Prostate Cancer, Perspectives and Recommendations from a Surgeon and Survivor

Pat Fox Fulgham, MD

May 18, 2024

North Texas Prostate Cancer Coalition

Prostate Cancer Symposium

Objectives

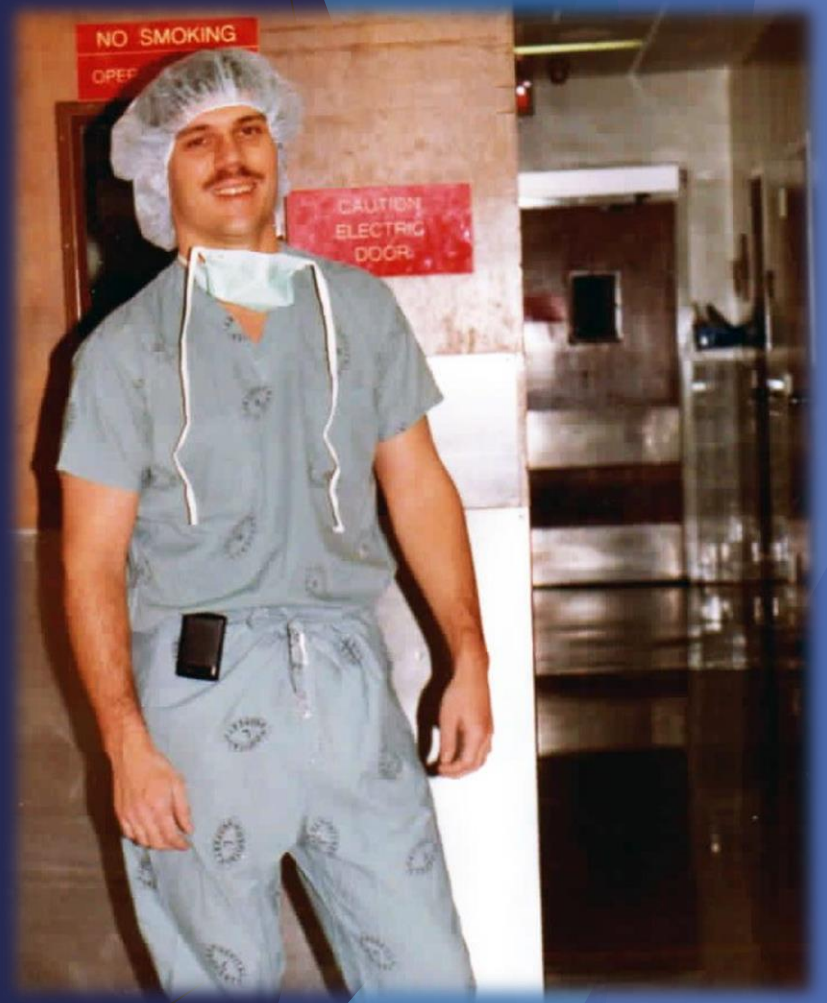
1) Personal story of prostate cancer from a prostate cancer surgeon.

2) Review current screening and risk stratification guidelines for prostate cancer in all men, addressing the disparities in outcomes for Black men.

3) Identify how new testing and technology may overcome barriers to screening and better inform decision making about biopsy and treatment.

4) Overview of the prostate cancer continuum

Surgeon and Survivor



Surgeon and Survivor

Pat Fulgham and John McConnell

Harry Spence, Paul Peters, Pat Fulgham, John Lang

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Parkland 1981

Presbyterian 1986

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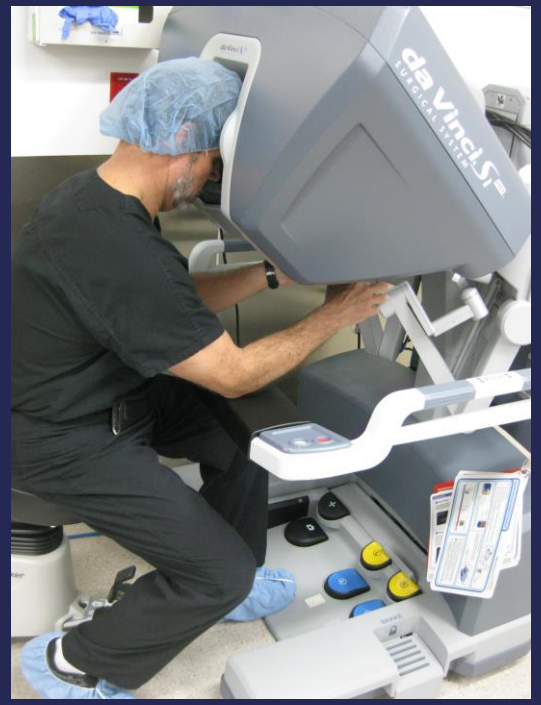
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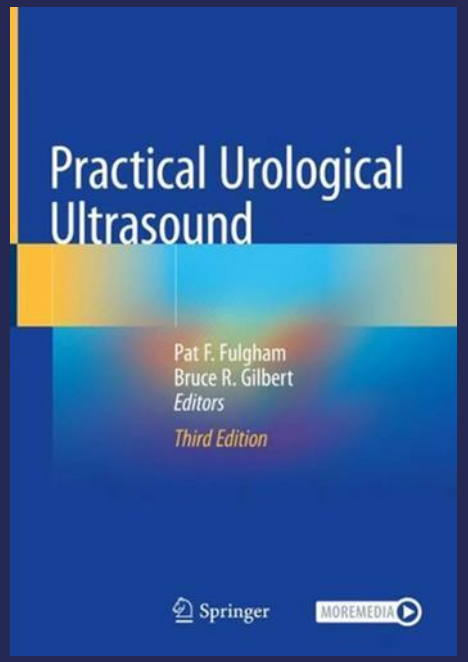
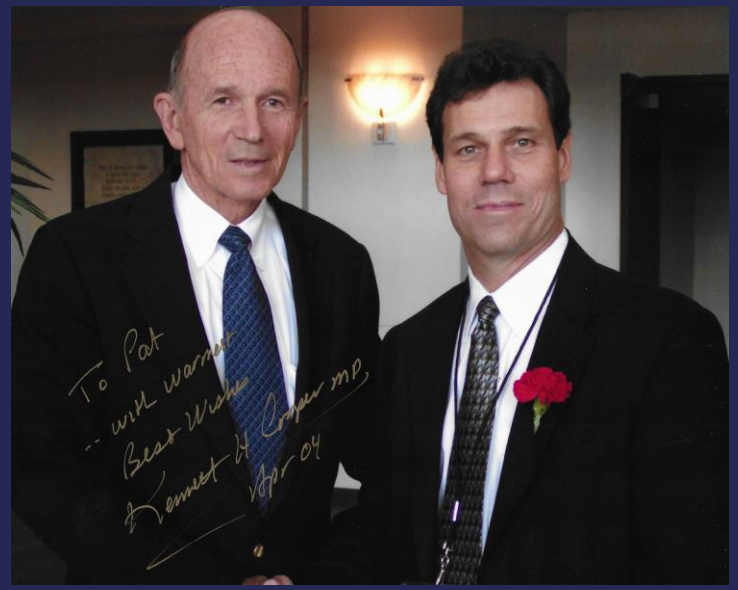

