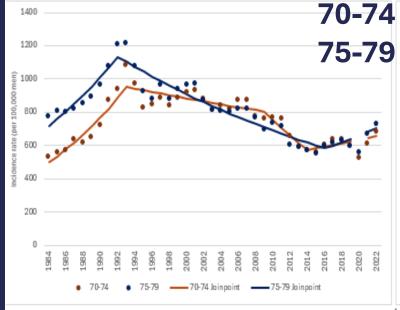
**Incidence Ages 50-74** 

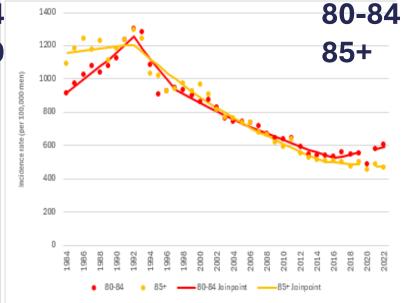
## INCIDENCE BY AGE

- In men 75 and older, peak incidence prior to screening onset, continual decline in incidence after screening
- Highest increase: 11% per year for 60-64
- 80-84-59% decrease in incidence 1992-2016.
   Significantly increasing 2016-2022
- Suggests screening was not simply "overdiagnosing" cases in older men with limited life expectancy



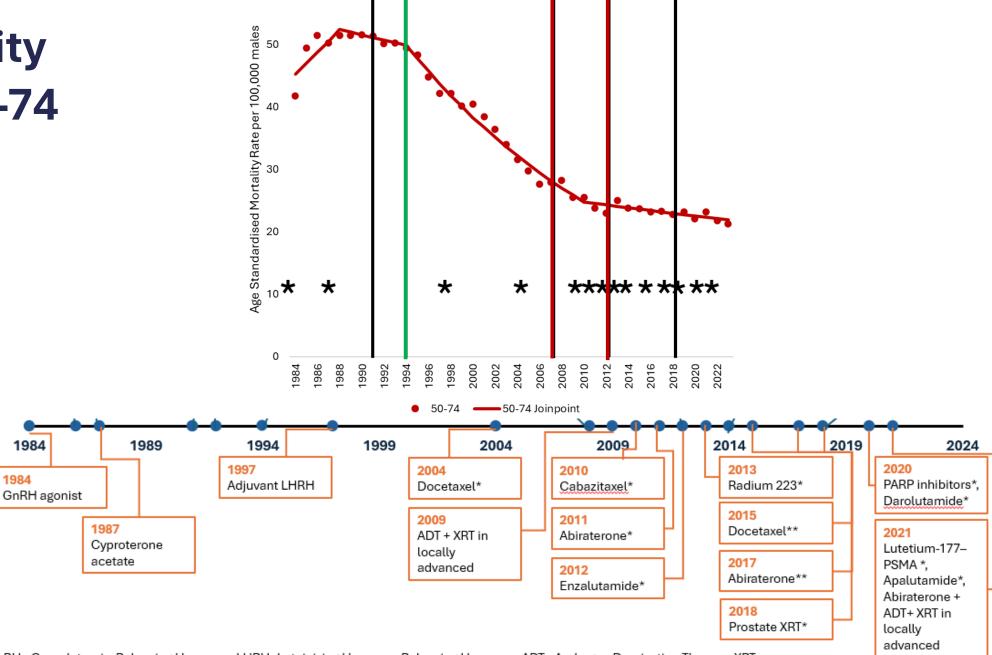






### **Mortality** Age 50-74

1984



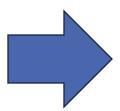
GnRH= Gonadotropin-Releasing Hormone; LHRH=Luteinizing Hormone-Releasing Hormone; ADT= Androgen Deprivation Therapy; XRT=

## CHANGES IN PROSTATE CANCER MORTALITY

#### 50-74

- 59% decrease 1990-2023
- 50% decrease 1990-2010

(only 9% decrease since 2010)



