Prostate Cancer Screening in 2026

KARIM MARZOUK MD FRCSC

Presenter Disclosure

Relationships with financial sponsors:

- Speakers Bureau/Honoraria: Bayer, Knight, Tersera
- Advisory Boards: Tolmar

Artificial Intelligence (AI) Disclosure:

- n/a

Asking the Right Questions

Should Canadian men be screened for prostate cancer ?

What age should screening begin ?

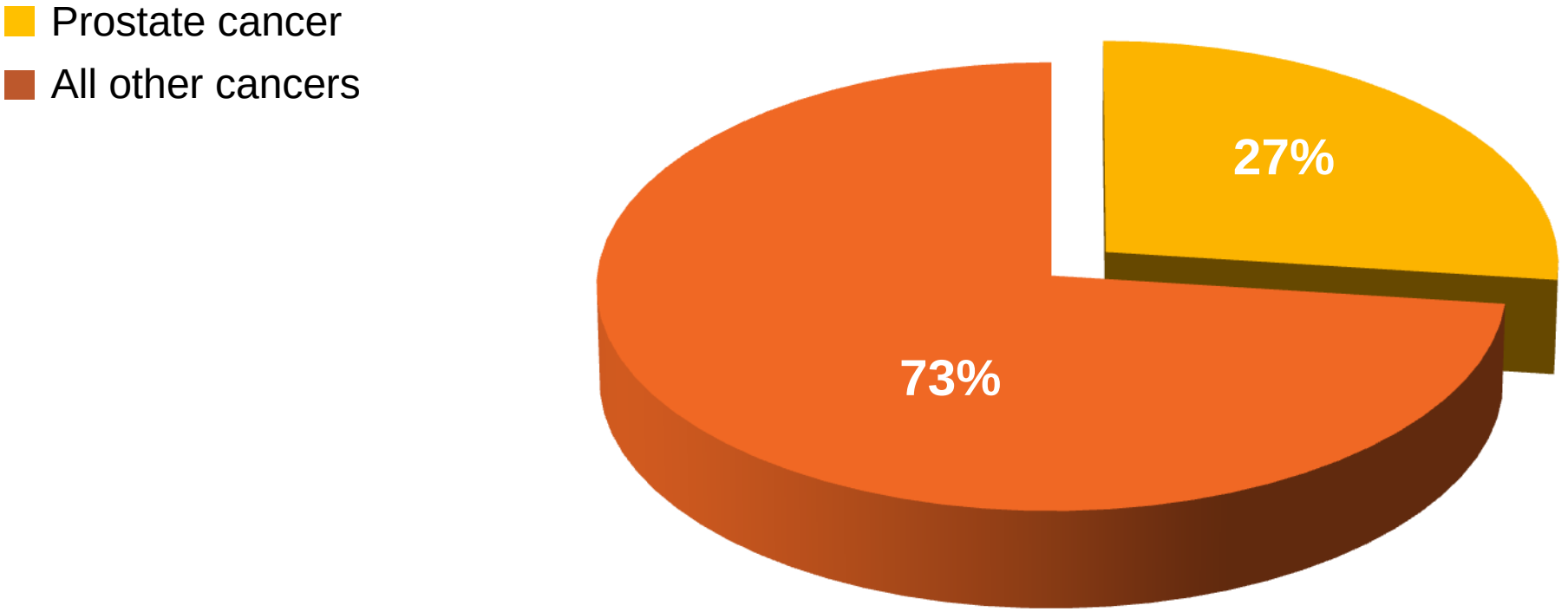
How often should screening be performed?

When can screening be stopped?

