INTRO TO PROSTATE CANCER: RISK FACTORS, SCREENING, IMAGING

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15 MAY 2024

AGENDA

- PROSTATE FUNCTION
- PROSTATE CANCER- WHAT & WHY IT MATTERS
- GLEASON SCORE, STAGING & RISK GROUP
- RISK FACTORS
- SCREENING OPTIONS/TESTS
  - PSA, DRE
  - BIOMARKERS
  - IMAGING

- QUESTION & ANSWER

SUPPORT GROUP LONG-TERM GOALS:

Improve Shared-Decision Making

Holistically support you physical, mental, and spiritual health

Help you advocate for yourself & have confidence in your treatment plan

Help you navigate the balance of quantity and quality of life

Help decrease treatment regret, feeling overwhelmed or intimidated

Help you understand where to look for information, resources, & support

CONFIDENTIALITY & CONSIDERATIONS

Information is live streamed, not recorded

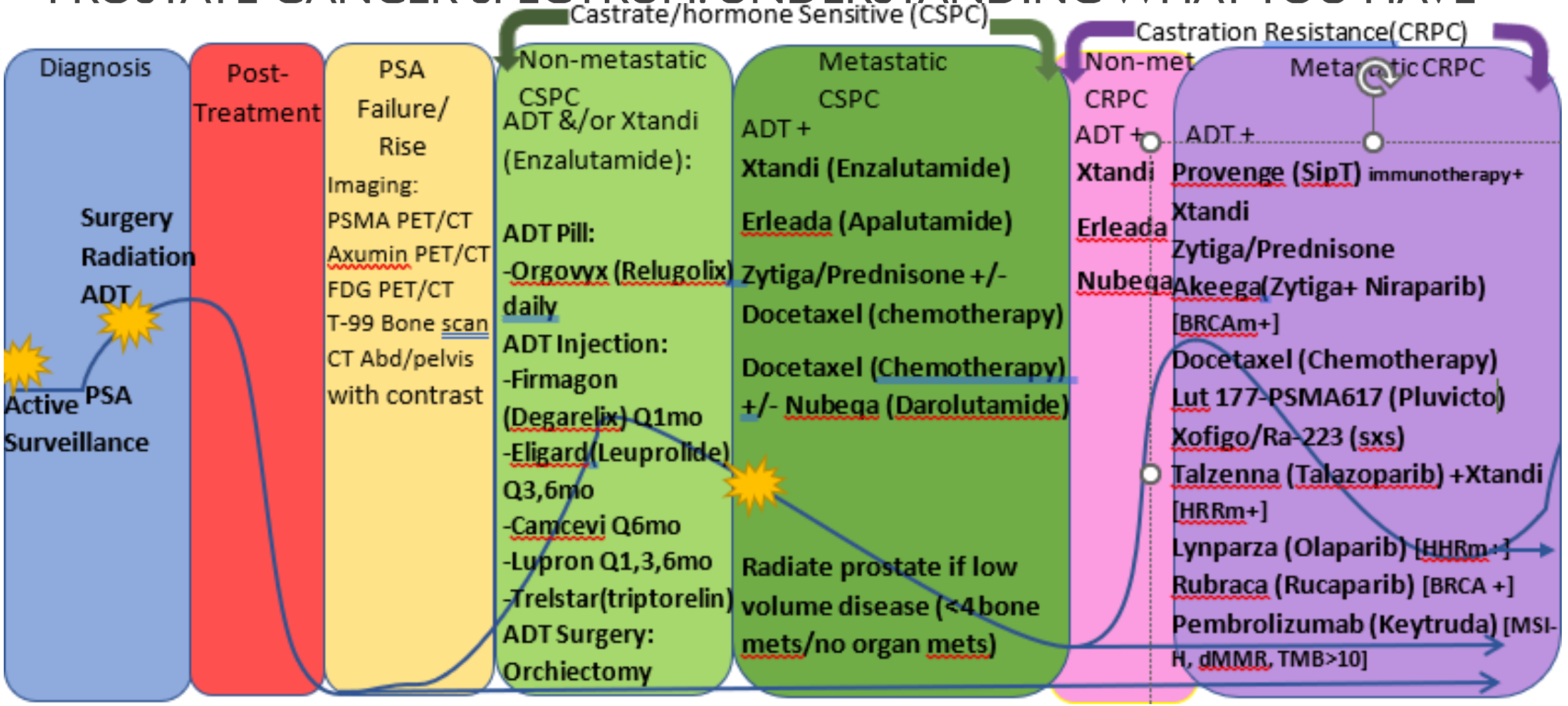
The information provided should *not replace* consultations with qualified health care professionals to meet your individualized medical needs

We are *not* here for Second Opinions but education and support

Be considerate/respectful and conscientious of others' time, feelings, and needs

Everyone is responding to their diagnosis and treatment in their own way at a different place in their prostate cancer journey

PROSTATE CANCER SPECTRUM: UNDERSTANDING WHAT YOU HAVE



Misconception: There's just one type or one treatment

YOUR TUCSON ADVANCED PROSTATE CANCER CLINIC (APCC)TEAM

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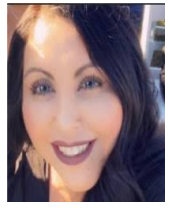

