Urology Review : Dine and Learn

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Objectives

- Bladder Cancer – What to know for a GP
  - Importance of timing
  - Dealing with BCG pt.’s
  - A quick look at diversions
- Prostate Cancer
  - Screening
  - Androgen Deprivation Therapy & Bone Health

Bladder Cancer

- 70 % Non-muscle invasive <T2.
  - Low risk 40% recurrence rate, 5 % progression,
  - High Risk 80% recurrence 20% progress.
  - Mainstay of treatments
    - Repeat cystoscopy and TURBTs
    - Mitomycin C in bladder
    - BCG therapy – q weekly x6 weeks, then q 3 weekly at 3,6, 12, 18, 24, 30 & 36 months.
- 30% Muscle invasive:
  - Treatment is Neoadjuvant Chemotherapy with Radical Cystectomy and Urinary Diversion
  - 50% 5 year survival rate.

Timing – THE GPs role is critical!

- May 17 2017 - **Gross hematuria and seen at walk in clinic a referral was made saying 'Prostatis'**
- Jul 6 2017 - seen in clinic with ? 1 cm lesion in trigone of bladder
- Aug. 7 2017 - Cystoscopy 1 cm bladder lesion seen.
- Sept. 6 2017 - TURBT MIBC
- Sep 25 2017 – Path retunrs & BCCA referral for NAC –
- Oct. 16 2017 - NAC refused due to neuro concerns.
- Nov. 28 - next available OR date for Cystectomy
- Dec. 12 2017 – Lymph node positive disease and re-referral for Adjuvant Chemo
- A wait longer that 12 weeks is associated with increased MORTALITY

- MESSAGE - Call the Urologist, or MAKE SURE referral Gets through. We all have fast tracks for gross hematuria patients and they should be seen and have cystoscopy

BCG Therapy

- Live attenuated TB.
- Risk of TB sepsis <0.5%, unless pt. has active hematuria, immunesuppressed, frail elderly.
- If febrile on BCG therapy > 38.5, not responsive to tylenol:
  - 1) evaluate for UTI
  - 2) Consider systemic TB as possibility.
- Main side effect is urinary urgency, frequency.

Radical Cystectomy

- 64% complication rate, 20% grade 3 complicaiton, 2% mortality.
- 3 types of urinary Diversion:
  - Ileal Conduit
  - Ileal Neobladder
  - Indiana Pouch

- All 3 types –
  - the bowel functions as bowels and resorbs urine causing an acidosis, hypernatremia.
  - Methotrexate and Dilantin are renaly excreted and absorbed in small bowel (Need to consider dosage)
  - Persistent Bacteriuria – don’t treat all positive cultures
  - Blockage / infection can present as nausea