Practical Urological Ultrasound
Pat F. Fulgham
Bruce R. Gilbert
Editors
Third Edition
Springer
MOREMEDIA


BD

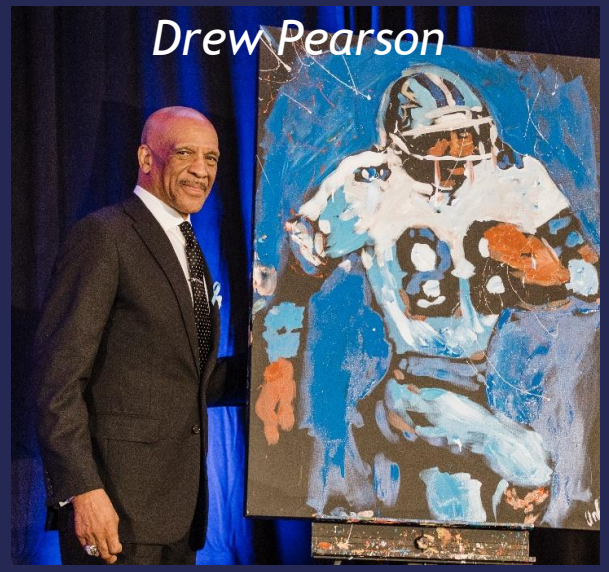


PRO'S & JOE'S
CELEBRITY GOLF TOURNAMENT
Celebrating Men's Health
2016
Brookhaven Country Club
Farmers Branch, TX

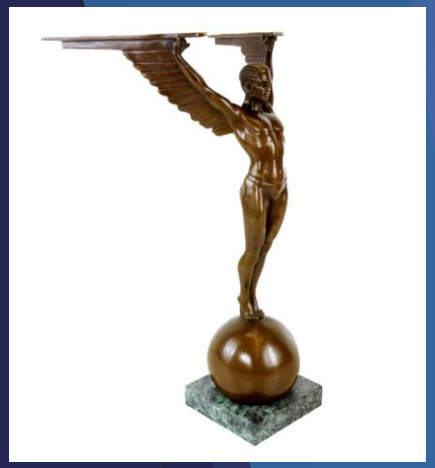
Dan Fulgham Memorial Dinner

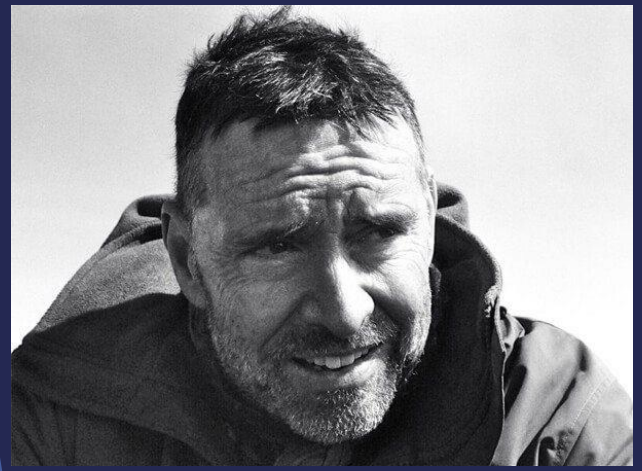
Man of Action Honorees

Lamar Hunt



Drew Pearson





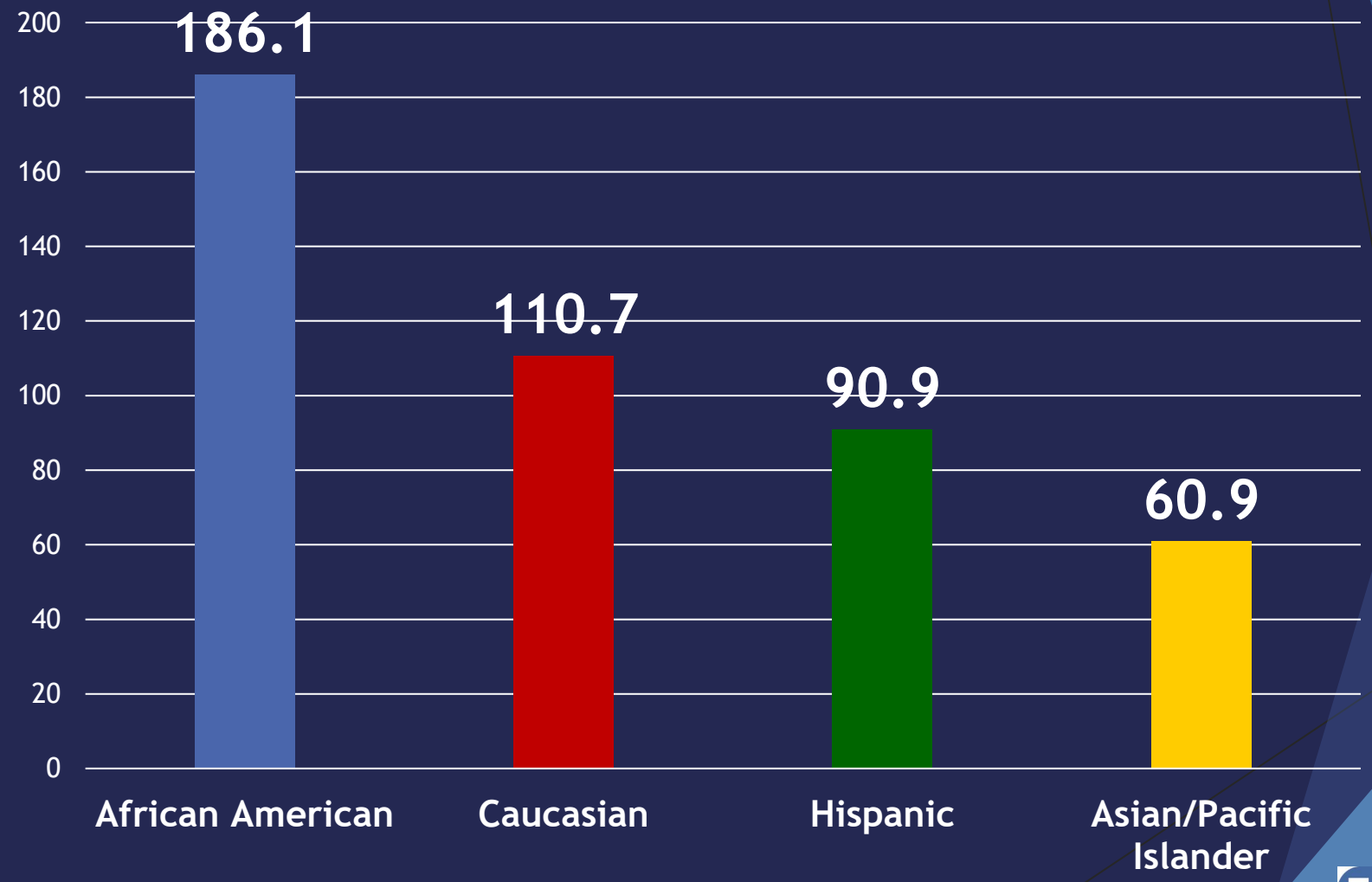
Todd Whitthorne

Brian Huth

The Controversy Regarding Screening for Prostate Cancer

- "Too much" screening may lead to over-treatment
- "Too little" screening may result in patients suffering from or dying of prostate cancer who could have been successfully treated or cured
- Using Prostate Cancer-Specific Mortality as the measure of "effectiveness" is superficial and undervalues the quality-of-life impact