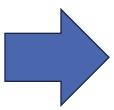
1990: 51.5 deaths/100,000 men

2010: 25.5 deaths/100,000 men

2023: 21.3 deaths/100,000 men

#### 75+

- Increasing mortality until 1995
- 37% decrease 1995-2012
- 15% decrease 2013-2023



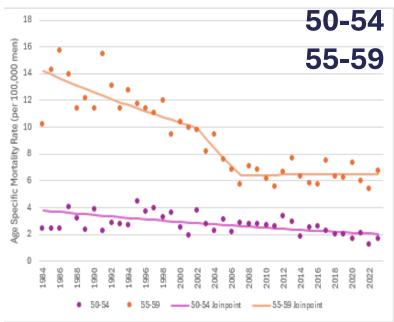
1995: 512.7 deaths/100,000 men

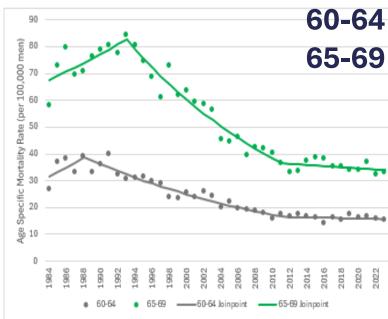
2012: 324.7 deaths/100,000 men

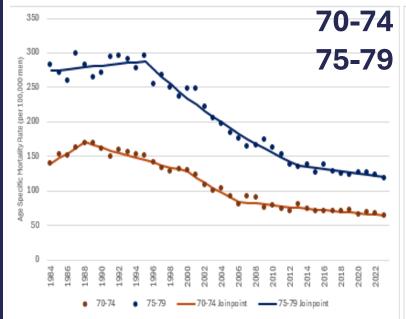
2023: 275.7 deaths/100,000 men

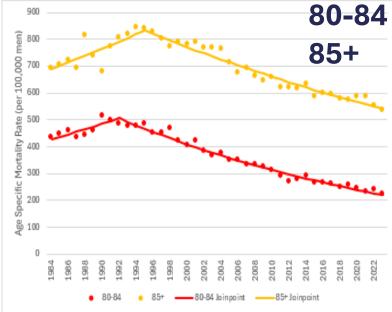
### MORTALITY BY AGE

- Mortality declined continuously from peak until 2013 in older men
- After 2013, mortality decline flattens out and no longer significant
- 90% of mortality reduction occurred before flattening out
- Significant mortality reductions in all age groups suggests cancers were not overdiagnosed









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## CHANGE IN STAGE IV

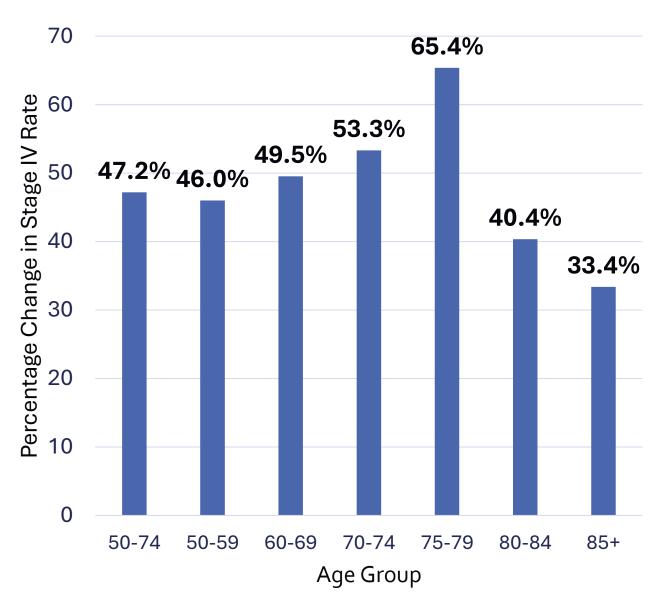
#### From 2010-2017

- Stage I-III rates only significantly decreased in ages 50-59 and 85+
- Stage IV rates increased significantly in 50-74 and 75+

#### From 2010-2021

- ~50% increase in rate of stage
   IV ages 50-74
- Largest increase in 75-79:65.4%