Prostate Cancer

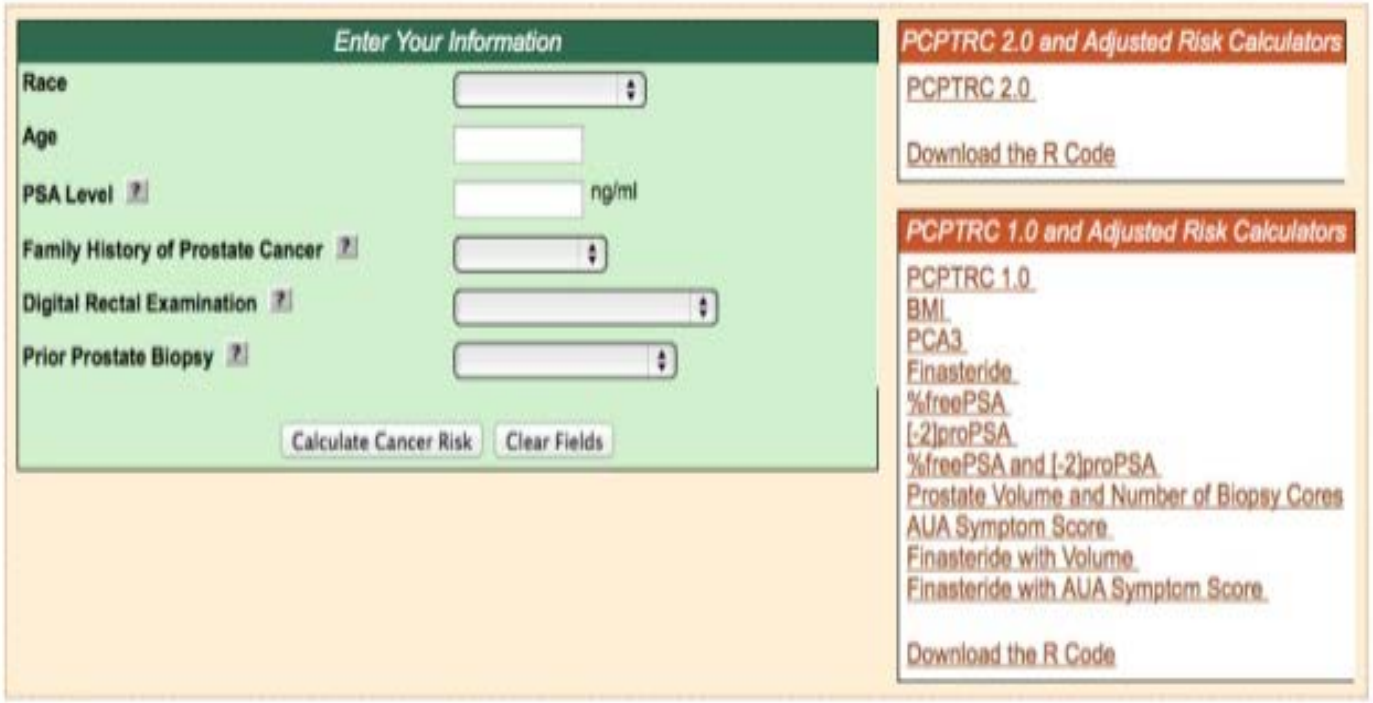
- Prostate cancer is the most common cancer in American men
- In 2015:
  - 220,800 new cases
  - Over 27,000 deaths (2nd leading cause of death)
  - Metastatic Prostate Cancer is associated with pain, urinary symptoms and poor Quality of Life

- Lifetime risk of diagnosis
  - 14% or 1 in 7 men