Prostate Cancer Incidence Based on Race in the United States (per 100,000)



Cancer Facts and Figures 2024

Why Prostate Cancer Matters

Current U.S. Statistics for Prostate Cancer 2024*

- About 299,010 new cases of prostate cancer
  - The incidence of prostate cancer continues to increase
- About 35,250 deaths from prostate cancer (2nd common cancer in men)
  - Number of deaths continues to increase after decades of previous decline, despite advances in treatment
- 1 in 8 men will develop prostate cancer in their lifetime
- 1 in 44 men will die of prostate cancer (1 in 4 men die of heart disease)

Cancer Facts and Figures 2024 (cancer.org)

Lack of Uniformity of Guidelines for Prostate Cancer Screening

Why are there so many variations in professional societal/institutional prostate cancer screening guidelines when all these entities have access to the same data?

American Urological Association

NCCN National Comprehensive Cancer Network®

AAFP

SUO Society of Urologic Oncology, Inc.

U.S. Preventive Services TASK FORCE 40 YEARS OF IMPROVING HEALTH

Prostate Cancer Screening Guidelines

Professional Societies / Institutional Organizations	Shared-decision	Average Risk	Increased Risk (Black men, Germline positive, FamHx, agent orange)	Digital Rectal Exam	PSA Upper-Level Thresholds
AUA /SUO (4/23) American Urological Association/Society of Urologic Oncology	Yes	Baseline PSA 45-50 yrs 50-69 yrs (q 2-4 yrs)	40-45 yrs	May use DRE along with PSA	40-49 2.5 ng/mL 50-59 3.5 ng/mL 60-69 4.5 ng/mL 70+ 6.5 ng/mL
NCCN (02/24) National Comprehensive Cancer Network	"Risk/benefit discussion"	45-75yrs **If PSA <1** repeat q 2-4 yrs **If PSA 1-3** repeat q 1-2 yrs	40-75 yrs **If PSA ≤3** repeat q 1-2 yrs	Recommend DRE as a complementary test that can be considered with PSA.	Although a serum PSA of 2.5 ng/mL has been used by many, a level of 3 ng/mL is supported by the trials and would more robustly limit the risk of over detection. A higher threshold of 4 ng/mL is recommended for patients who choose to continue PSA screening past the age of 75 years
AAFP (2018) American Academy of Family Physicians *Currently under review*	"…men who desire PSA screening, it should only be performed after engaging in shared decision making."	55-70 yrs Repeat 2-4 yrs	Same as average risk	No evidence to support DRE	None listed
USPSTF (2018) United States Preventive Services Task Force	"…discuss potential benefits and harms…"	55-69 yrs	Based on available evidence, not able to make separate, specific recommendation		None listed

Why Current Screening Practices are Not Good Enough

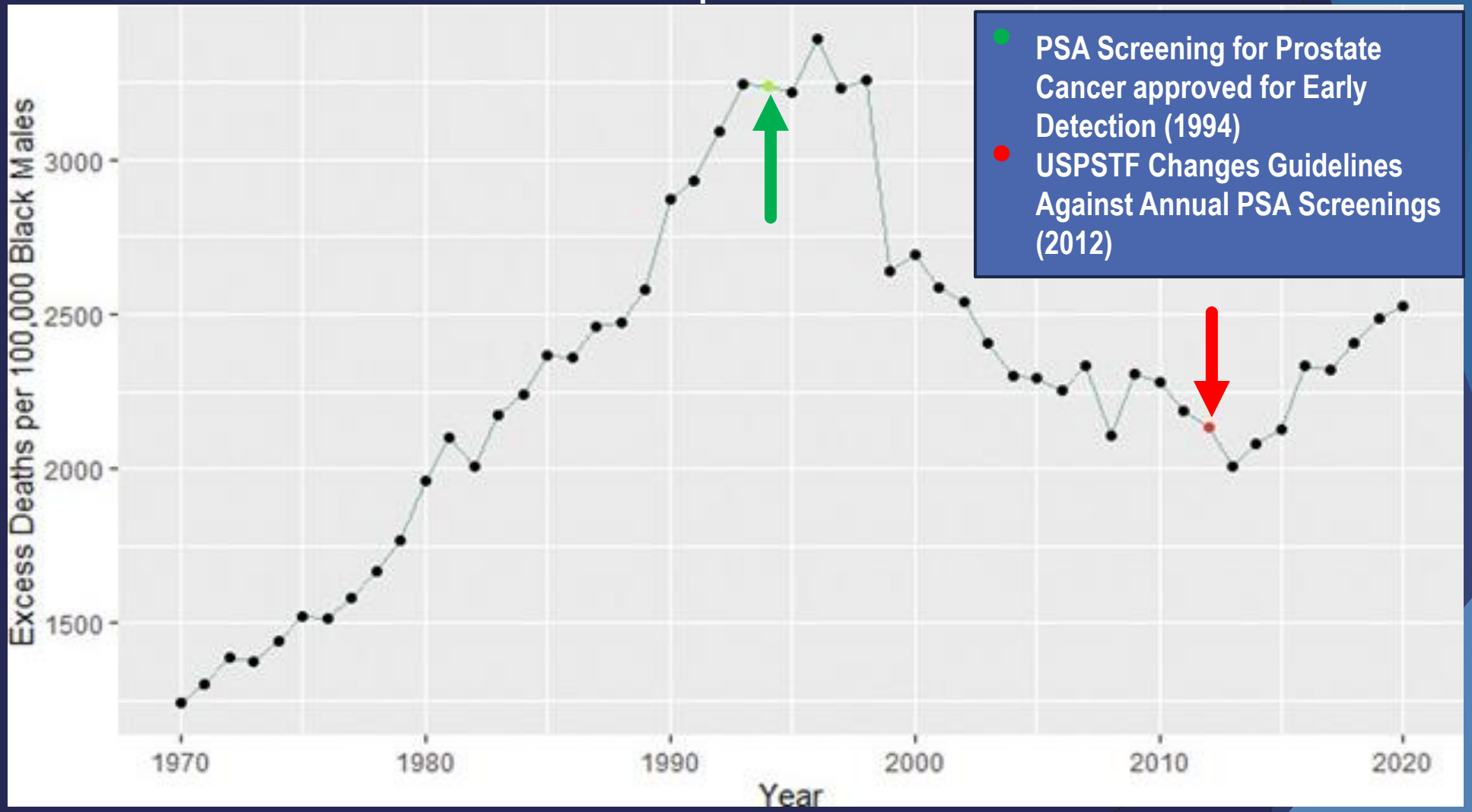
How Black Men Fare under the Current Paradigm

