

PSA Screening, Rx versus Surveillance, timing of post op RT and treatment of Oligometastatic Prostate Cancer

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Sentinel findings in screening, diagnosis and management of prostate cancer

DISCLOSURES

None

Learning Objectives

- Understand how to interpret apply the level 1 evidence regarding the use of screening PSA
- Understand level 1 evidence guiding whether mpMRI should be obtained prior to prostate biopsy in men with an elevated PSA
- Understand the level 1 evidence guiding whether to treat or monitor clinically localized PC
- Understand the level 1 evidence guiding the approach to a patient with oligoM1 PC

Variations in PSA

- **PSA > 2.5, > 4.0 ng/ml**
 - 23%, 44% normal next year on serial blood draws
- **Confounders**
 - Assay variation, Ejaculation, bicycle, horseback.., infection, inflammation, instrumentation, biopsy
- **Eliminate confounders before using PSA to recommend biopsy or Rx**

Prostate Cancer Randomized Screening Studies

- **Contamination**

- Powered for 38% in **PLCO**
- **85%*** had at least 1 PSA level by year 5
- **15%** in ERSPC an CAP

- **Non-attendance**

- **15% PLCO, 36% ERSPC, 64% CAP**

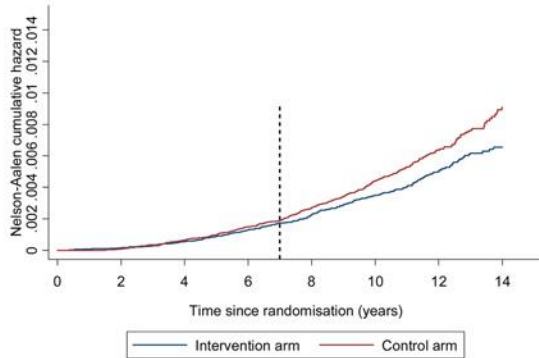
- **Screening Interval and Difference in PSA testing**

- **PLCO (q1 yr)** **85% vs 85% or 0%**
- **ERSPC (q4 yrs)** **64% vs 15% or 49%**
- **CAP (once)** **36% vs 15% or 21%**

***Pinsky et al., *Clin Trials* 2010 7: 303**

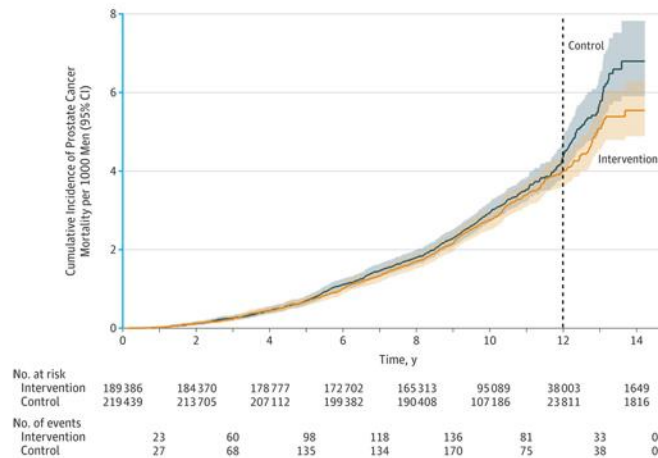
Prostate Cancer Specific Mortality

ERSPC



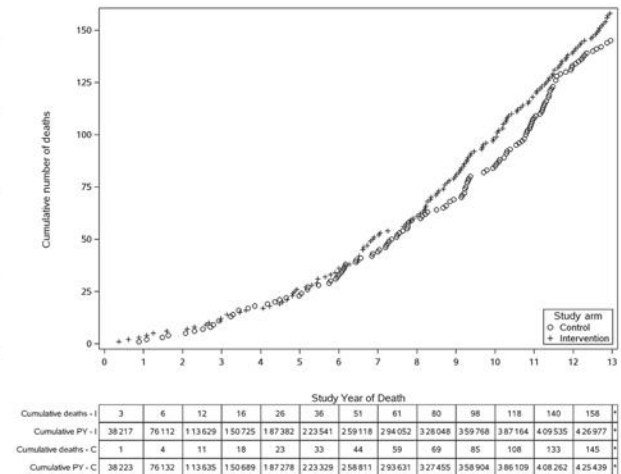
49%

CAP



21%

PLCO



0%

Difference in PSA screening between arms

DISCUSSION

- **Using these data, who to screen?**
 - **Benefit after 6 to 7 yrs with q1-4 yr screening**
 - USPTF now recommends to **discuss PSA screening**
 - » **African American (AA) men** at high risk for aggressive PC were not in the trials to any significant degree
 - » In **4654 AA men** PSA screened q yr for 5 years vs less
 - » **Less M1** (0.61 [0.47-0.81], $p < 0.01$) and **less PC death** (0.75 [0.59-0.95], $p = 0.02$)
 - **Young men**
 - PSA performs better in the absence of BPH
 - **Longer life expectancy or Healthy**
 - More likely to benefit from early detection
 - BRCA1,2.. Testing for men with FH if **age at dx < age 60**

MRI/TRUS vs MR vs TRUS bx

12%, 60%, 83% with PI RADS 3,4, 5 PC have \geq Gleason 3 + 4 or \uparrow

– 2103 men (median PSA 6.7, T1c in 54%)

- MR (2 cores/lesion) and 12 core TRUS guided bx
 - 404 had whole mounted RP (gold standard)

Biopsy	Upgrading 3 + 4 or \uparrow	Upgrading 4 + 3 or \uparrow	Downgrading to 3 + 3
Both	6.7	3.5	3.7
MRI	18.3	8.7	2.5
12 core TRUS	30.2	16.8	2.2