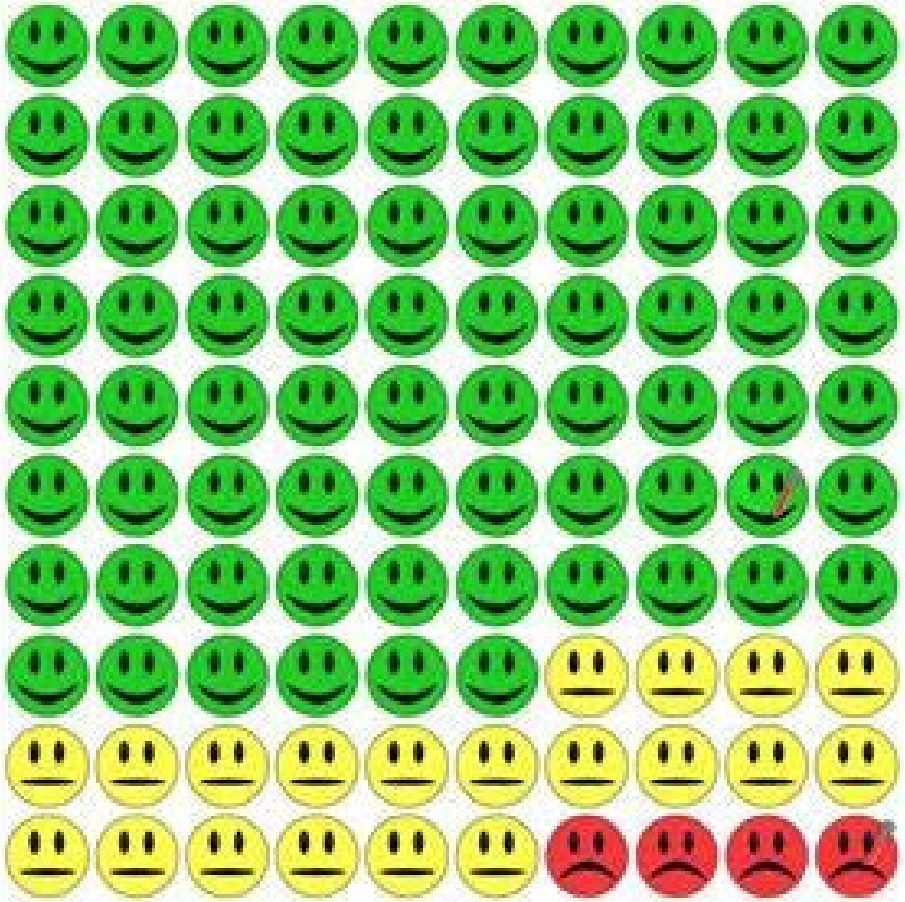
- Risk Factors:
  - Age (median age at diagnosis 67)
  - Race
    - African Americans: 1.6x more likely diagnosed, 2.4x increased death
  - Family History
    - One first-degree relative: 2x increased lifetime risk
    - Two or more: 4x increased lifetime risk
  - Diet, Obesity, Smoking, Genetics, Agent Orange exposure