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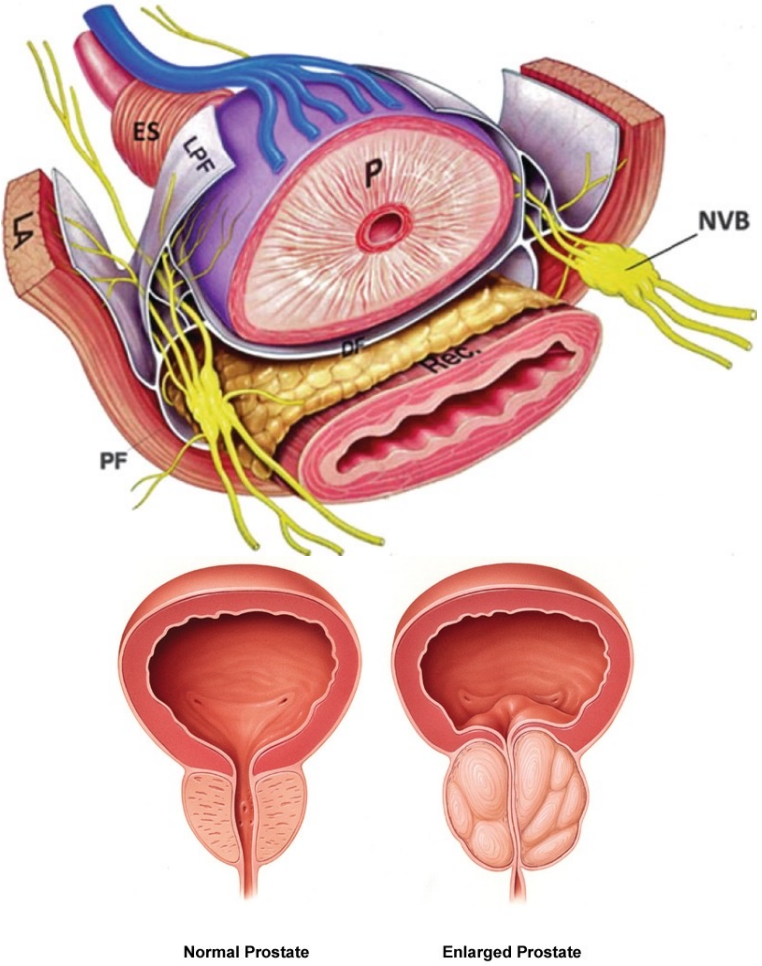
DISCLOSURES