Why Prostate Cancer Screening is Important

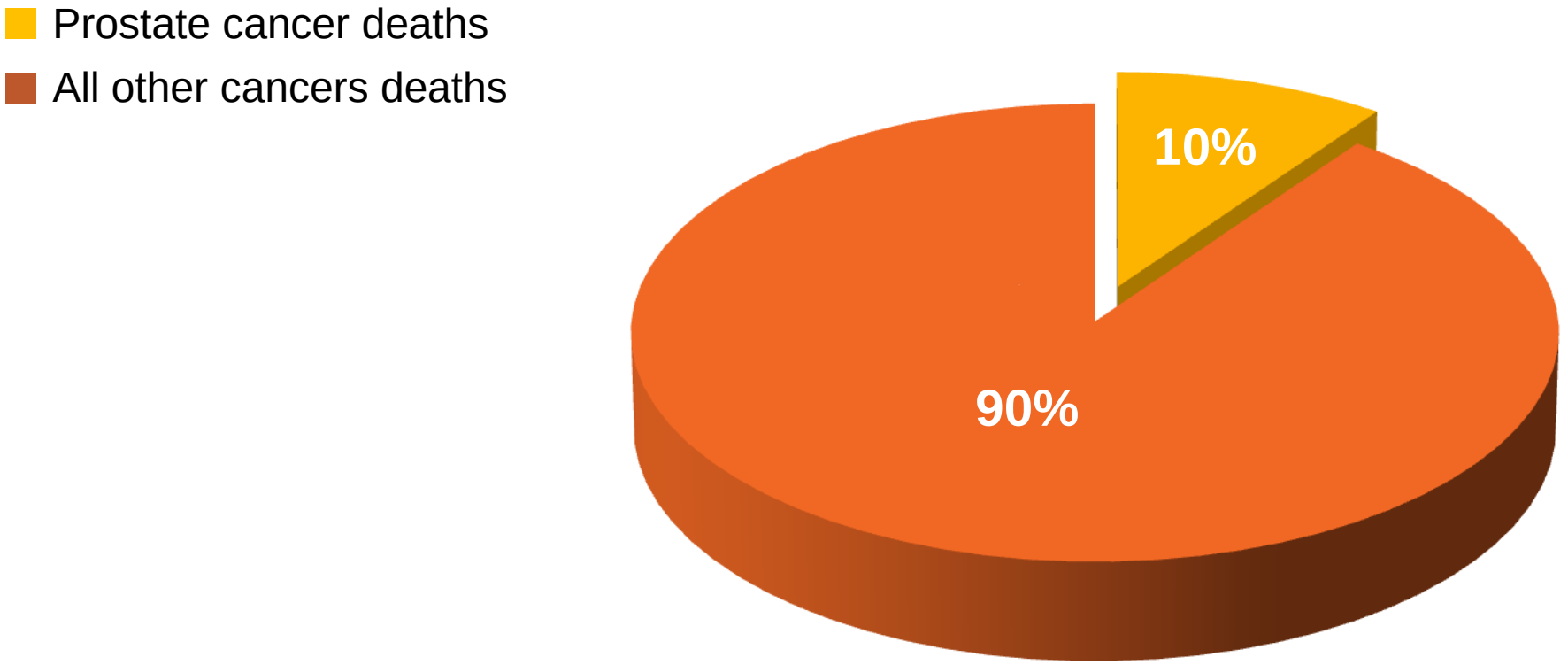
The most common male malignancy

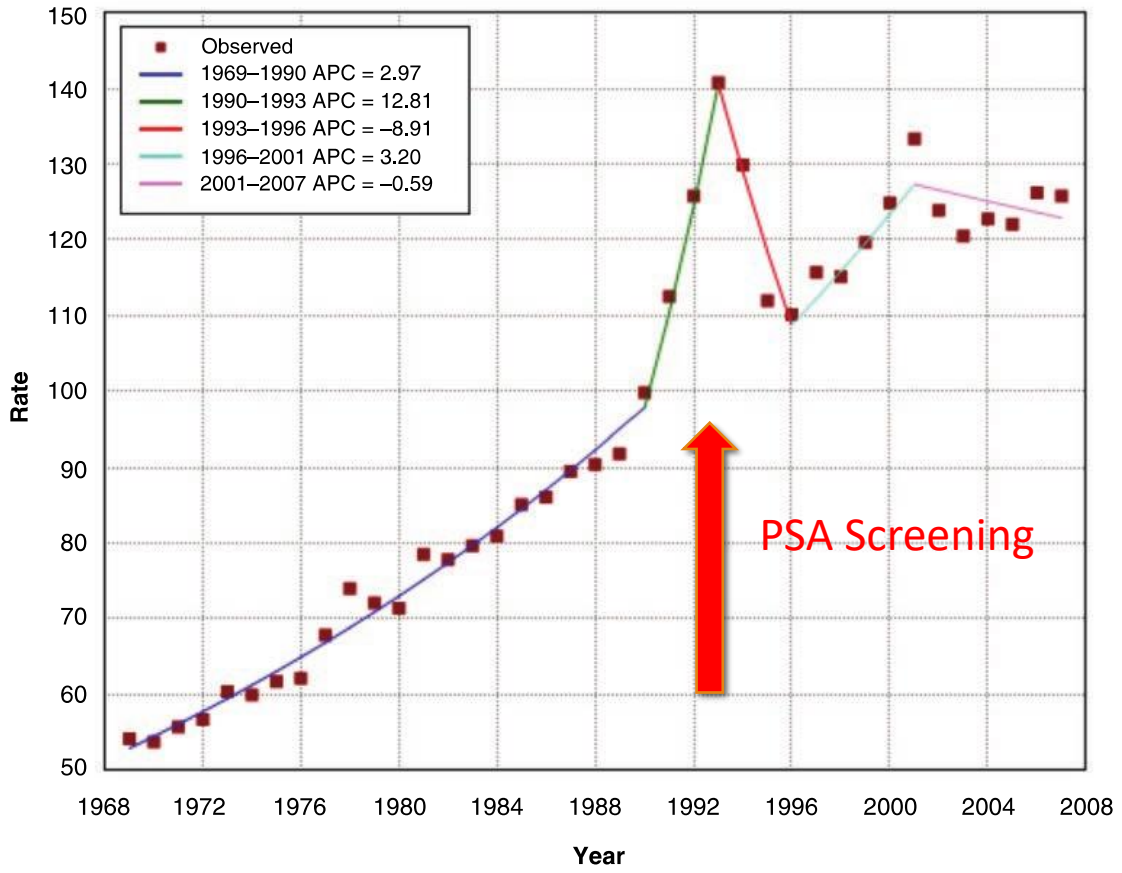
29,300 Canadian men



Why Prostate Cancer Screening is Important

2nd leading cause of cancer death
5000 deaths annually





Age standardized incidence & annual percent change of prostate cancer incidence in Canada

Dickenson et al. CMAJ Open. (2016)

PSA screening & prostate cancer mortality

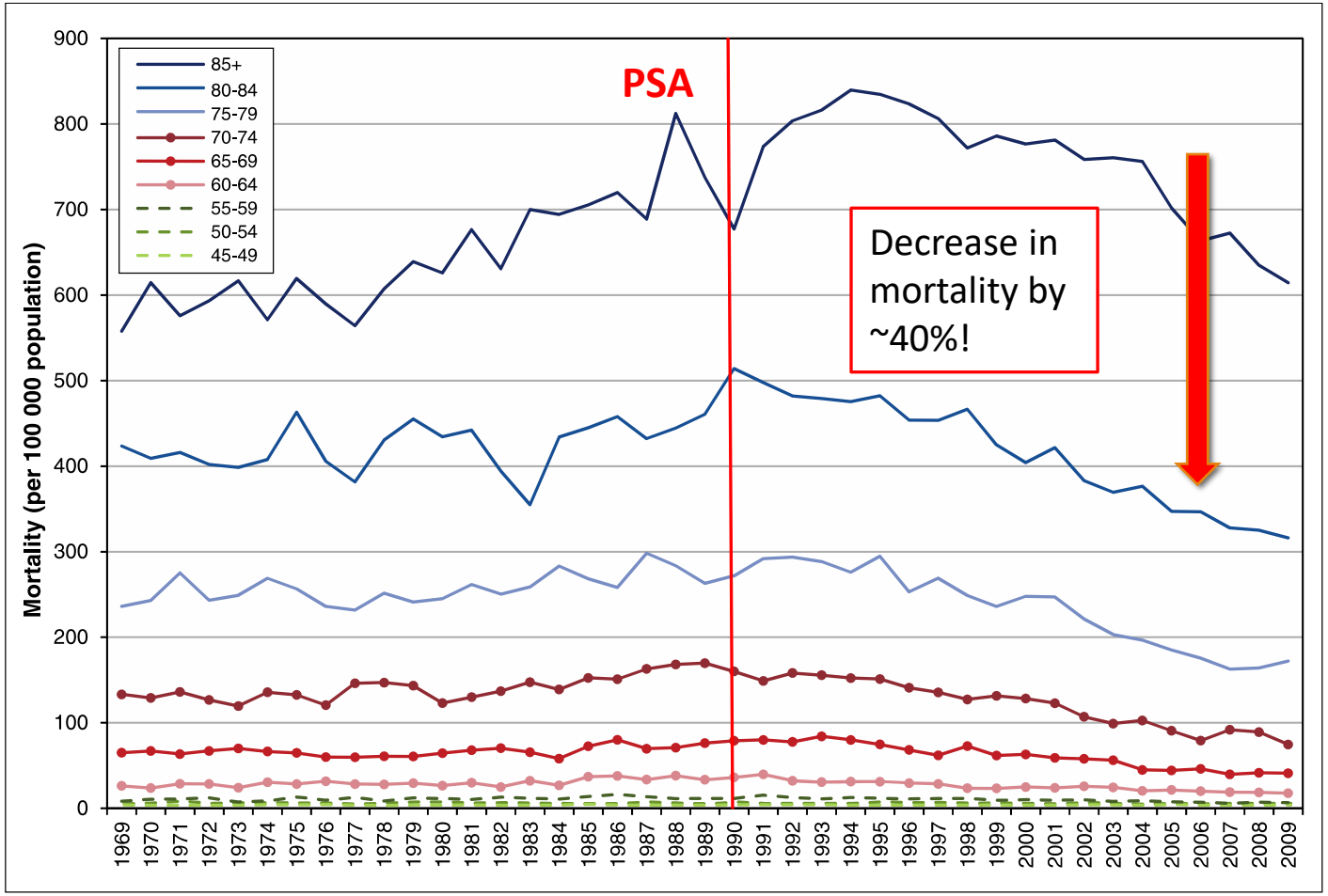


Figure 5: Mortality by age group, 1969–2009, Canada.

Dickenson et al. CMAJ Open. (2016)

CMAJ GUIDELINES CME

Recommendations on screening for prostate cancer with the prostate-specific antigen test

Canadian Task Force on Preventive Health Care*

The recommendations apply to all men without a previous diagnosis of prostate cancer.

- For men aged less than 55 years, we recommend not screening for prostate cancer with the prostate-specific antigen (PSA) test. (*Strong recommendation*; *low-quality evidence.*)
- For men aged 55–69 years, we recommend not screening for prostate cancer with the PSA test. (*Weak recommendation*; *moderate-quality evidence.*)
- For men 70 years of age and older, we recommend not screening for prostate cancer with the PSA test. (*Strong recommendation*; *low-quality evidence.*)