Brawley et al, World J Urol 2012

Screening: To Assessing Risk of Diagnosis Prostate Cancer



Google for prostate cancer risk calculator



Based on the provided risk factors a prostate biopsy performed would have a:

- 4% chance of high-grade prostate cancer,
- 20% chance of low-grade cancer,
- 76% chance that the biopsy is negative for cancer.
- About 2 to 4% of men undergoing biopsy will have an infection that may require hospitalization.

Source: UT Health Science Center

Why all the controversy?

- PSA is not a perfect test
- Confounders
  - BPH
  - Infections (UTI, prostatitis)
  - Ejaculation
  - Catheterization
  - Medication
  - Urinary Retention
  - Trauma

No safe PSA threshold…

- PSA <4 ng/mL

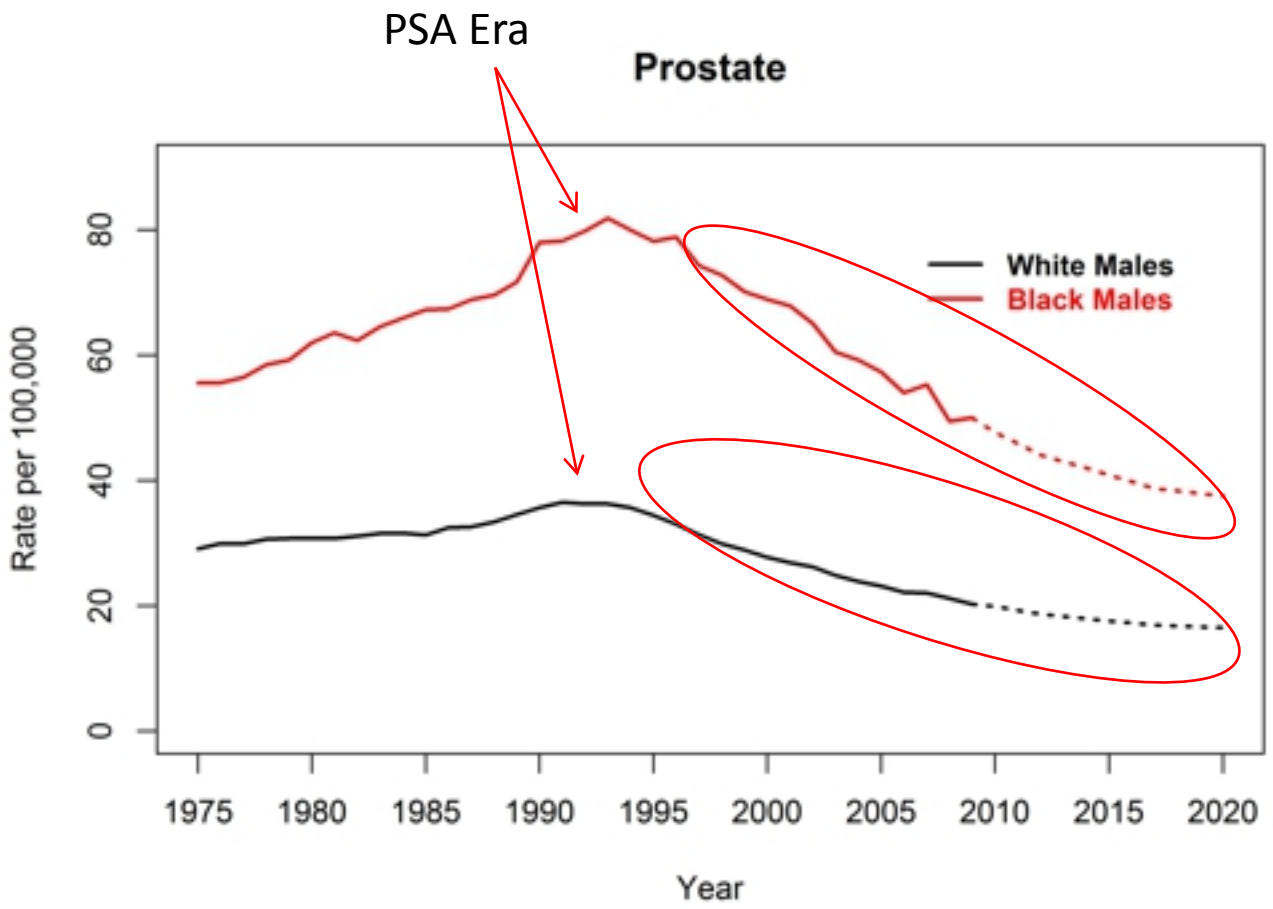
PSA level	Prevalence of Prostate Cancer	High-Grade Disease
3.1 - 4.0	26.9%	25.0%
2.1 - 3.0	23.9%	19.1%
1.1 - 2.0	17.0%	11.8%
0.6 - 1.0	10.1%	10.0%
<0.5	6.6%	12.5%

Thompson et al, JAMA 294:66-70, 2005.
Thompson et al, NEJM 350:2239-46, 2004.

Prostate Cancer Dilemma

- Goal of treatment: Prevent death & morbidity
- Not all men diagnosed with prostate cancer need treatment
- We cannot predict with certainty who will die
- Potential for over-treatment
- All treatments have side effects

PSA and Prostate Cancer Mortality



Prostate Cancer Intervention Side Effects

- Biopsy side effects
  - Sepsis, Bleeding, Discomfort
- Treatment side effects
  - Transient incontinence, ED, stricture, long-term bowel or bladder irritation
- Overtreatment of clinically insignificant cancer
  - Very Low Risk Prostate Cancer doesn’t need treatment due to benign course, or can be treated at a later date.
  - Int mediate and High risk cancer treatment recommended
  - Advanced Prostate Cancer will progress despite certain therapies.

Why recommend against screening for prostate cancer?

Screening and consequent treatment, as currently practiced, are often harmful:

- Too much screening of elderly men with a short life expectancy
- Too liberal criteria for biopsy
- Too aggressive treatment of low risk cancers
- Inadequate treatment of high risk cancers
- Treatment largely administered by low volume providers (higher risks of side effects and lower risks of cure)

Vickers AJ, Lilja H. Time for another rethink on prostate cancer screening. Nat Rev Clin Oncol. 2011; 9:7-8.

What were these recommendations based on?