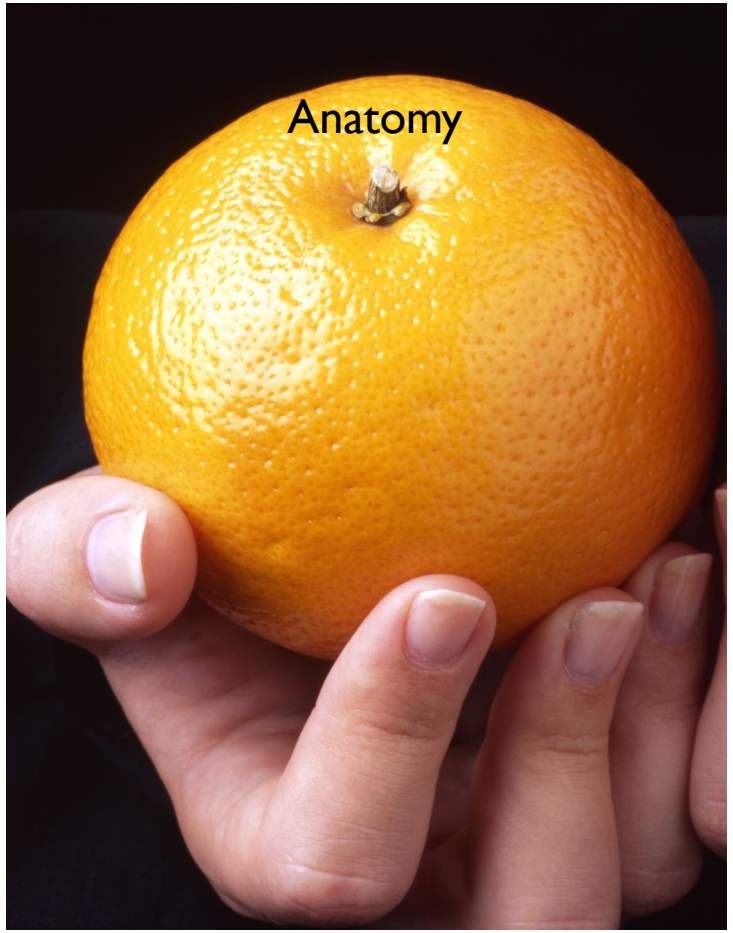
Janssen BioTech

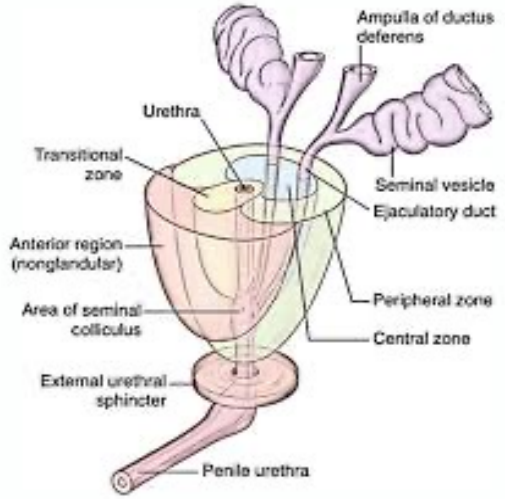
Tempus Labs

Dendreon

PROSTATE CANCER JOURNEY







WHAT'S IT FOR? *ELIMINATES SEMEN/SEXUAL FUNCTION*

HOW IS IT UNIQUE? *PROSTATE IS ANDROGEN(HORMONE) SENSITIVE*

WHERE? *SITS IN LINE WITH URINARY TRACT- URINATION ELIMINATION AND EJACULATION*

Ecosystem Analogy: Invasive species

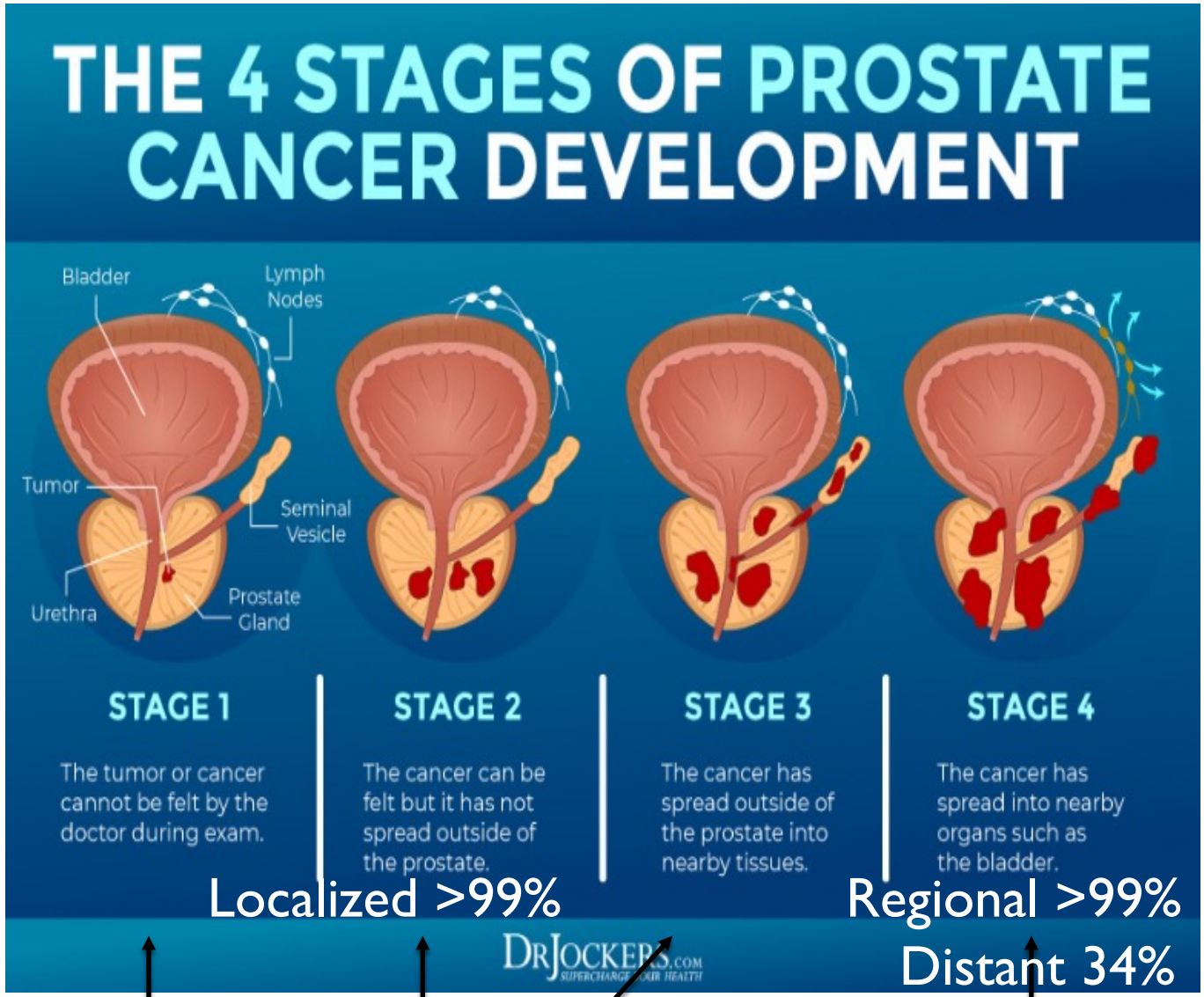
What causes you to die?

INSIDE A TUMOR: WHAT IS CANCER? VIDEO SERIES (YOUTUBE.COM)

PROSTATE CANCER STAGING

- **Stage 1:** one side of prostate

  (confined to prostate)
- **Stage 2:** both sides of prostate, nodule on exam **(confined to prostate)**
- **Stage 3:** Extends beyond capsule of prostate or into seminal vesicle
- **Stage 4**: **metastatic** to lymph node, organ or bone
  - Hormone/castrate ***sensitive***
  - Hormone/castrate ***resistance***