- Develop disease **3-9 years younger** than their counterparts
- **1.8x** more likely to be diagnosed
- **2x** more likely to die of it
- **1 of 8 Black men** with prostate cancer die of it
- **1 of 16 White men** with prostate cancer die of it

- **Survival of prostate cancer is highly correlated with how early (clinical stage) it is diagnosed.**

The Consequences of the USPSTF Recommendation

Estimated Prostate Cancer-Specific Excess Deaths in Black Males



J of Urology, 22:5S. May 2024. MP68-05 EXCESS DEATH AND POTENTIAL LIFE YEARS LOST AMONG BLACK PROSTATE CANCER PATIENTS (1970-2020)Nana A. Frimpong*, Philadelphia, PA; Sarah K. Holt, Daniel Carson,Yohali Burrola-Mendez, Jenney Lee, Erika Wolff, John L. Gore,Yaw A. Nyame, Seattle, WA

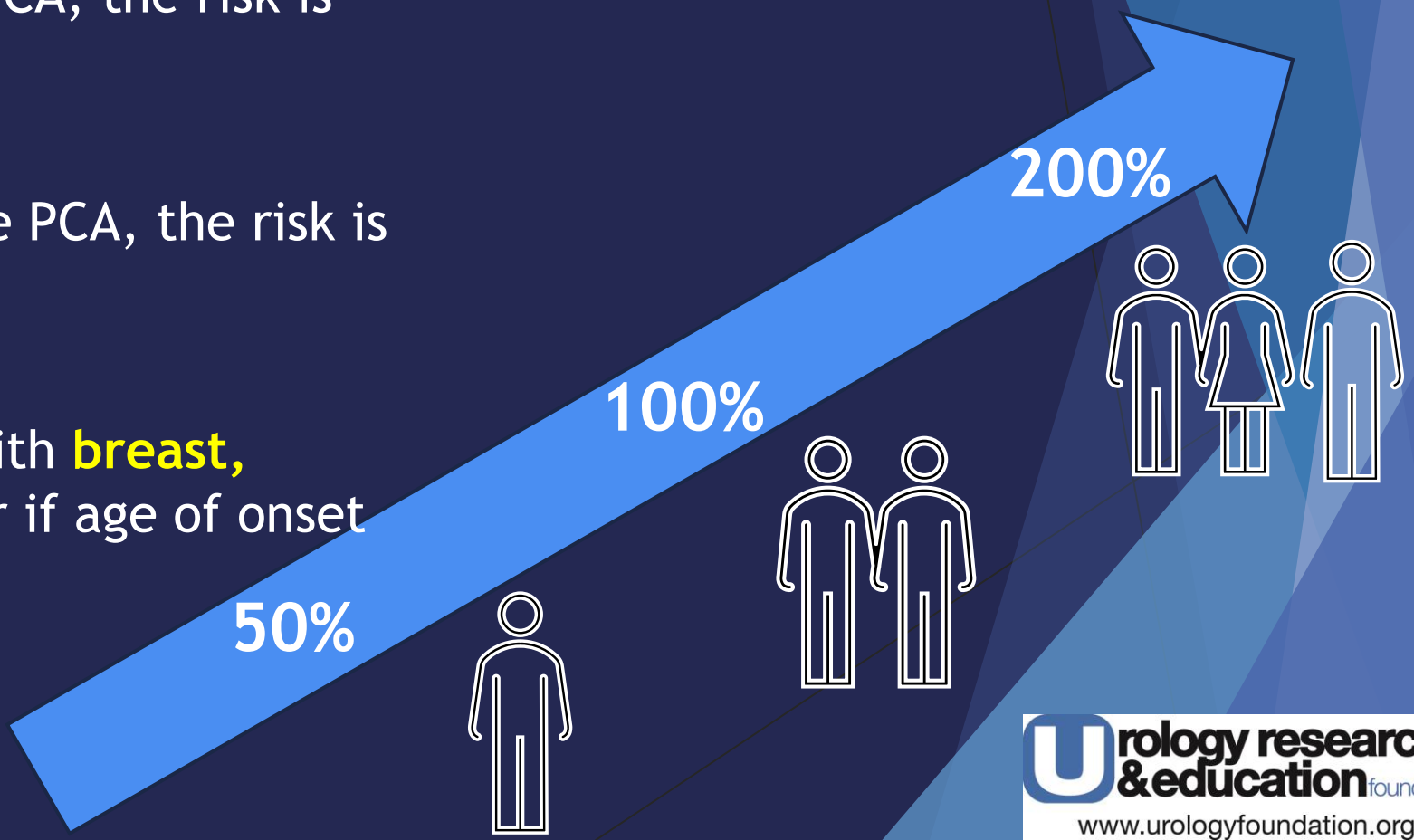
My Family History of Prostate Cancer

PGF
Died at 87
PGM
Mother
Father
Died at 87
PUncle
Died at 87
twins
PUncle
Died at 52 (heart)
Me
Dx at 66
Wife
Daughter-In-law
Son
Daughter
Son-in-law
Grand son
Grand daughter
Grand son

Genetic Risks: Why Family History Matters

Identifying men at increased risk based on family history:

- If 1 first-degree relative has PCA, the risk is increased by 50%
- If 2 first-degree relatives have PCA, the risk is increased by 100%
- If multiple family members with **breast, ovarian, colon, pancreatic** or if age of onset <50 years, > 200%



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Genetic Testing Explained

Knowing that your relative with prostate cancer has a germline mutation may help you decide whether to undergo testing at an earlier age. Also, if you (yourself) have aggressive or advanced prostate cancer you may want to know if you have a genetic or a somatic mutation that might affect your treatment options.

Germline Testing	Somatic Testing
Strong family history of prostate cancer	All men with aggressive or advanced prostate cancer at the time of diagnosis
Family history of multiple cancers including breast, ovarian, colon, pancreatic	Evidence of recurrence after treatment
Family member diagnosed with cancer at age <50	Progression of disease while on treatment
Men diagnosed with prostate cancer <50	
Men diagnosed with aggressive or advanced prostate cancer	

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Why Are Black Men at Increased Risk for Prostate Cancer?