- PLCO Study
  - Prostate, Lung, Colorectal, Ovarian Screening
  - US based study, concluded in 2009
  - Men 55-74, 10 study centers across US, 1993-2001
- ERSPC Study
  - European Randomized study for Screening of Prostate Cancer
  - Originally published in 2009
  - Men 55-69, 7 European centers, 1991-2003

PLCO Limitations

- **Selection Bias:**
  - 44% of those enrolled underwent PSA testing before study
- **Cross-over Contamination:**
  - 52%-79% controls had PSA testing
- **Low Adherence:**
  - Only 41% of the patients in the screening arm with positive PSA values underwent prompt biopsy within 1 year
  - Only 40% had biopsy when PSA went up

- *Is this a true randomized trial comparing PSA screened to unscreened population?*

- *Or just comparing "opportunistic" screening to annual screening?*

Problems with recommendation against screening

- European randomized trial has not reached its primary endpoint
- Inappropriate inclusion of very different trials in meta-analysis
- Lack of appreciation for the strong relationship between PSA and prostate cancer mortality
- Inadequate consideration of time-to-event (long delay between elevated PSA and death from prostate cancer)
- Overall mortality is not an appropriate endpoint
- Mortality risk of surgery exaggerated (0.5%)

ERSPC

- Correcting for selection bias and noncompliance, RR reduction of 29%.
- To prevent 1 death at 13 years follow-up, need to screen 781 and number needed to treat 27
- Impact of screening on PCa mortality improved with additional follow-up

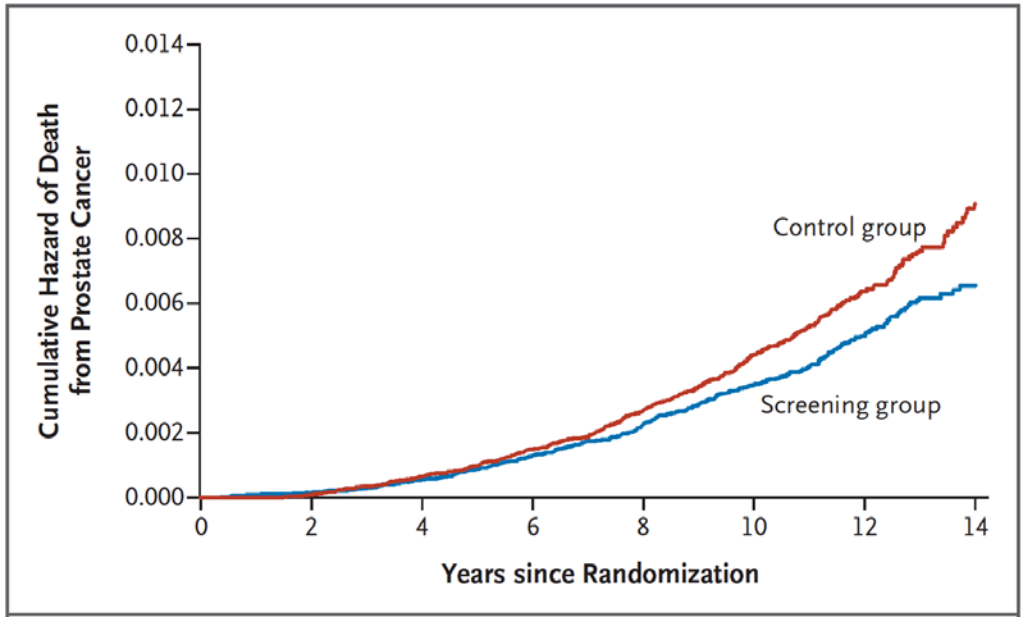


Figure 2. Cumulative Hazard of Death from Prostate Cancer among Men 55 to 69 Years of Age.