Acknowledging the harms of screening

Screening has not been selective

- screening of elderly men with a short life expectancy

Large proportion of cancers diagnosed by screening are low-risk

- Likely clinically insignificant

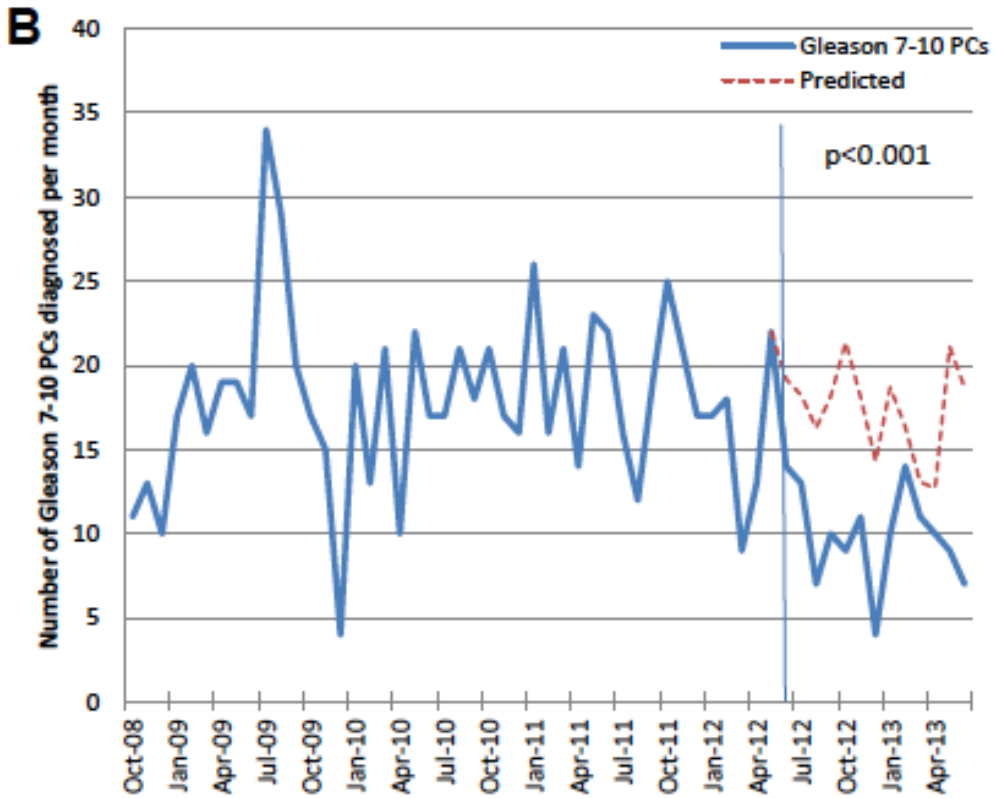
Too liberal criteria for biopsy

- Sepsis rates are increasing

Too aggressive treatment of low-risk cancer

- Historical underutilization of active surveillance

Impact of Task Force Recommendations

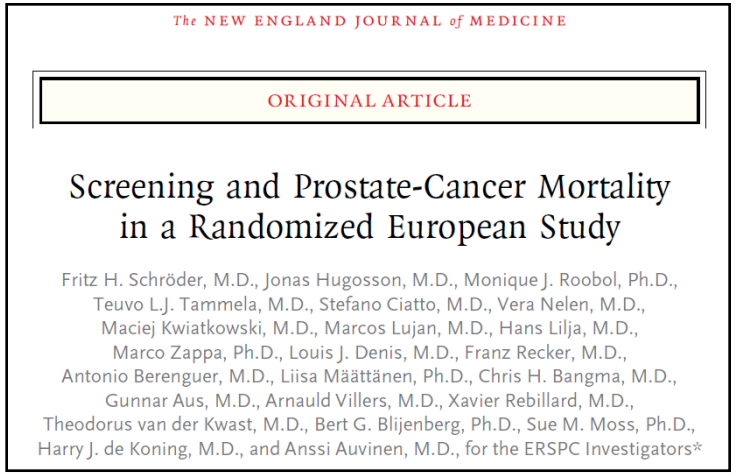


Bhindi B et al. J Urol 2015;193:1519-1524

Should Canadian men be screened for prostate cancer ?



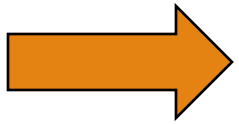
Two Major PSA Screening Trials


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Screening and Prostate-Cancer Mortality in a Randomized European Study

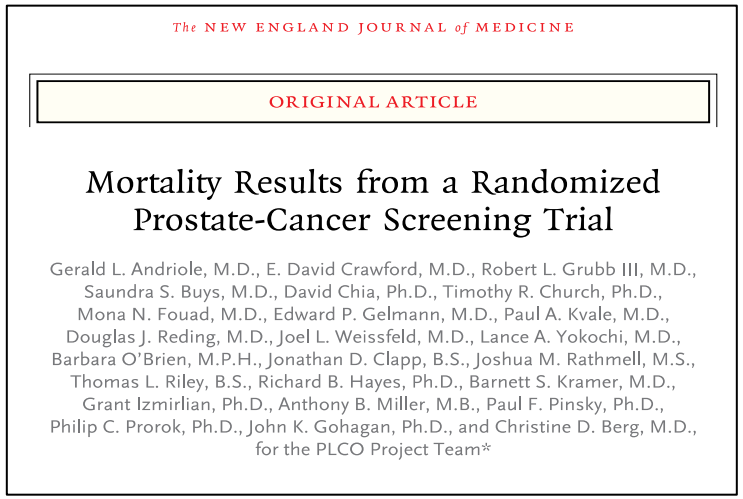
Fritz H. Schröder, M.D., Jonas Hugosson, M.D., Monique J. Roobol, Ph.D., Teuvo L.J. Tammela, M.D., Stefano Ciatto, M.D., Vera Nelen, M.D., Maciej Kwiatkowski, M.D., Marcos Lujan, M.D., Hans Lilja, M.D., Marco Zappa, Ph.D., Louis J. Denis, M.D., Franz Recker, M.D., Antonio Berenguer, M.D., Liisa Määttänen, Ph.D., Chris H. Bangma, M.D., Gunnar Aus, M.D., Arnauld Villers, M.D., Xavier Rebillard, M.D., Theodorus van der Kwast, M.D., Bert G. Blijenberg, Ph.D., Sue M. Moss, Ph.D., Harry J. de Koning, M.D., and Anssi Auvinen, M.D., for the ERSPC Investigators*



182,000 men, age 55-69

PSA q4 years

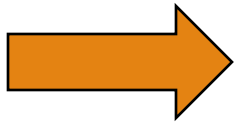
21% reduction in PCa mortality


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Mortality Results from a Randomized Prostate-Cancer Screening Trial

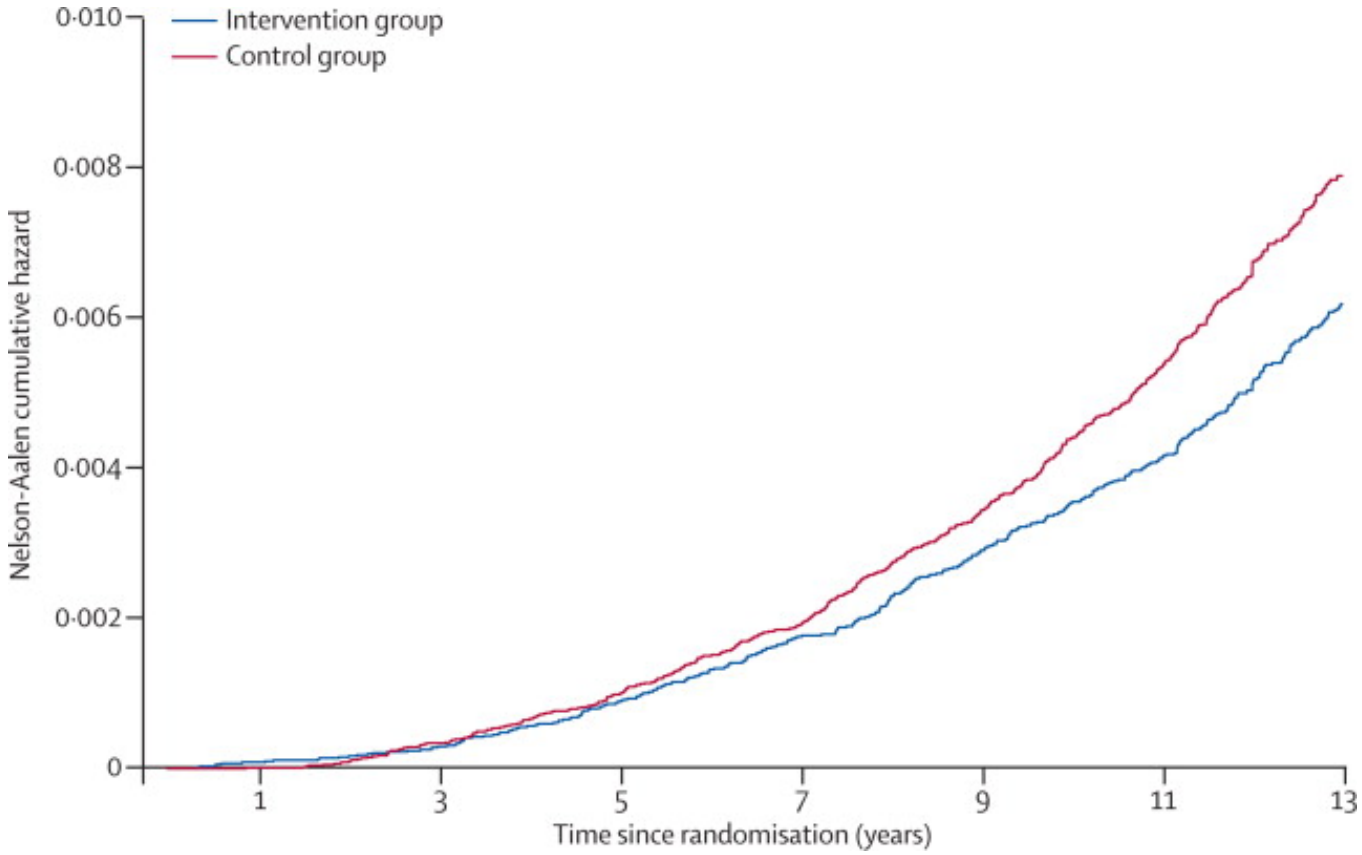
Gerald L. Andriole, M.D., E. David Crawford, M.D., Robert L. Grubb III, M.D., Saundra S. Buys, M.D., David Chia, Ph.D., Timothy R. Church, Ph.D., Mona N. Fouad, M.D., Edward P. Gelmann, M.D., Paul A. Kvale, M.D., Douglas J. Reding, M.D., Joel L. Weissfeld, M.D., Lance A. Yokochi, M.D., Barbara O'Brien, M.P.H., Jonathan D. Clapp, B.S., Joshua M. Rathmell, M.S., Thomas L. Riley, B.S., Richard B. Hayes, Ph.D., Barnett S. Kramer, M.D., Grant Izmirlian, Ph.D., Anthony B. Miller, M.B., Paul F. Pinsky, Ph.D., Philip C. Prorok, Ph.D., John K. Gohagan, Ph.D., and Christine D. Berg, M.D., for the PLCO Project Team*