- Increased androgen receptor density
- Increased testosterone levels at all ages
- Possible increased androgen exposure in utero
- Increased genetic DNA repair pathway mutations
- Dietary and environmental risks
- Lack of access to health care (economic)
- Historical lack of trust in medical system (cultural)

Explanations for the Disparity in Outcomes for Black Men with Prostate Cancer

- Probable explanations:
  - **Current screening paradigm not as effective in Black Men**
    - The risk of prostate cancer for Black men with a PSA of 4 is equivalent to that of White men with a PSA of 13.4 ng/dL*
  - **Diagnosed at a later stage**
    - **Black men have treatment outcomes which are equal, at every stage of diagnosis, to other men**
- Suggested contributing factors:
  - Access to care: Economic and cultural factors
  - Black men “offered” less-effective treatments (controversial)

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*Lee KM, Bryant AK, Lynch JA, et al. Association between prediagnostic prostate-specific antigen and prostate cancer probability in Black and non-Hispanic White men. *Cancer*. 2024; 130(2): 224-231. https://doi.org/10.1002/cncr.34979

How PSA Informs the Risk of Prostate Cancer

At every level of PSA, Black men have a higher risk of having prostate cancer and of having a more aggressive prostate cancer.

Predicted Biopsy Results	Caucasian (PSA 4.0)	Black (PSA 4.0)	Caucasian (PSA 13.4)	Black (PSA 13.4)
Aggressive	7%	18%	19%	39%
Non-aggressive	23%	22%	27%	22%
No cancer	70%	60%	54%	39%

Lee KM, Bryant AK, Lynch JA, et al. Association between prediagnostic prostate-specific antigen and prostate cancer probability in Black and non-Hispanic White men. *Cancer*. 2024; 130(2): 224-231. https://doi.org/10.1002/cncr.34979

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Recommendations for Screening Black Men by the Prostate Cancer Foundation (Jan 2024)

- *Black men should obtain information about PSA screening for prostate cancer.*
- *Among Black men who elect screening, baseline PSA testing should occur between ages 40-45.*
- *Depending on the PSA value and health status, annual screening should be strongly considered.*
- *Personalized prostate cancer surveillance and/or treatment can prevent potential harms from overdiagnosis.*

https://ascopubs.org/doi/10.1200/JCO.2024.42.4_suppl.264 (Jan 2024)

Proposed Paradigm for Screening and Risk Stratification for All Men

- Men at increased risk on the basis of race or family history, begin screening at age 40 and repeat annually until age 75 or until life expectancy is less than 10 years.
- Men at average risk begin screening at age 45 and repeat annually until age 75 or life expectancy of less than 10 years.

Proposed Paradigm for Screening and Risk Stratification

Men ≤ 60 PSA should be < 2.5
Men >60 PSA should be < 4.0
Elevation > 0.35 ng/mL in a year (PSA velocity)

- **Screening to include:**
  - History including targeted family history
  - Digital rectal exam
  - Repeat abnormal PSA in 6-12 weeks (40% will normalize)
  - PSA and/or variants (e.g., PSAII (PSA and %free PSA), PHI, 4K, PSA density)
  - Utilize risk calculators (https://www.riskcalc.org/PCPTRC/)

- **If increased risk based on above, then:**
  - See a urologist for further risk stratification
  - If appropriate, consider the following prior to prostate biopsy:
    - Biomarkers (Exodx, PCA3, and others)
    - Perform imaging (mpMRI, ultrasound, PSMA-PET CT)
  - Genetic information, if available, may be considered

If increased risk is confirmed and overall health, age and co-morbidities permit, see urologist

Prostate Cancer Risk Calculators

PCPT Risk Calculator answers the question:

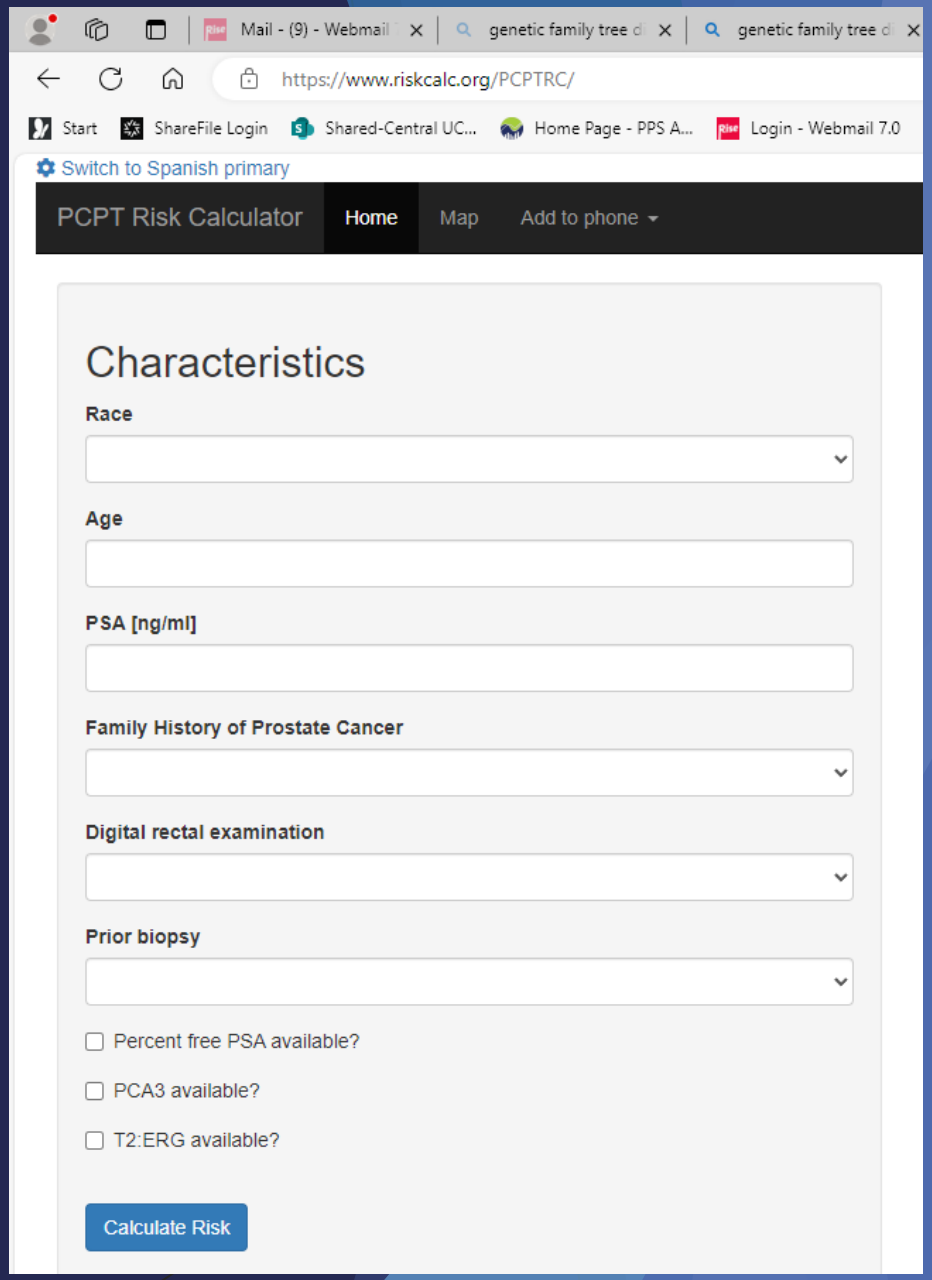
"What is the likelihood of having clinically significant disease?"