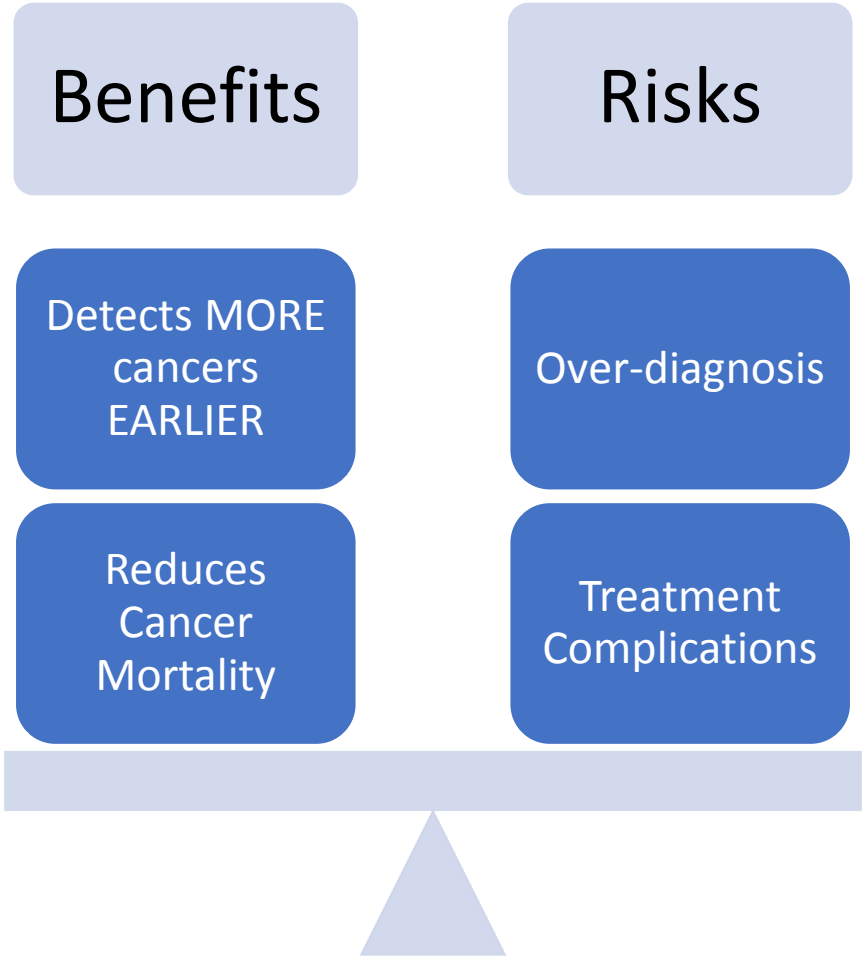
Values are not included for centers in France because of the short follow-up period (median, 4.6 years). The Nelson–Aalen method was used to calculate the cumulative hazard of death from prostate cancer.