5 year survival rate

Localized >99%

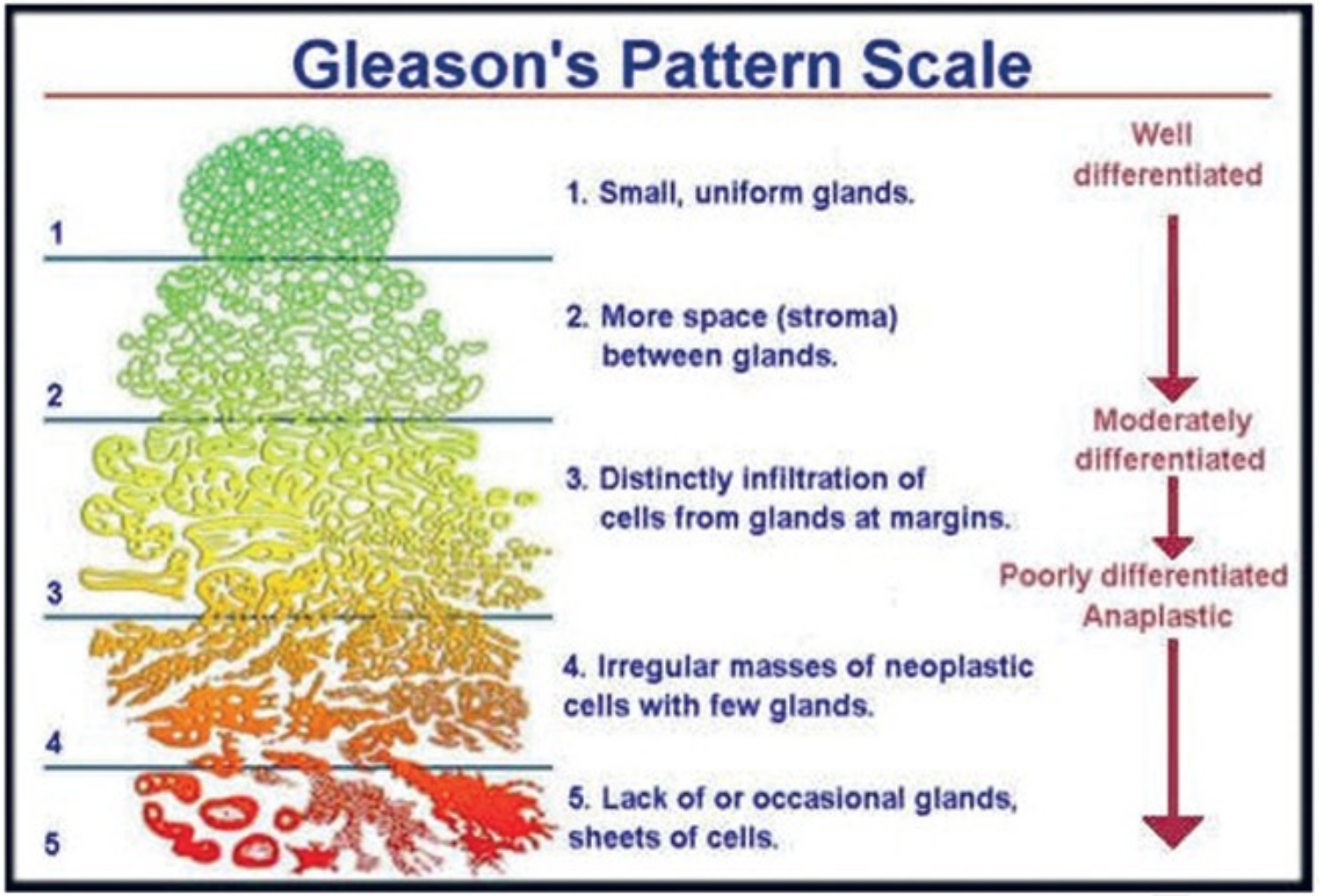
Regional >99%

Distant 34%

nonmetastatic

metastatic

PROSTATE CANCER GLEASON SCALE



Less aggressive

Grade Group	Gleason Score
Grade Group 1	Gleason Score ≤ 6
Grade Group 2	Gleason Score 7 (3 + 4)
Grade Group 3	Gleason Score 7 (4 + 3)
Grade Group 4	Gleason Score 8
Grade Group 5	Gleason Score 9-10