The PCPT Risk Calculator considers race as a factor.

https://www.riskcalc.org/PCPTRC/

There are other on-line calculators which include additional information such as biomarkers and imaging:

https://www.prostatecancer-riskcalculator.com



Caucasian

66 yrs old

PSA 5.3

Positive family hx

Normal DRE

No prev bx

% free PSA 13%

Characteristics

Race: Caucasian

Age: 66

PSA [ng/ml]: 5.3

Family History of Prostate Cancer: Yes

Digital rectal examination: Normal

Prior biopsy: Never had a prior biopsy

☑ Percent free PSA available?

Percent free PSA: 13

Risk of prostate cancer if biopsy were to be performed

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

14% chance of high-grade prostate cancer,

36% chance of low-grade cancer,

40%

50% chance that the biopsy is negative for cancer.

About 2 to 4% of men undergoing biopsy will have an infection that may require hospitalization.

Please consult your physician concerning these results.

If you are Caucasian, click here for a new update to the PCPTRC that incorporates detailed family history into a risk of prostate cancer calculation.

African American

66 yrs old

PSA 5.3

Positive family hx

Normal DRE

No prev bx

% free PSA 13%

Characteristics

Race: African American

Age: 66

PSA [ng/ml]: 5.3

Family History of Prostate Cancer: Yes

Digital rectal examination: Normal

Prior biopsy: Never had a prior biopsy

☑ Percent free PSA available?

Percent free PSA: 13

Risk of prostate cancer if biopsy were to be performed

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

30% chance of high-grade prostate cancer,

31% chance of low-grade cancer,

61%

39% chance that the biopsy is negative for cancer.

About 2 to 4% of men undergoing biopsy will have an infection that may require hospitalization.

Please consult your physician concerning these results.

How the Application of Risk Stratification Improves Outcomes in All Men

Some men may be able to avoid prostate biopsy

- Urinary biomarkers have a high-negative predictive value **89%***
  - Easy to do. Some biomarkers don't require a rectal exam and can be done with a home-test kit.

- A "negative" prostate MRI predicts a lower risk of a significant cancer but may miss 20-30% of significant cancers

Men confirmed to be at increased risk may be diagnosed earlier when treatment is more likely to be effective

Survival	Localized	Distant
5-year survival	100%	36.6%
10-year survival	99.1%	29.2%

https://seer.cancer.gov/statfacts/html/prost.html

**European Urology. 74(2018):731-738*

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Proposed Paradigm for Screening and Risk Stratification for All Men

- If increased risk, then:
  - See a urologist for further risk stratification. If appropriate, consider:
    - **Urinary biomarkers***
      - Without DRE: ExoDx, MiR Sentinel
      - Post-DRE: PCA3, MPS, SelectMDx, TMPRSS2:ERG
    - Perform imaging: mpMRI prostate, ultrasound, PSMA-PET CT

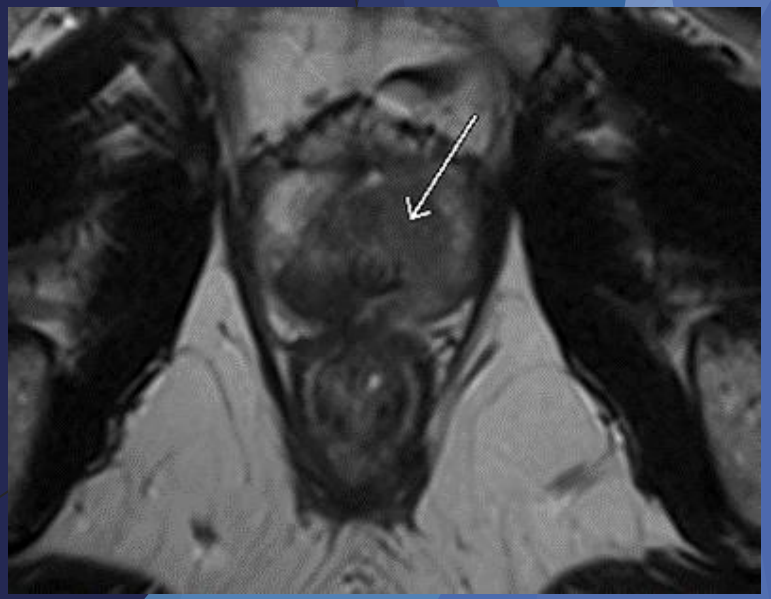
- If increased risk is confirmed and overall health, age and co-morbidities permit, discuss prostate biopsy with urologist

*2023 AUA Guidelines for Prostate Cancer Screening: Table 6.

Pursuing Elevated Prostate Cancer Risk

- **Biomarkers:**
  - ExoDx (urine test)
    - Does not require DRE
    - Can be obtained at home and mailed in
    - Has a binary outcome (<15.6 low risk, >15.6 high risk)
    - 89% negative predictive value for significant disease

- **Imaging:**
  - mpMRI is the preferred imaging test at present
    - PI-RADS 3 35% probability of positive biopsy
    - PI-RADS 4 60% probability of positive biopsy
    - PI-RADS 5 80% probability of positive biopsy