MD Anderson Cancer Center
Making Cancer History®

Schroder et. al. NEJM, 2012

Schroder et. al. Lancet, 2014

Balancing Act of Prostate Cancer Screening



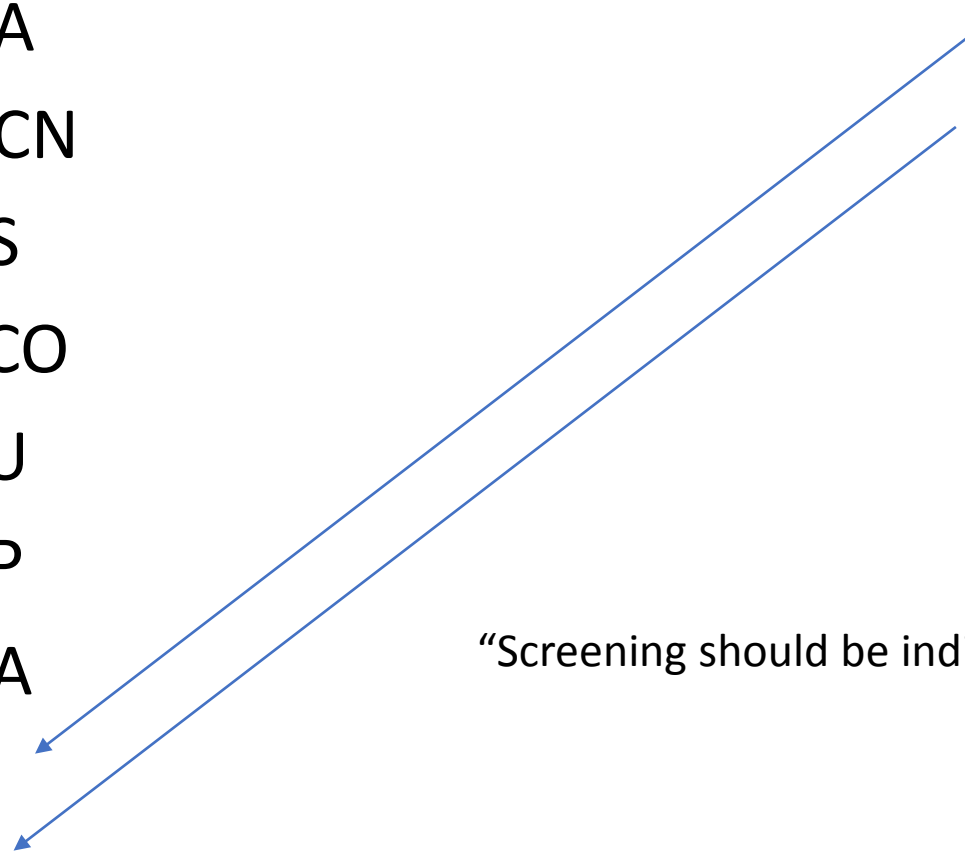
Recommendations from Professional Organizations

Screening Recommended

- AUA
- NCCN
- ACS
- ASCO
- EAU
- ACP
- CUA

Screening NOT Recommended

- ~~USPTF~~
- ~~AAFP~~
- CPSTF (last update 2014)



"Screening should be individualized"

NCCN Guidelines - 2015

- **START**
  - Baseline testing at age 45
  - Risk-adapted screening based on baseline PSA
- **HOW OFTEN**
  - If baseline PSA< 1 ng/mL → every 2-4 years
  - If baseline PSA≥ 1 ng/mL → every 1-2 years
- **STOP**
  - ≥75 years old OR <10 year life expectancy
- Special Considerations
  - High Risk Patients (AA, +FHx): no consensus, same schedule
  - Genetic syndromes (*BRCA1/2,* Lynch syndrome): start screening at 40

How to Increase the Benefits and Reduce the Risks of Screening for Prostate Cancer

- Screen, But Screen Less:
  - Risk adjust screening by age and PSA (reduce frequency of screening)
- Improve Screening:
  - Reduce false positive PSA results by adding additional markers (4 kallikrein panel or -2(pro)PSA, PSMA, MRI), (Limit Uneccessary Biopsies)
- Don’t Treat all patients:
  - Active surveillance for low risk cancers (reduce harms of unnecessary therapy)
- When you treat patients, treat them well:
  - Refer patients who need treatment to high volume physicians or centers (reduce harm of necessary therapy)

Vickers A, Roobol M, Lilja H. *Annu. Rev. Med*. 2012. 63:161–70.

Bone Health in Prostate Cancer

Androgen Deprivation Therapy

- Prostate cancer has a predisposition for bone met's
- Androgen Deprivation results in Osteoporosis.
- Fracture Risk for patients on continuous ADT is extremely high (>15 % /year)
- All men on ADT should:
  - Be on Ca2+ and Vitamin D
  - Should get DEXA Bone Scans
  - Should get bisphosphonates or Denosumab (RANK-Ligand mAb) if osteoporotic, prior fracture, or if have bone metastasis.

What is your risk?

See mskcc.org

→ search prediction tools

→ Click ‘ prostate cancer’

→ calculate:

-risk of having prostate cancer given PSA

-risk of male death with vs. from prostate cancer

-risk of outcome following prostatectomy

-risk of recurrence after prostatectomy

-risk of cure with salvage treatment….