76,683 men, age 55-74

PSA annually

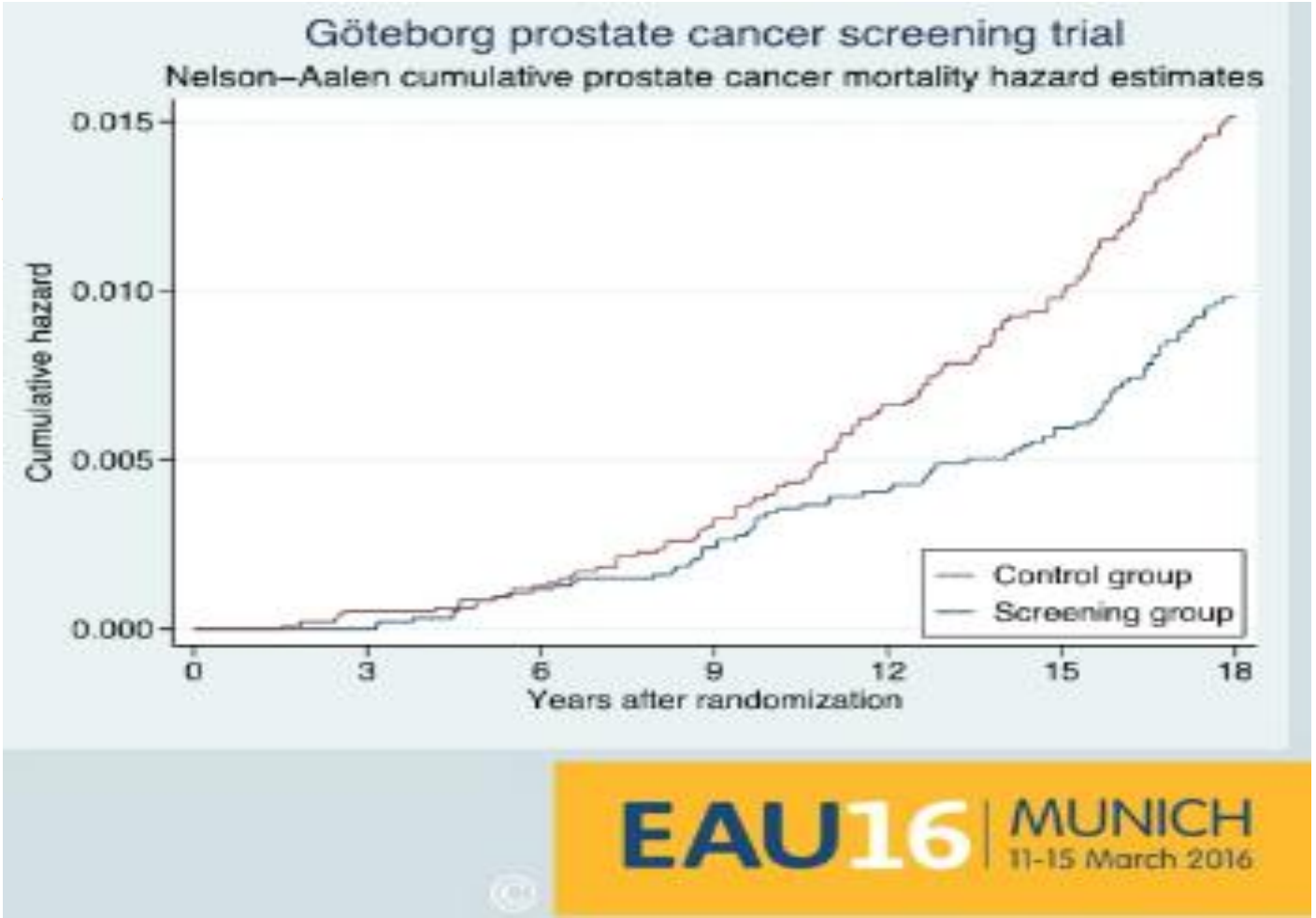
No difference in PCa mortality



ERSPC Trial
13 year f/u

Schroder F et al. The Lancet 2014;384:6-12

Prostate cancer deaths reduced by ≈ 40% at more than 14 years follow-up in Göteborg trial



42%

RR 0.65 at 18 years
(95% CI 0.49-0.87)
S: 0.98%
C: 1.50%

NNS = 139
NND = 13

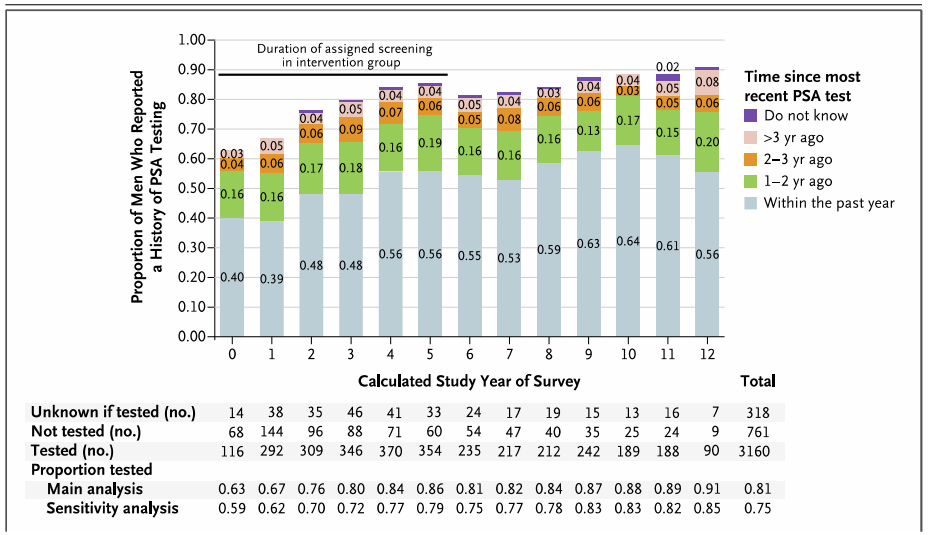
Hugosson, Carlsson, Lilja et al. *Lancet Oncol.* 2010;11:725-32.
Arnsrud Godtman R, et al. *EAU annual meeting* 2016.

Why the discrepancy with PLCO?

High contam

Opportunistic vs. Organized screening !!

The NEW ENGLAND JOURNAL of MEDICINE



Unknown if tested (no.)	14	38	35	46	41	33	24	17	19	15	13	16	7	318
Not tested (no.)	68	144	96	88	71	60	54	47	40	35	25	24	9	761
Tested (no.)	116	292	309	346	370	354	235	217	212	242	189	188	90	3160
Proportion tested														
Main analysis	0.63	0.67	0.76	0.80	0.84	0.86	0.81	0.82	0.84	0.87	0.88	0.89	0.91	0.81
Sensitivity analysis	0.59	0.62	0.70	0.72	0.77	0.79	0.75	0.77	0.78	0.83	0.83	0.82	0.85	0.75

Years of study	PSA test in Controls PLCO
0-5	78.9%
6-17	85.9%

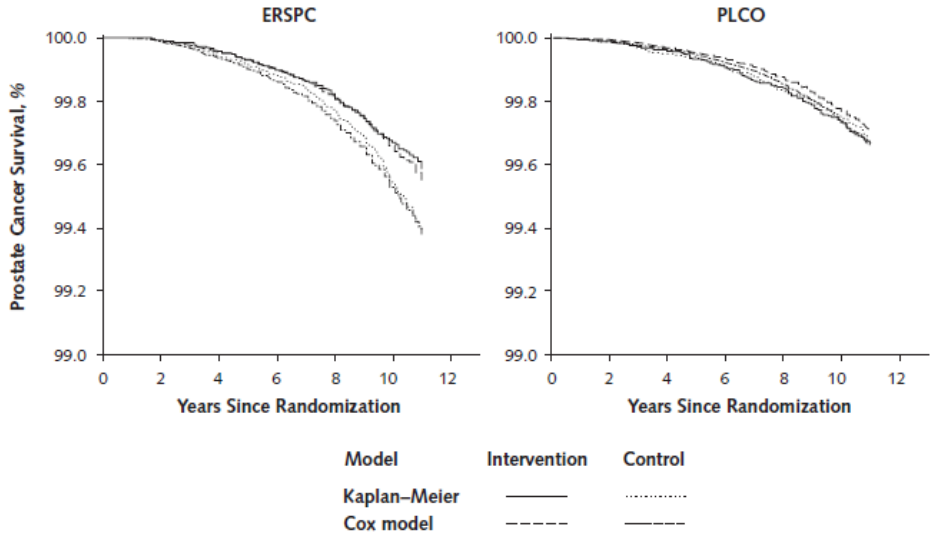
Shoag J et al NEJM 2016;374:18
Pinsky et al Cancer 2017;123:592-599