More aggressive

PROSTATE CANCER RISK GROUP

1 PSA
2 PSA Density
3 Rectal Exam
4 Gleason Grade
5 Volume of positive biopsy cores

National Comprehensive Cancer Network®

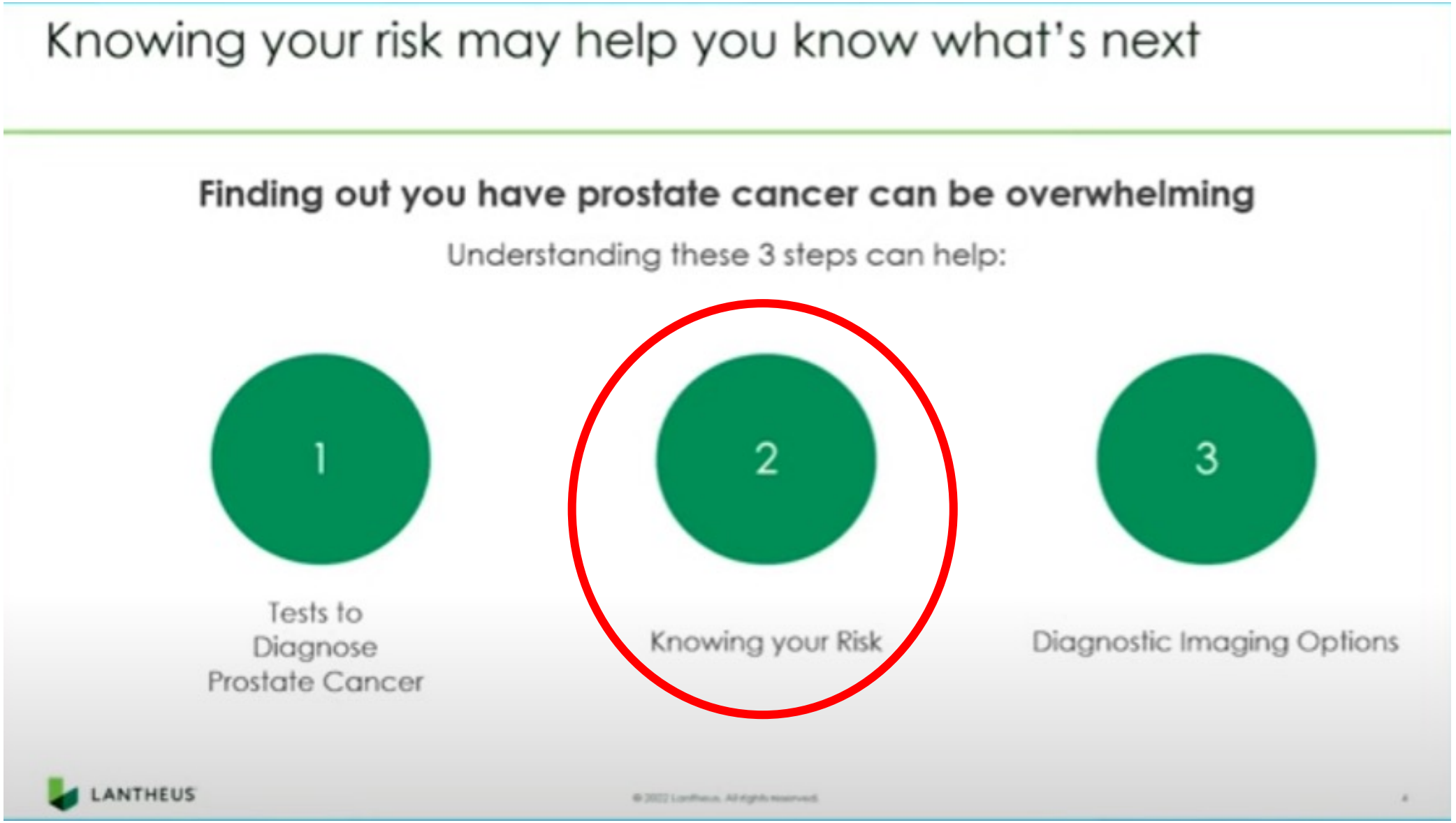
NCCN Guidelines Version 1.2024
Prostate Cancer

NCCN Guidelines Index
Table of Contents
Discussion

INITIAL RISK STRATIFICATION AND STAGING WORKUP FOR CLINICALLY LOCALIZED DISEASE[i]

Risk Group	Clinical/Pathologic Features (Staging, ST-1)			Additional Evaluation[f,m]	Initial Therapy
Very low[j]	Has all of the following: • cT1c • Grade Group 1 • PSA <10 ng/mL • <3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core[k] • PSA density <0.15 ng/mL/g			• Confirmatory testing can be used to assess the appropriateness of active surveillance (PROS-F 2 of 5)	PROS-3
Low[j]	Has all of the following but does not qualify for very low risk: • cT1–cT2a • Grade Group 1 • PSA <10 ng/mL			• Confirmatory testing can be used to assess the appropriateness of active surveillance (PROS-F 2 of 5)	PROS-4
Intermediate[j]	Has all of the following: • No high-risk group features • No very-high-risk group features • Has one or more intermediate risk factors (IRFs): • cT2b–cT2c • Grade Group 2 or 3 • PSA 10–20 ng/mL	Favorable intermediate	Has all of the following: • 1 IRF • Grade Group 1 or 2 • <50% biopsy cores positive (eg, <6 of 12 cores)[l]	• Confirmatory testing can be used to assess the appropriateness of active surveillance (PROS-F 2 of 5)	PROS-5
		Unfavorable intermediate	Has one or more of the following: • 2 or 3 IRFs • Grade Group 3 • ≥ 50% biopsy cores positive (eg, ≥ 6 of 12 cores)[l]	Bone and soft tissue imaging[g,h] • If regional or distant metastases are found, see PROS-8 or PROS-13	PROS-6
High	Has no very-high-risk features and has exactly one high-risk feature: • cT3a OR • Grade Group 4 or Grade Group 5 OR • PSA >20 ng/mL			Bone and soft tissue imaging[g,h] • If regional or distant metastases are found, see PROS-8 or PROS-13	PROS-7
Very high	Has at least one of the following: • cT3b–cT4 • Primary Gleason pattern 5 • 2 or 3 high-risk features • >4 cores with Grade Group 4 or 5			Bone and soft tissue imaging[g,h] • If regional or distant metastases are found, see PROS-8 or PROS-13	PROS-7