P < 0.0002 for **upgrading** and p = 1.0 for **downgrading**

Using both: **4% downgraded** and **7% upgraded**

ProtecT

- PSA screen x 1 to men Age 50 – 69 (**59.1**) yrs
 - Report death from PC in 2016 at median f/u ~ 10 yrs
 - ~550 primary care centers in England/Wales
 - ~450,000 randomized
 - 228,966 offered PSA
 - » 100,444 attended appt with RN
 - **82,429 (36%) had PSA**; 8,566 had PSA > 3 to 19.9
 - 7,414 had 10 core bx and 2896 (PC)
 - 1643 randomized: AM, RP_{open}, 74 Gy RT_{3-6mos} ADT
 - ~3/4 T1c, 1/4 T2
 - ~77%, **20%**, 2% were GS, 6, **7**, 8 to 10 respectively
 - median PSA 4.6

ProtecT

- **Patient Population**

- **< 1% African American**
- **Family History PC (7%)**

- **Excluded**

- **PSA > 20, only 2% GI 8 to 10 (high risk)**
- **under age 50**
- **over age 70**

ProTect

- **Metastasis (DM)**

- Bone, Visceral, LN or PSA > 100

- 6.4 vs. 2.4 to 3.0 per 1000 person yrs* (p = 0.004)

- **Hazard Ratio: Death from Prostate Cancer**

- RP vs AM **0.63 [0.21, 1.93]** ***0.9 vs 1.5**

- RT/ADT vs AM **0.51 [0.15, 1.69]** ***0.7 vs 1.5**

- RT/ADT vs RP **0.80 [0.22, 2.99]** ***0.7 vs 0.9**

- **Pre-randomization stratum (Age > 65)**

- Interaction p-value = 0.09

- Most PC death in men randomized to AM

Prostate RT in men with castrate sensitive M1 PC

- Randomized Controlled Trials
 - HORAAD
 - ADT +/- RT (70/2 or 57.76/3.04 --- 3x/wk)
 - STAMPEDE
 - ADT + Docetaxel (12/15) +/- RT (55/2.75 or 36/6 q week)

Does the addition of Prostate RT to SOC for men with castrate sensitive M1 PC prolong overall survival?

RESULTS

Trial	Number	OVERALL SURVIVAL		
		HAZARD RATIO [95% CI]		
Accrual period	Median Follow up	ALL	Minimal M1	Other M1
HORAAD	432	0.90	0.68*	1.06
2004 -2014	47 months	[0.70–1.14] p = 0.40	[0.42 to 1.10]	[0.80 to 1.39]
STAMPEDE	2061	0.92	0.68**	1.07
2013 - 2016	37 months	[0.80 to 1.06] p = 0.27	[0.52 to 0.90] p = 0.007	[0.90 to 1.28] p=0.42

* < 5 bone mets (37%)

** ≤ 3 bone and no visceral mets (40%)

Men **NOT** stratified by metastatic burden prior to randomization

DISCUSSION

- Taking together these data **raise the possibility of a survival benefit** for prostate RT in men with castrate sensitive M1 PC
- **≤ 3 bone and no visceral metastasis**

Targeted Systemic RT

- ^{177}Lu -PSMA-617 (**Beta-emitter**)
 - M1CRPC that was PSMA + on ^{68}Ga PSMA-11 scan
 - At least 1 prior AR pathway inhibitor and taxane Rx
- 2:1 Randomization to Lu (4-6 cycles) + SOC vs SOC
 - Co Primary endpoints – OS and Radiographic PFS
- N = 831, median f/u: 20.9 mos
 - OS HR: 0.62 [0.52, 0.74]: 15.3 vs 11.3 mos
 - Radiographic PFS/Death HR: 0.40 [0.29, 0.57]: 8.7 vs 3.4 mos
- Higher Grade 3 events (52.7% vs 38.0%) – **fatigue/anemia**
 - Opportunity to ▼ toxicity with **alpha emitter** (e.g. PSMA-TTC)
 - Other PSMA based therapies being studied (**I-131-1095 and 1404**)

All of the following occurring within 1 week of a PSA test can cause a false elevation except

- **(A) Ejaculation**
- **(B) Instrumentation (e.g. Foley)**
- **(C) Prostatic inflammation (Prostatitis)**
- **(D) Prostate Infection**
- **(E) Ingesting Saw Palmetto**

Which of the following men should not consider PSA screening?

- (A) 75 yo Caucasian, moderate comorbidity
- (B) 50 yo African American, no PMH
- (C) 65 yo Caucasian, minimal comorbidity, brother with BRCA-2 mutant, High-risk PC

Which of the following is not a Rx option for healthy 67 yo man with Gleason 7 prostate cancer?

- (A) Radical Prostatectomy with the possible need for adjuvant Radiation and or Testosterone**
- (B) Suppression Therapy (TS Rx)**
- (C) External Beam RT + Seed boost Rx + TS Rx**
- (D) External Beam + TS Rx**
- (E) Active Surveillance**

Rx of the 1° may improve OS in men with newly dx'd M1 PC and

- (A) Widely metastatic PC**
- (B) 3 or fewer bone and no visceral metastasis**
- (C) Both bone and visceral metastasis**
- (D) Visceral metastasis only**
- (E) A short life expectancy due to comorbidity**

Which treatment has been shown to prolong survival in men with M1, castrate resistant prostate cancer?

- (A) Radical prostatectomy**
- (B) Radiation Therapy**
- (C) ^{177}Lu -PSMA-617**
- (D) Active Surveillance**
- (E) Testosterone suppression therapy**