Annals of Internal Medicine ORIGINAL RESEARCH

Reconciling the Effects of Screening on Prostate Cancer Mortality in the ERSPC and PLCO Trials

Alex Tsodikov, PhD; Roman Gulati, MS; Eveline A.M. Heijnsdijk, PhD; Paul F. Pinsky, PhD; Sue M. Moss, PhD; Sheng Qiu, MS; Tiago M. de Carvalho, MS; Jonas Hugosson, MD; Christine D. Berg, MD; Anssi Auvinen, MD; Gerald L. Andriole, MD; Monique J. Roobol, PhD; E. David Crawford, MD; Vera Nelen, MD; Maciej Kwiatkowski, MD; Marco Zappa, PhD; Marcos Luján, MD; Arnauld Villers, MD; Eric J. Feuer, PhD; Harry J. de Koning, MD; Angela B. Mariotto, PhD; and Ruth Etzioni, PhD

Figure 2. Prostate cancer survival from randomization in the ERSPC and PLCO, estimated by Kaplan–Meier or Cox regression model using mean lead time estimated with the empirical approach.



Similar reduction in prostate cancer specific mortality in both PLCO and ERSPC

Revised USPSTF Recommendations

U.S. Preventive Services TASK FORCE

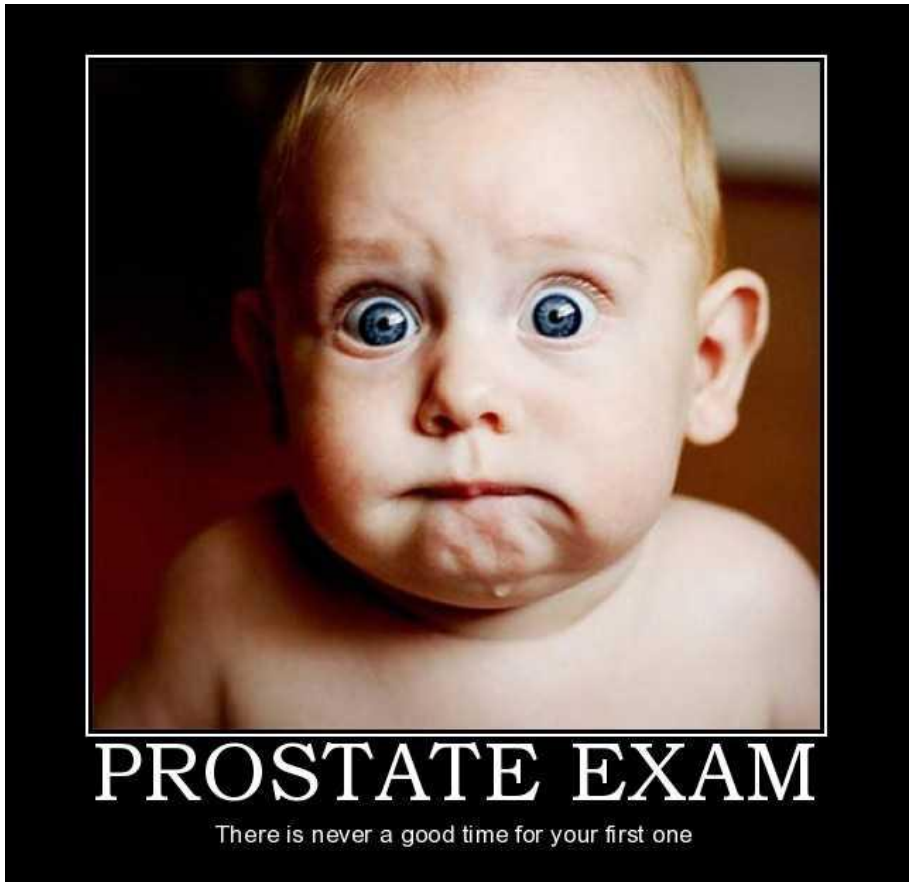
May 2018

Draft: Recommendation Summary

Population	Recommendation	Grade (What's This?)
Men ages 55 to 69 years	The USPSTF recommends that clinicians inform men ages 55 to 69 years about the potential benefits and harms of prostate-specific antigen (PSA)– screening for prostate cancer after discussion with a clinician, so that each man has an opportunity to understand the potential benefits and harms of screening and to incorporate his values and preferences into his decision.	C ?

Canadian Task Force on Preventive Health Care

What age should screening begin ?



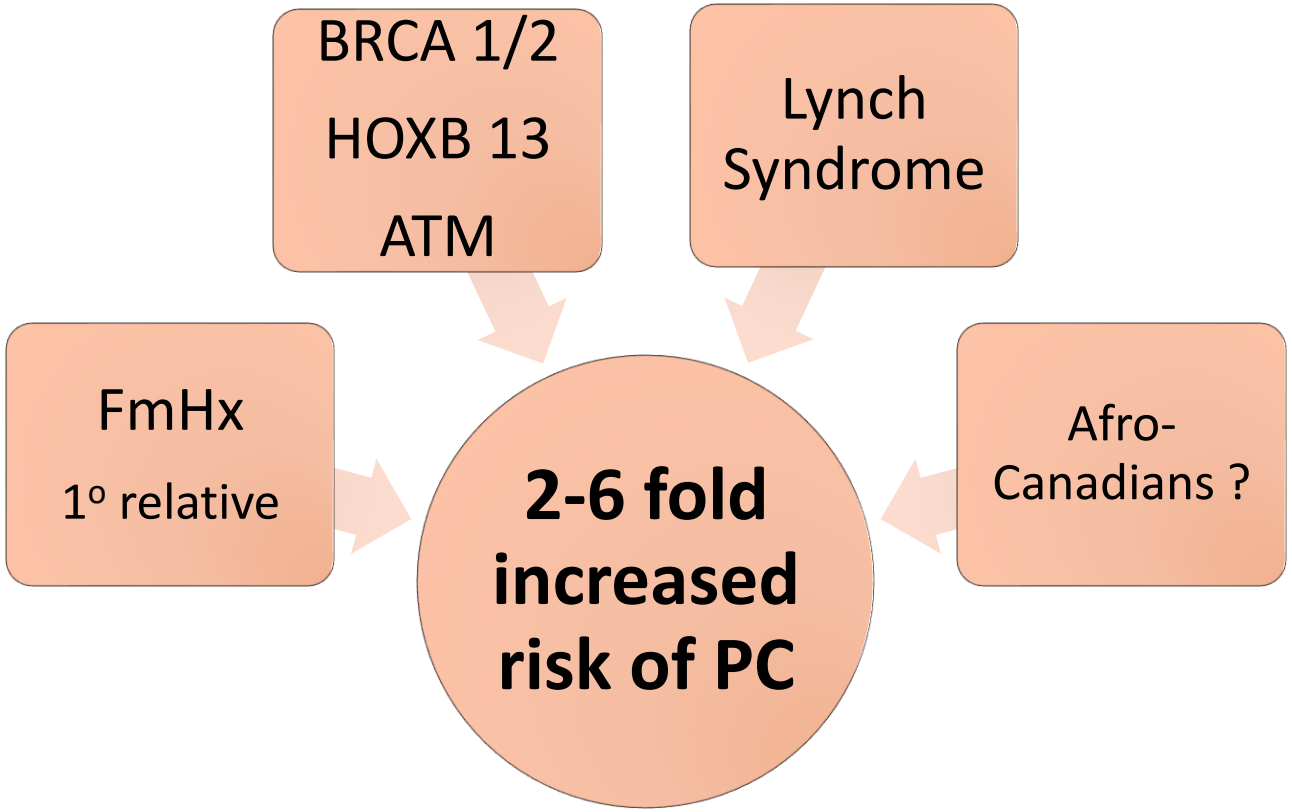
When to start screening

Guideline	CUA	NCCN	MSKCC	EAU-ESTRO	ASCO, ACS, ACP	AUA, USPSTF (draft)
Age	50	40-45	45	50; 45 if family history or African-American	50	55