PROSTATE CANCER JOURNEY

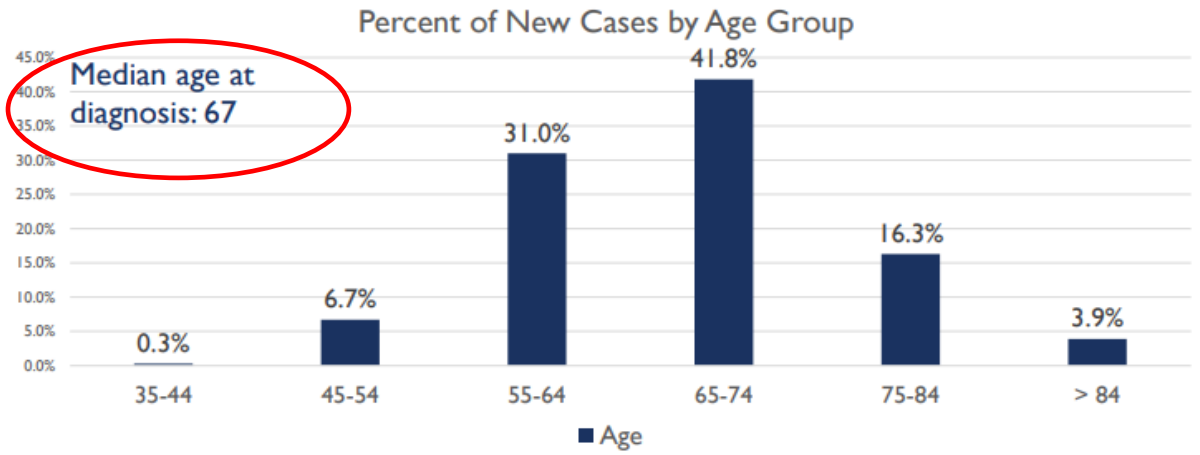


PROSTATE CANCER RISK FACTORS

1 Age
2 Race
3 Family History/Genetics
4 Environmental Exposures
5 Medications
6 Diet/Lifestyle

RISK FACTORS: AGE

PROSTATE CANCER STATS



PSA SCREENING

- Age adjusted PSA reference ranges:

Age	PSA (ng/mL)
< 50	≤ 1.5
50 – 54	≤ 2.0
55 – 59	≤ 3.0
60 – 69	≤ 4.0
≥ 70	≤ 6.0

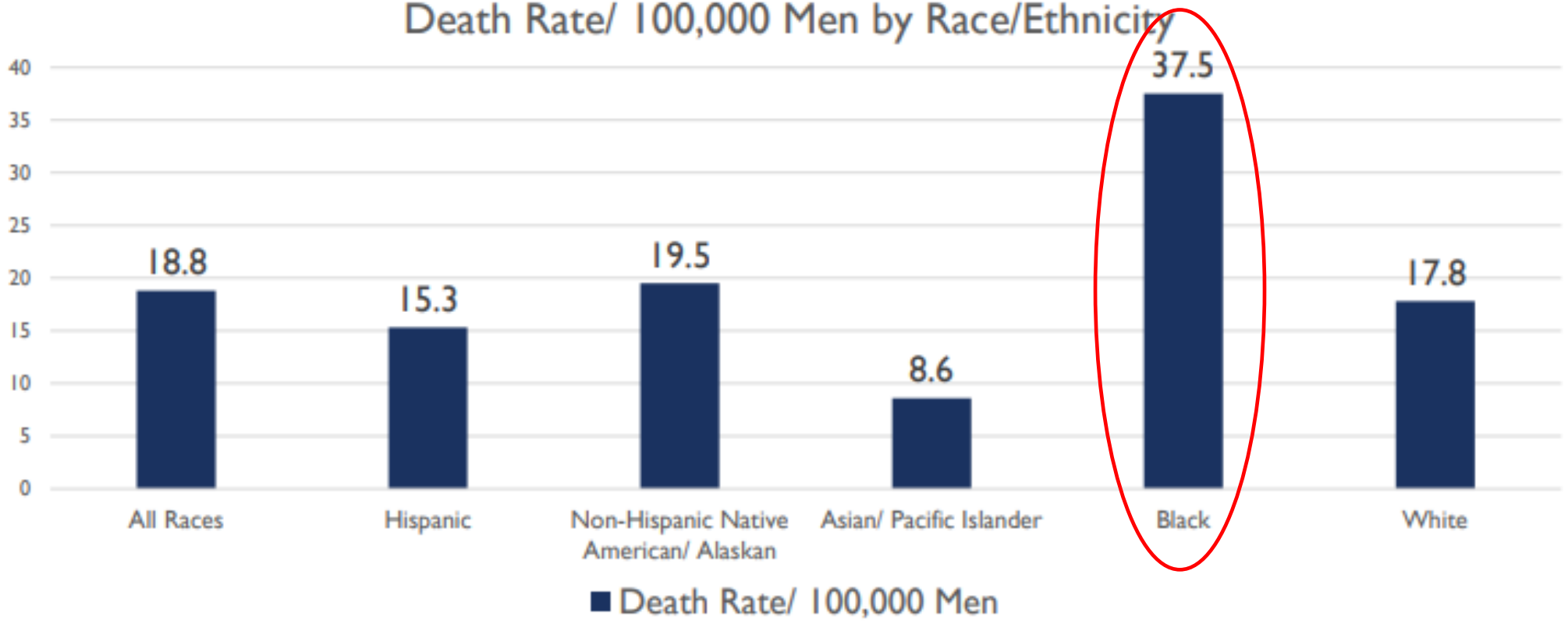
US SSA: MALE LIFE EXPECTANCY

Age	Death probability w/in 1-yr	Life expectancy (yrs)
70	2.6%	13.59
71	2.8%	12.94
72	3.0%	12.3
73	3.3%	11.67
74	3.7%	11.05
75	4.1%	10.46
76	4.5%	9.88
77	4.9%	9.32
78	5.4%	8.77
79	6.0%	8.25
80	6.6%	7.74
81	7.2%	7.25
82	8.0%	6.77
83	8.9%	6.31
84	9.8%	5.88
85	10.9%	5.47

US Social Security Actuarial Life Table 2020 (2023 TR). https://www.ssa.gov/oact/STATS/table4c6.html. Accessed 12/27/2023.

RISK FACTORS: RACE/ANCESTRY

PROSTATE CANCER STATS



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

RISK FACTORS: GENETICS/FAMILY HISTORY

b If there is a known or suspected cancer susceptibility gene, referral to a cancer genetics professional is recommended. Individuals harboring germline mutations in prostate cancer risk genes may have an elevated lifetime risk of prostate cancer and, in the case of certain genes or mutations, an *elevated risk of early onset and/or potentially lethal prostate* cancer (eg, **BRCA2**).