### Percent Increase in Stage IV Prostate Cancer 2010-2021



### SURVIVAL BY STAGE

 Survival by stage remained stable or increased over time (2011-2017)

Stage I-III remain ~100%

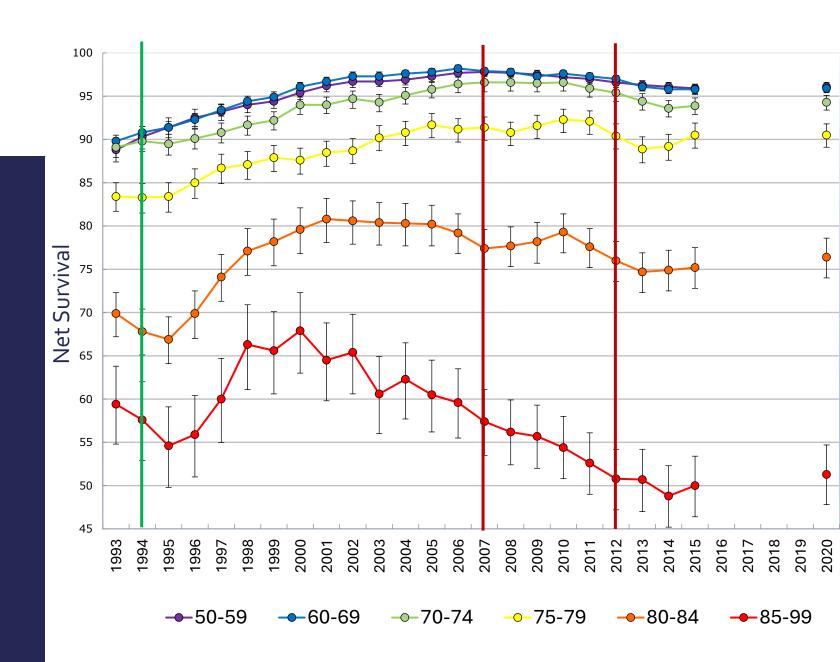
Stage IV survival increases, reflecting treatment innovations

• 50-74: 49.4% → 56.6%

• 75+: 26.6% → 29.2%

### **NET SURVIVAL**

- Survival increased after the early 1990's by ~8 percentage points
- Survival peaked ~ 2007
- Survival decreased after this time
- Most recent survival lower than ~20 years ago
- Decreased survival due to increasing proportion of stage IV cases



### **BOTTOM LINE**

- This study uses national cancer data to audit the impacts of screening guideline changes
- Prostate cancer trends in Canada reflect US PSA screening recommendations
- After screening became widespread, prostate cancer diagnosis shifted to an earlier age. Cases increased rapidly in younger men and decreased among men 75 and older
- Prostate cancer mortality dropped by over 50% after screening started,
   with the biggest changes seen among men in their late 50s and 60s

### **BOTTOM LINE**

- After US recommendations against screening, mortality reductions lessened and stage IV increased among both younger and older men
- Stage IV increased by about 50% among men 50-74
- Despite multiple new life prolonging treatments for patients which have increased survival in stage IV cancer, overall survival has decreased due to increasing incurable cases



### TO PSA OR NOT?

- In absence of formal screening recommendations in Canada, screening is opportunistic
- Opportunistic screening = screening without guardrails. Drives:
  - Inequity
  - Inappropriate practices
  - Limits ability to implement innovations to decrease overdiagnosis/overtreatment
- If we restrict to just those "high risk" we will miss majority of cases

### THAT WAS THEN... THIS IS NOW

- Time to stop measuring PSA screening based on practices of yesteryear
- Time to acknowledge the significant strides which have been made to minimise overdiagnosis and treatment.
- Time to acknowledge the rise in potentially preventable stage IV prostate cancer in men of all ages, with its financial burden, pain, suffering and lives cut short
- Time to focus less on overdiagnosis and more on **underdiagnosis**
- Time to rethink prostate cancer screening.



### QUESTIONS