Basis for CUA recommendations

Goteborg – “Level 1” evidence for benefits starting at age 50

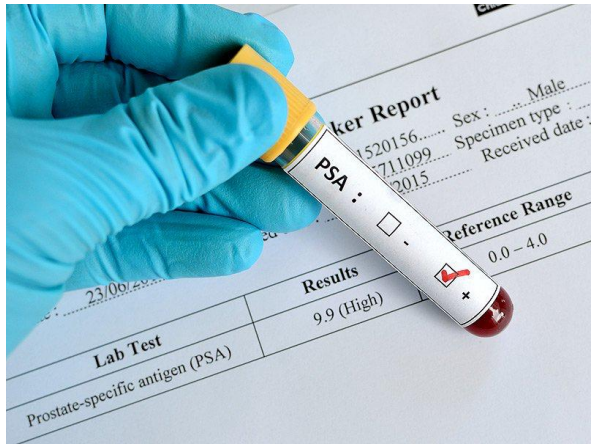
High risk populations



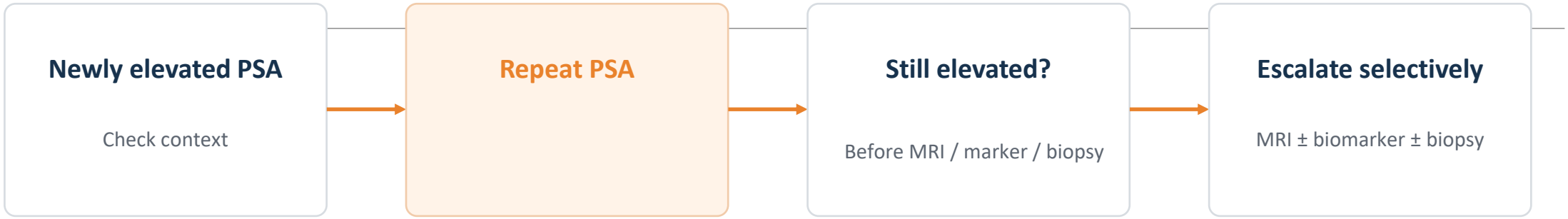
Consider screening earlier: 40-45 yrs

How to screen ?





A newly elevated PSA is a signal to repeat—not a biopsy order



25–40%

of newly elevated PSA values normalize on repeat testing

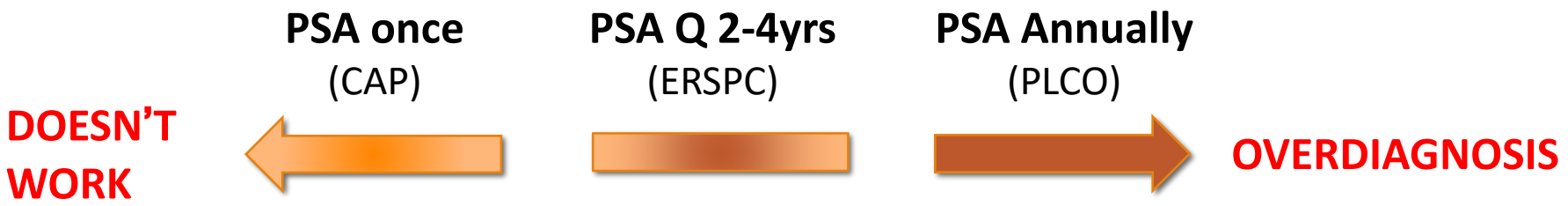
Before repeating, ask about:

UTI / prostatitis symptoms • recent instrumentation or catheterization • urinary retention • 5-ARI use • prior PSA trajectory

Do not use empiric antibiotics solely to "treat the PSA" in an asymptomatic patient.

AUA/SUO Early Detection Guideline 2023–2026

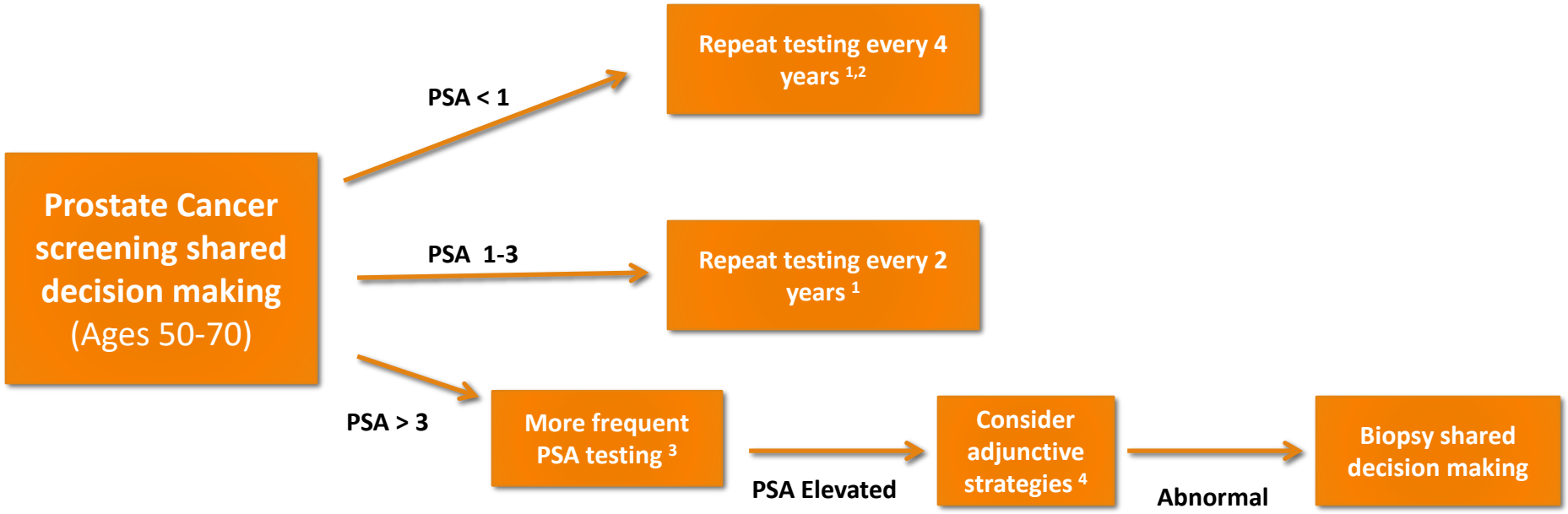
Frequency of screening



Baseline PSA can risk-stratify men

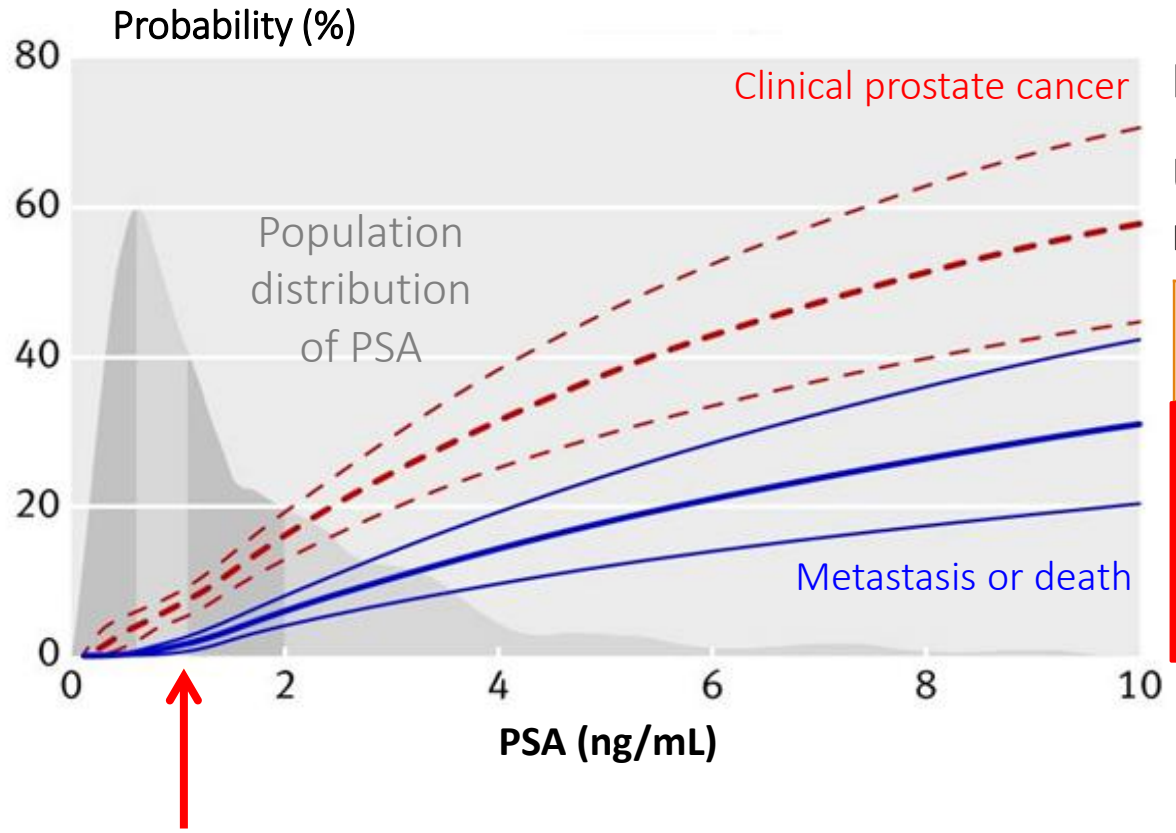
- Men with PSA <1ng/ml represent low risk group