Such risk genes include, but are not limited to, BRCA2, BRCA1, ATM, CHEK2, PALB2, HOXB13, MLH1, MSH2, MSH6, PMS2, EPCAM, and TP53

RISK FACTORS: GENETICS/FAMILY HISTORY

a One 1st or 2nd degree relative (uncle, cousin):

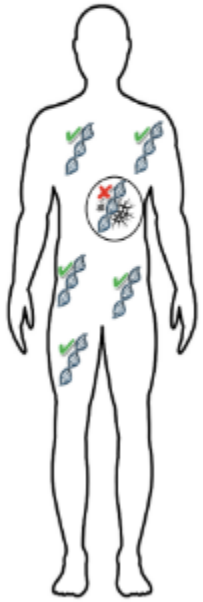
- Metastatic prostate cancer
- Ovarian cancer
- Breast cancer in a relative assigned male at birth
- Breast cancer diagnosed in a relative assigned female at birth at age ≤45 years
- Colorectal or endometrial cancer at ≤50 years
- Pancreatic cancer

≥Two 1st or 2nd degree relatives (uncle, cousin):

- Breast
- Prostate (but not clinically localized Grade Group 1)
- Colorectal
- Endometrial cancer at any age

RISK FACTORS: GENETICS/FAMILY HISTORY

Somatic vs. Germline Testing

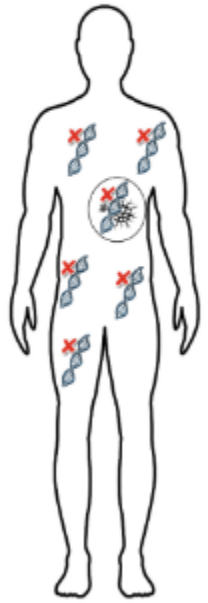


Somatic:

- Performed on a piece of the **tumor** or cancer
- Looks at **genomic variants in cancer cells**
- Done to help find the best medication or treatment for an individual tumor or cancer
- May aid in diagnosis of certain cancers
- Does not provide information about inherited risk or cancer risk for others in the family.

Germline:

- Performed on usually a blood or saliva sample
- Looks for **genetic variants** that are **in all cells of the body**
- Provides information about **inherited cancer risk** and the risk for future cancers
- May have implications for treatment for certain cancers
- May help the whole family better understand what to do for cancer screening and ways to reduce the risk for cancer



RISK FACTORS: GENETICS/FAMILY HISTORY

WHAT IF I DON'T HAVE KIDS?

Do you have brothers, sisters, nieces or nephews?

DO YOU WANT TO KNOW IF THERE IS A TOOL IN YOUR TOOLBOX?

In mCRPC patients, PARP Inhibitors stop the PARP from doing its repair work in the cancer cells and they die

RISK FACTORS: GENETICS/FAMILY HISTORY

Summary:

Somatic testing (ie Tempus xT, xF

Who: Advanced stage GU cancer patients patients;

Which Test: xT on tissue if available, adequate for sequencing;
xF: to complement tissue especially if potential for inadequate tissue specimen; or as a stand alone

When: At advanced stage dx, as information may inform current/future tx decisions
Consider reassessment at progression (ie xT on metastatic bx and/or xF plasma based)

Why: Expanding number of tumor agnostic biomarkers linked to FDA approved therapies many of which may have
benefit that exceeds otherwise standard therapy options

Germline
(Prostate Cancer)

Who: Advanced stage (Metastatic/Regional) - regardless of age or family history
High or very high risk Localized regardless of age of family history
Many others (FHx, Ancestry, Personal history, consider in intermediate risk intraductal/cribiform etc..)
Incidental variant identified on somatic test such as xT

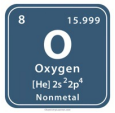
Which test: Broad panel validated germline test such as Tempus xG

When: Early/at Dx

Why: Therapeutic implications: (iPARPs, other); Familial and personal cancer risk implications

- **RISKS:**
- **2008 Genetic Information Nondiscrimination Act (GINA) Law**
  - **Disability & Health Insurance protected**
    - **Life & Long-term care insurance not protected**
- **Cascade Testing**
- **Variants of Uncertain significance**
- **Genetic counseling**