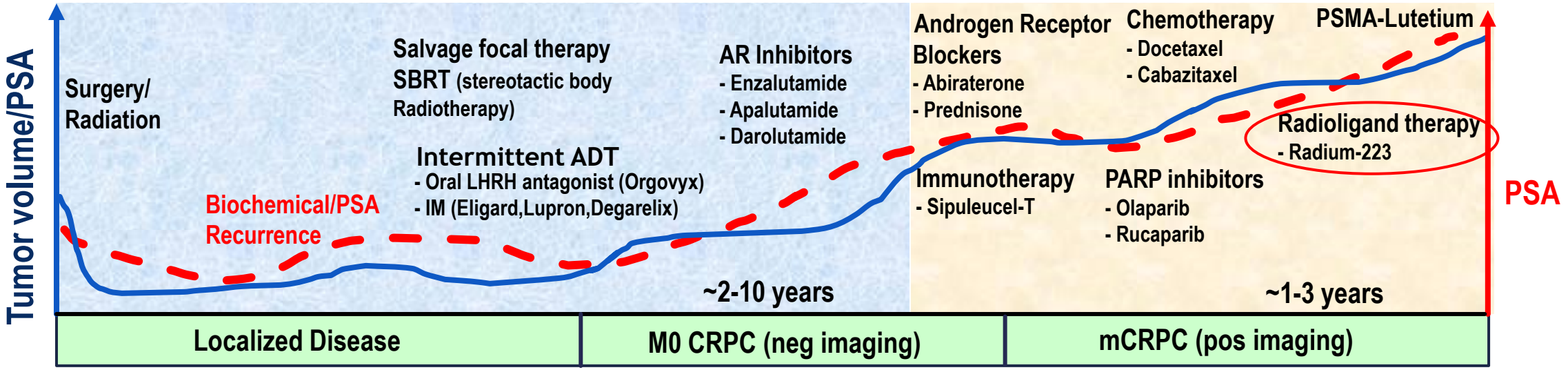


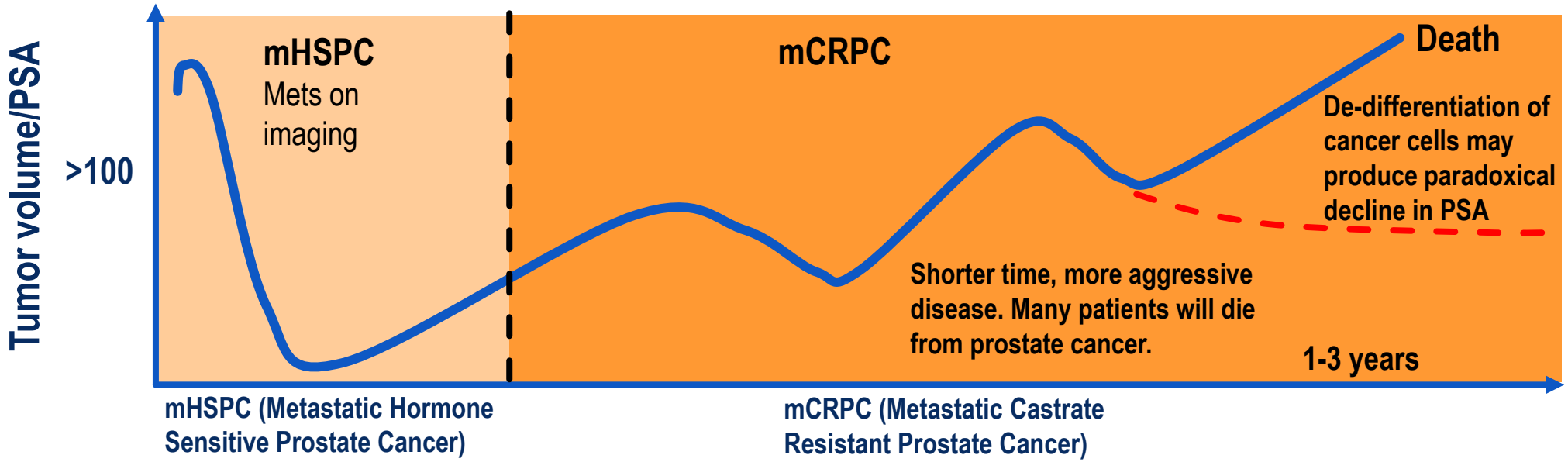
Take Home Points on Screening and Early Diagnosis

- Know your family history
- Control your risk factors (Heart-healthy = Prostate-healthy)
- Do annual PSA-related screening beginning at 45 (40 if you are of Black ethnicity or have a strong family history). Insist on it, even if your doctor demures.
- Take advantage of risk calculators, biomarkers, and imaging before deciding about biopsy

Disease Continuum of Prostate Cancer

Usual prostate cancer course: from localized to metastatic





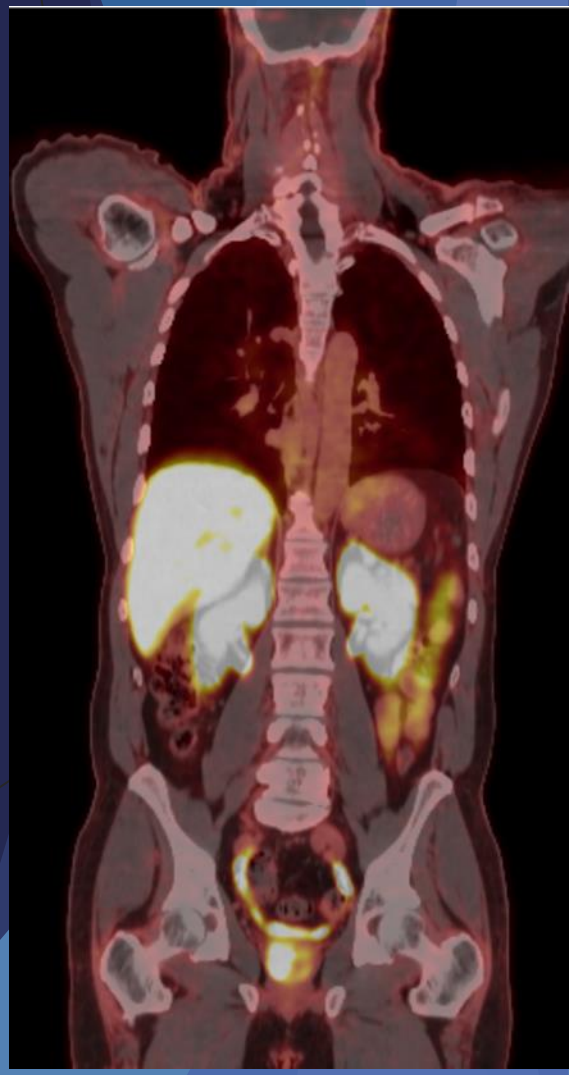
Biochemical Recurrence of Prostate Cancer

- What is biochemical recurrence?
  - Detectable PSA after radical prostatectomy
  - After XRT: Two consecutive increases in PSA after the PSA reaches its lowest point

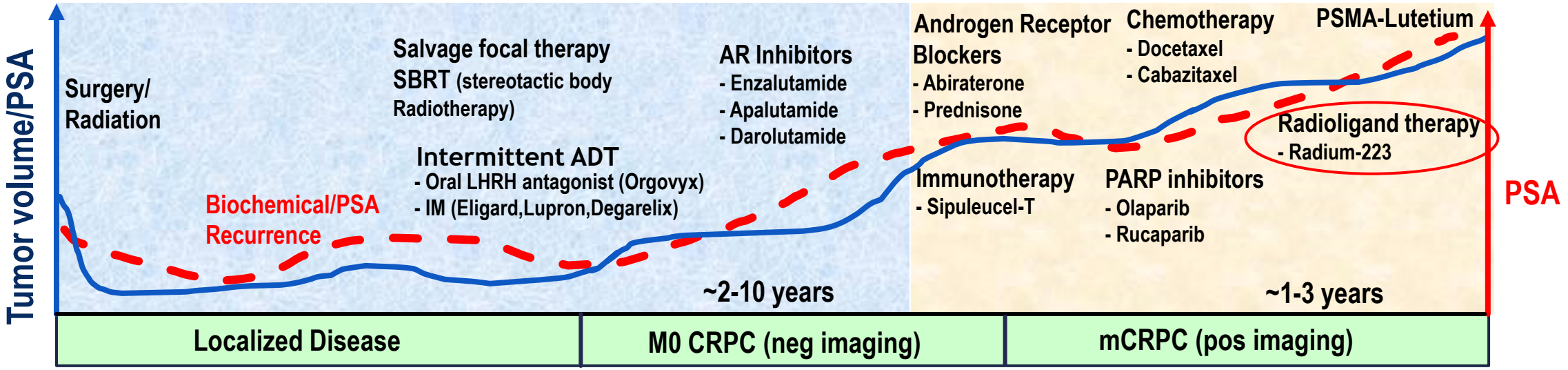
Imaging to Investigate Biochemical Recurrence