CUA Guidelines 2022



1. Discontinuation of screening if life expectancy < 10 years
2. Consider discontinuation of screening if Age >60 and PSA remains < 1
3. More frequent testing intervals can be considered, the optimal frequency is unknown
4. ie; Risk calculators, free PSA, biomarkers

Don’t screen men > 60 with PSA ≤ 1 ng/mL



Reduces overdiagnosis

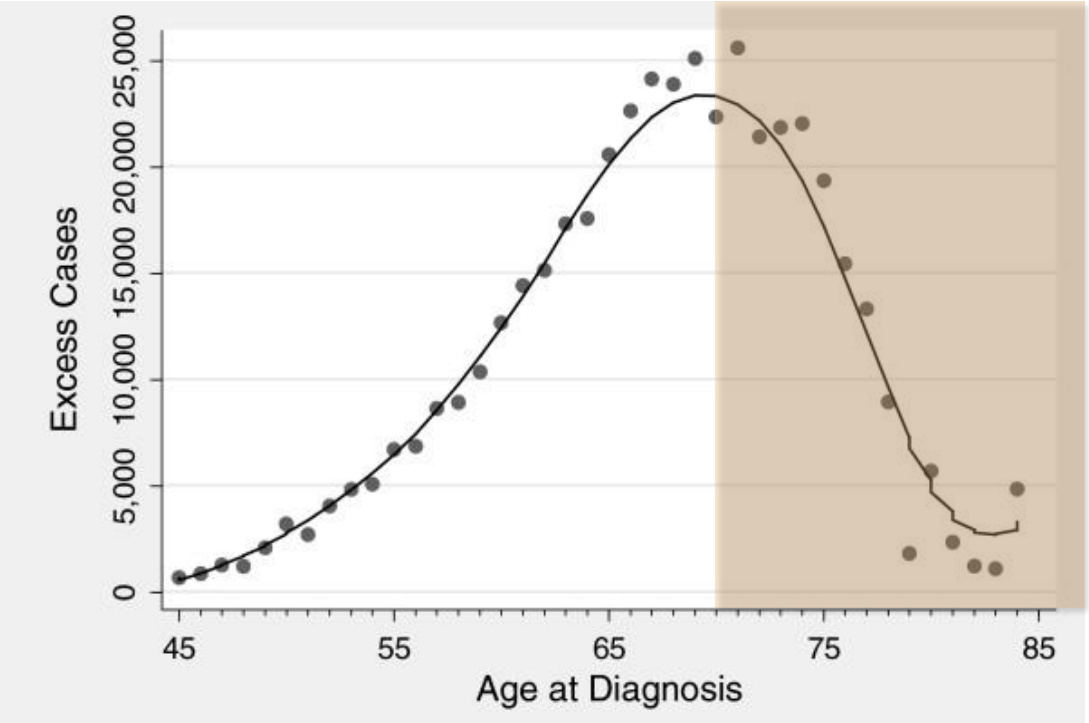
Unlikely to develop clinically relevant prostate cancer

Outcome	Risk by age 85	AUC (95% CI)
Metastasis	**0.5%**	0.86 (0.79-0.92)
Prostate cancer death	**0.2%**	0.90 (0.84-0.96)

Vickers A, et al. *BMJ*. 2010; 341:c4521.

Don’t screen older men

Stopping screening at age **70** → **42%** reduction in overdiagnosis



Vickers AJ et al. *BMC Med*. 2014;12:26

Should we stop screening at 70?

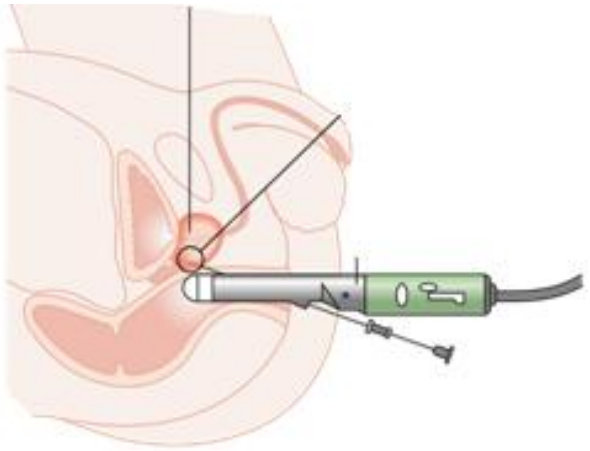
Subgroup analysis from ERSPC failed to identify a benefit to screening over age 70

BUT

Men in excellent health who wish to be screened screening?

- Can be offered, noting lack of evidence
- Age is a poor surrogate for life expectancy

What else is there beyond PSA?



PSA

Risk calculators

PCA3

mpMRI

ConfirmMDx

MiPS

STHLM3

SelectMDx

PHI

4Kscore

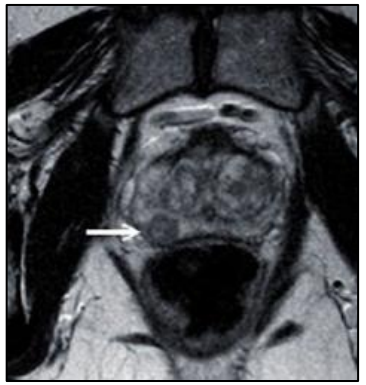
ExoDx Prostate Intelliscore

1980

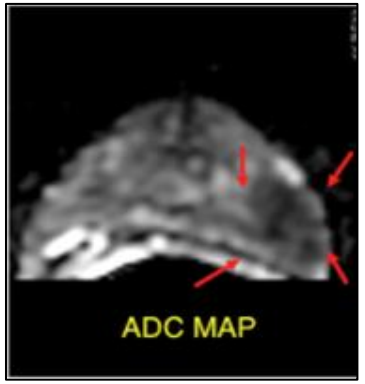
2020

Prostate MRI





T2WI



DWI –ADC

Imaging based biopsy selection

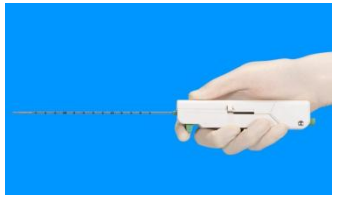
PSA elevated
(screened men)



normal

Observe

Abnormal



Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study

Hashim U Ahmed, Ahmed El-Shater Bosaily*, Louise C Brown*, Rhian Gabe, Richard Kaplan, Mahesh K Parmar, Yolanda Collaco-Moraes, Katie Ward, Richard G Hindley, Alex Freeman, Alex P Kirkham, Robert Oldroyd, Chris Parker, Mark Emberton, and the PROMIS study group†*

The Lancet. Published online January 19,2017

575 men underwent mpMRI followed by TPM & TRUS biopsy

- 230 (40%) diagnosed with Gleason ≥4+3
- mpMRI more accurate sensitivity & NPV vs. TRUS bx

	MP-MRI, % (95% CI)	TRUS-biopsy, % [95% CI]	Test ratio* [95% CI]	p value
Primary definition (Gleason score ≥4+3 or cancer core length ≥6 mm), prevalence of clinically significant cancer 230 (40%, 36–44%)				
Sensitivity test	93 (88–96)	48 (42–55)	0·52 (0·45–0·60)	p<0·0001
Specificity test	41 (36–46)	96 (94–98)	2·34 (2·08–2·68)	p<0·0001
PPV	51 (46–56)	90 (83–94)	8·2 (4·7–14·3)	p<0·0001
NPV	89 (83–94)	74 (69–78)	0·34 (0·21–0·55)	p<0·0001

Specificity and PPV of MRI are poor

NPV 89% = 11% with ”normal” MRI that have Gleason ≥4+3

Ahmed H et al. Lancet.2017;389:815-822

MRI is now embedded in Canadian and US biopsy decision-making

CUA / CCO 2022

- Biopsy-naïve + elevated risk: mpMRI before biopsy if a candidate for curative management.
- Positive MRI: targeted + systematic biopsy to maximize csPCa detection.
- Negative MRI: may forgo biopsy with ongoing follow-up.
- Quality matters: negative MRI can miss clinically significant disease.

Canadian recommendation is explicitly MRI-forward.

AUA / SUO 2023 → 2026

- MRI before initial biopsy may be used to increase GG2+ detection.
- 2026 amendment revised the strength of evidence for biopsy-naïve MRI based on newer randomized data.
- Suspicious MRI: targeted biopsy; systematic cores may be added.
- Negative MRI + persistently elevated GG2+ risk: systematic biopsy remains appropriate.

2026 change: stronger evidentiary footing—not “MRI rules out cancer.”

CUA 2022; AUA/SUO 2023, amended 2026

A negative MRI lowers risk; it does not erase it

AUA pooled estimate in biopsy-naïve patients

91%

NPV of PI-RADS 1–2 for GG2+ cancer

≈1 in 10

may still harbor GG2+ disease

Residual-risk modifiers after a negative MRI

- PSA density
- Strong family history / Black ancestry
- Pathogenic germline variant
- Abnormal DRE / concerning PSA trajectory
- Local MRI quality and reader expertise

Clinical rule

Negative MRI + low residual risk → surveillance is reasonable. Negative MRI + high residual risk → biopsy remains on the table.

AUA/SUO 2023–2026; CUA 2022

PSA Derivatives

PSA Velocity

>0.75 ng/ml/year (>0.35ng/ml/year when PSA <4.0)
Little evidence of PSAV is predictive of biopsy results

High velocity alone is not an indication for biopsy

Sustained rise over time is concerning
Consider repeating PSA at shorter intervals

Vickers A et al. JCO 2009;27:398-403
Vickers A et al. Urology 2014;83:592-598

PSA Derivatives

PSA Density

Higher density implies higher probability prostate cancer*

- >0.15ng/ml/cm^3

Problems with PSAD

Requires imaging

Inter-observer variability of measurement

Conflicting results from other prospective studies**

- 31% of cancers missed using PSAD cutoff (men with PSA 4-10)

*Allan R et al. J Urol. 2003;170:370-372. Radwan M et al. J Urol. 2007; 69:1121-1127

**Lujan M et al. Pros Can Prostatic Dis. 2001;4:146-9. Djavan B et al. Urology.2002;60:4-9

PSA Derivatives

Percent Free PSA

Lower %fPSA suggests greater risk of PCa

PCa ~56% of men with %fPSA <10%
Pca ~8% of men with %fPSA >25%

Like total PSA, can fluctuate

- Sensitivity ~ 92%
- Specificity ~ 23% (false positive rate 77%)

Catalona WJ et al. JAMA. 1998:279:1542-1547

Summary

Screening can reduce PC mortality in Canadian men

Maximizing detection of aggressive disease & minimizing harms

The way forward

Awareness in men’s health

Shared decision making



PSA screening summary

Do's:

Screen healthy men 50-70 yrs old

- Earlier for men (40-45yrs) with a family history of lethal/aggressive prostate cancer

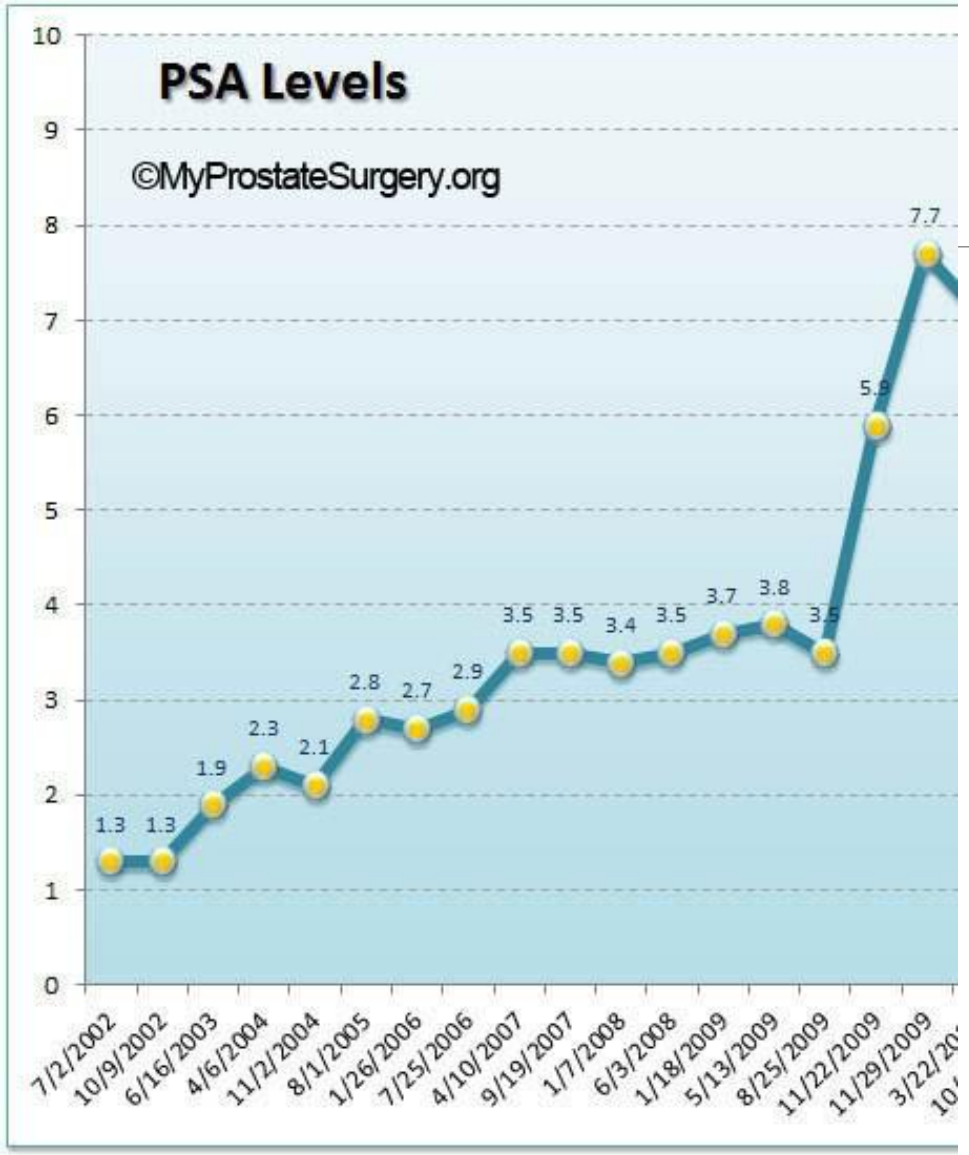
Can stop screening for men >60 with PSA <1.0

If PSA is elevated, repeat the PSA in 1-2 months

- 40% will decrease over time

Provide a history of previous PSA's

- If available


PSA Levels
©MyProstateSurgery.org
10
9
8
7
6
5
4
3
2
1
0
1.3
1.3
1.9
2.3
2.1
2.8
2.7
2.9
3.5
3.5
3.4
3.5
3.7
3.8
3.5
5.9
7.7
7/2/2002
10/9/2002
6/16/2003
4/6/2004
11/2/2004
8/1/2005
1/26/2006
7/25/2006
4/10/2007
9/19/2007
1/7/2008
6/3/2008
1/18/2009
5/13/2009
8/25/2009
11/22/2009
11/29/2009

PSA screening summary

Don’t’s

Screen unhealthy men 50- 70 yrs old

- Life expectancy < 10 yrs

Screen men >75 yrs old

Screen men with active infection/UTI

CUA Guidelines 2022

CUA GUIDELINE

Canadian Urological Association recommendations on prostate cancer screening and early diagnosis

Ricardo A. Rendon, MD[1]; Ross J. Mason, MD[2]; Karim Marzouk, MD[3]; Antonio Finelli, MD[4]; Fred Saad, MD[5]; Alan So, MD[6]; Philippe D. Violette, MD[7,8]; Rodney H. Breau, MD[9]