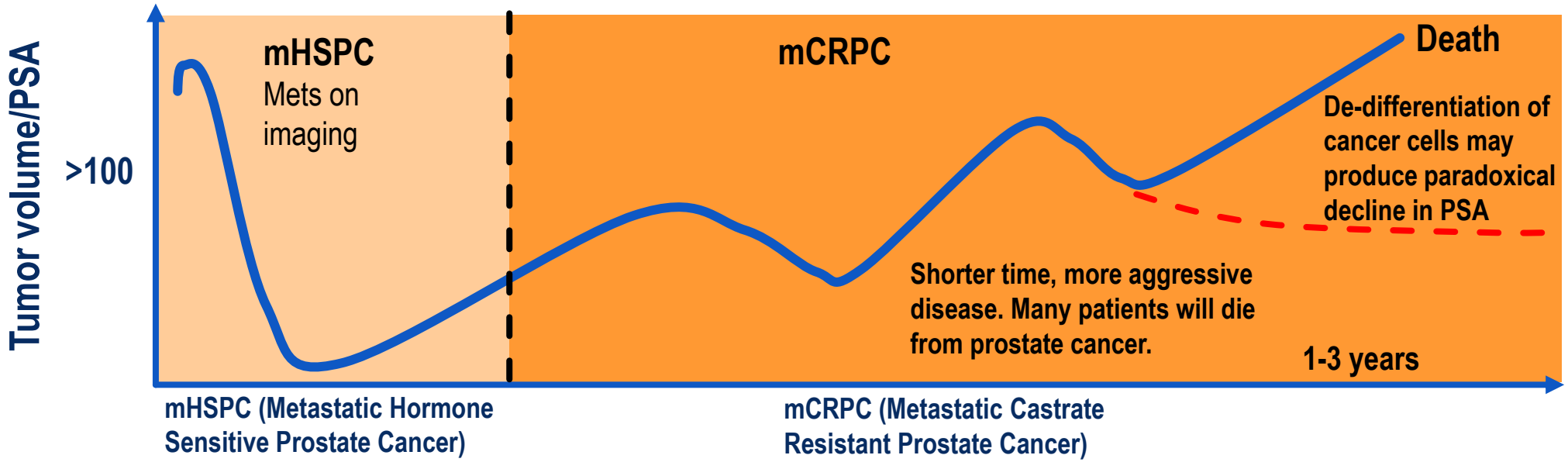
PSMA-PET CT is Exquisitely Specific (90%) but Not Sensitive (30%)

- F-18 PSMA
  - Relevant clinical trial using Posluma & Orgovyx (IIT)
- Gallium-68
- Copper-64
  - Relevant clinical trials:
    - Clarify (Clarity Pharmaceuticals)
    - Solar Stage, Solar Recur (Curium)



Usual prostate cancer course: from localized to metastatic



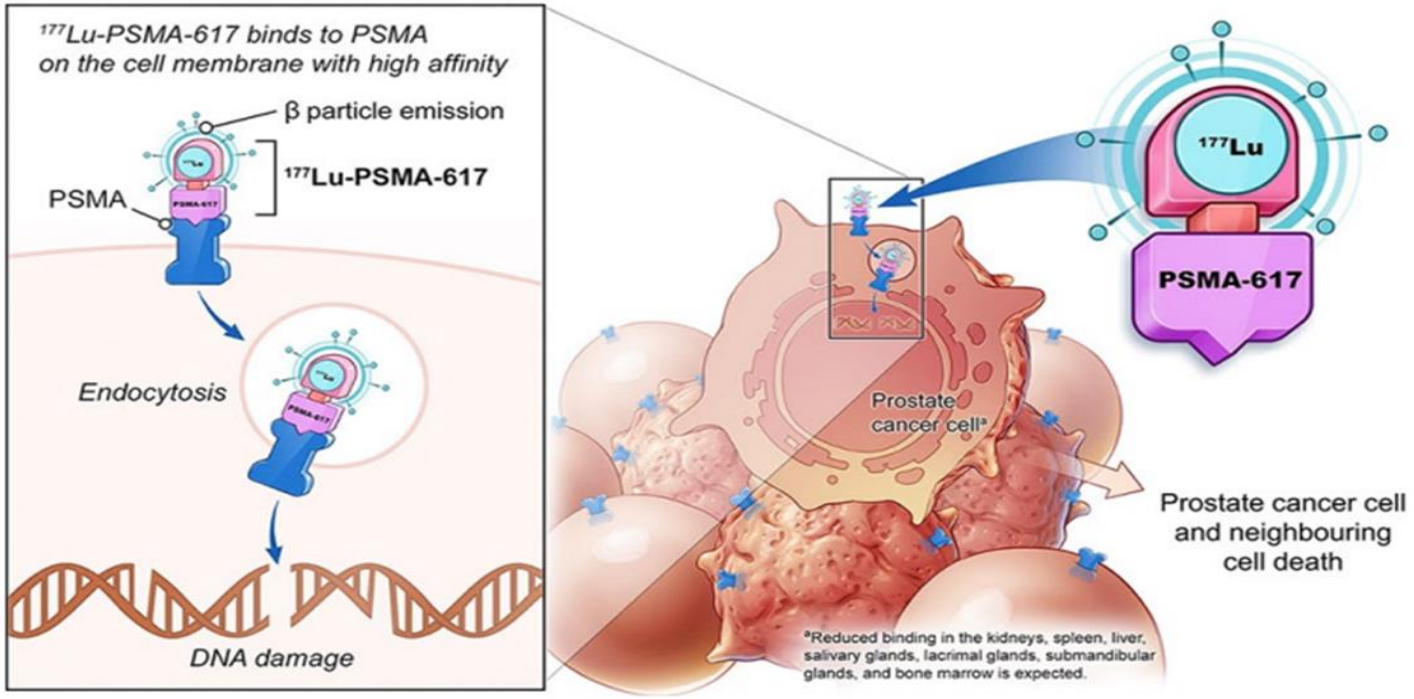


PSMA-based Radioligand Therapy

Novartis-PSMA Care Trial

^{177}Lutetium-PSMA-617

- Beta-emitter lutetium
- Targeted to prostate specific membrane antigen (PSMA), highly expressed on prostate cancer cells
- Able to target both soft tissue and bone lesions



Treatment After Recurrence

Active Surveillance

Radical treatment (prostatectomy, radiotherapy)

Focal Treatment

Modifications of ADT, salvage focal therapy, PSMA-based radioligand therapy, PSMA-based combination drug therapy, chemotherapy

Clinical Trials

Questions ??

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