RISK FACTORS: ENVIRONMENT EXPOSURE



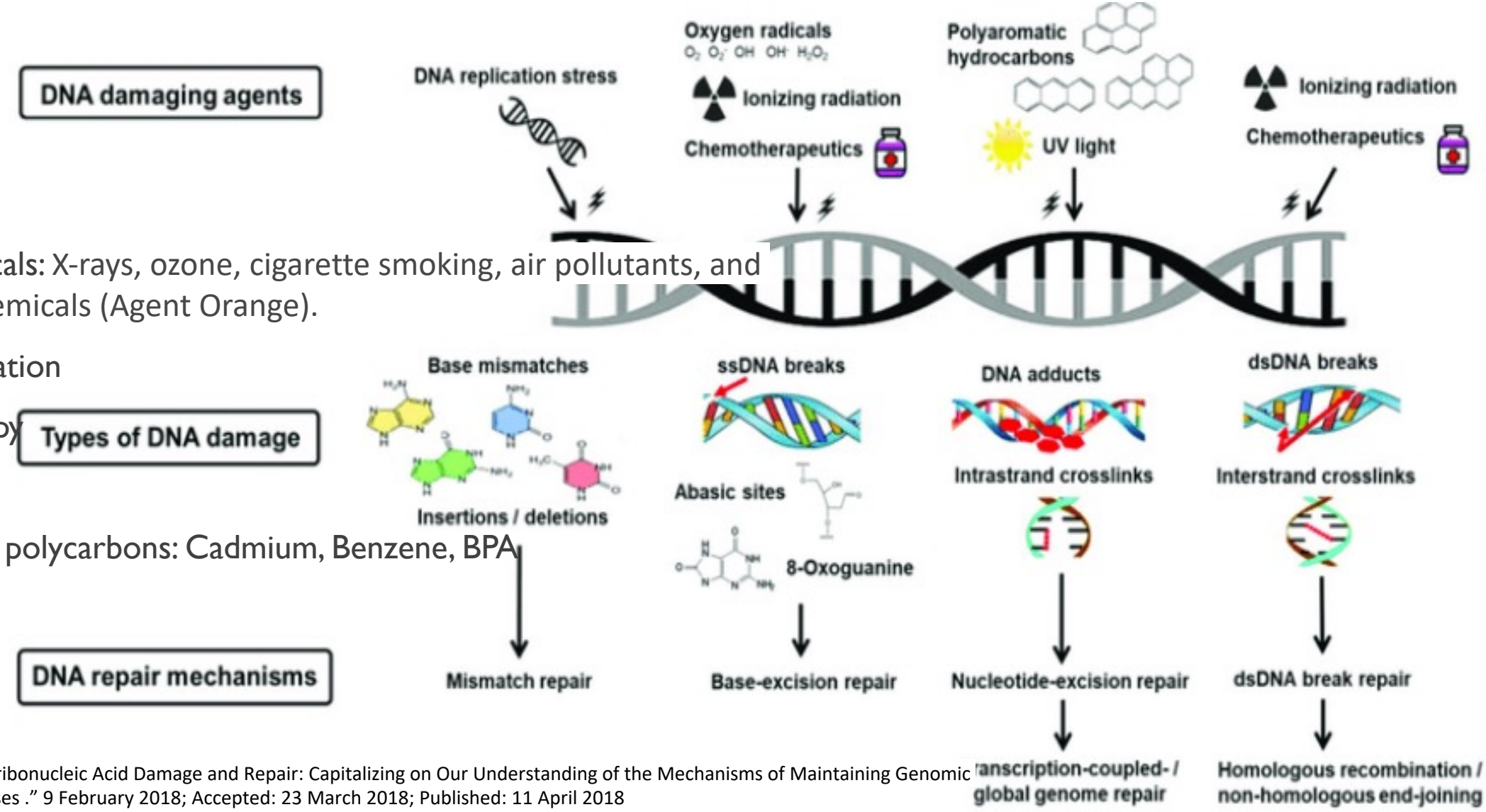
- Oxygen radicals: X-rays, ozone, cigarette smoking, air pollutants, and industrial chemicals (Agent Orange).

- Ionizing Radiation

- Chemotherapy

- UV Light

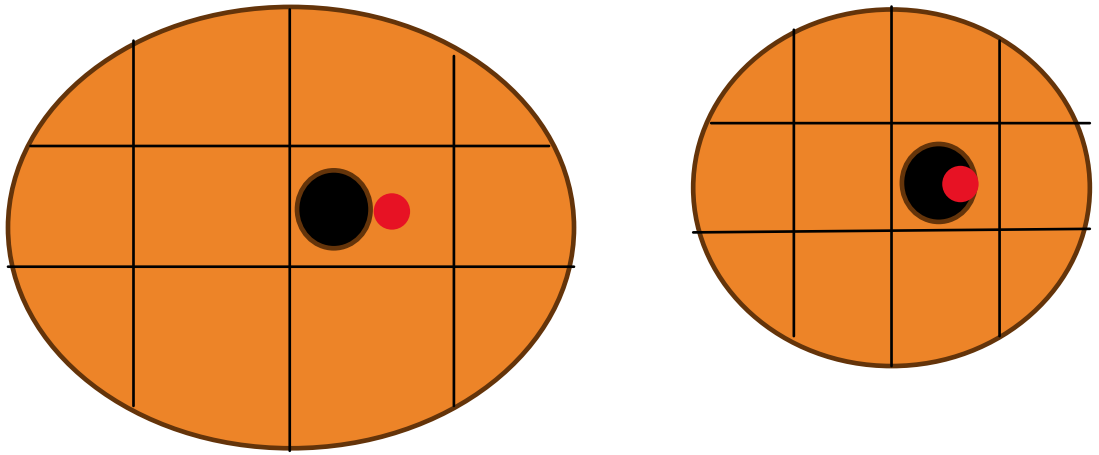
- Polyaromatic polycarbons: Cadmium, Benzene, BPA



Helena, Jolene M, et al. “Deoxyribonucleic Acid Damage and Repair: Capitalizing on Our Understanding of the Mechanisms of Maintaining Genomic Integrity for Therapeutic Purposes .” 9 February 2018; Accepted: 23 March 2018; Published: 11 April 2018

RISK FACTORS: MEDICATIONS

- Finasteride & Dutasteride "controversy"
  - 2003 Prostate Cancer Prevention Trial (PCPT)
  - Detection bias
    - Shrinks prostate ~25%
    - Cuts PSA ~50%



RISK FACTORS: SHOULD I CHANGE MY DIET?

Defined low-risk subjects:

1) Not currently smoking or had quit for ≥10 years

2) Body mass index <30 kg/m² *(no obesity)*

3) engaged in ≥3 hours of vigorous activity/week and/or walked briskly ≥7 hours/week *(not sedentary)*

4) consumed ≥4 servings of tomato sauce/week (more tomatoes)

5) consumed ≥2 servings of fish/week (more Fish)

6) consumed <3 servings of processed red meat/week (less meat)

Supplements:

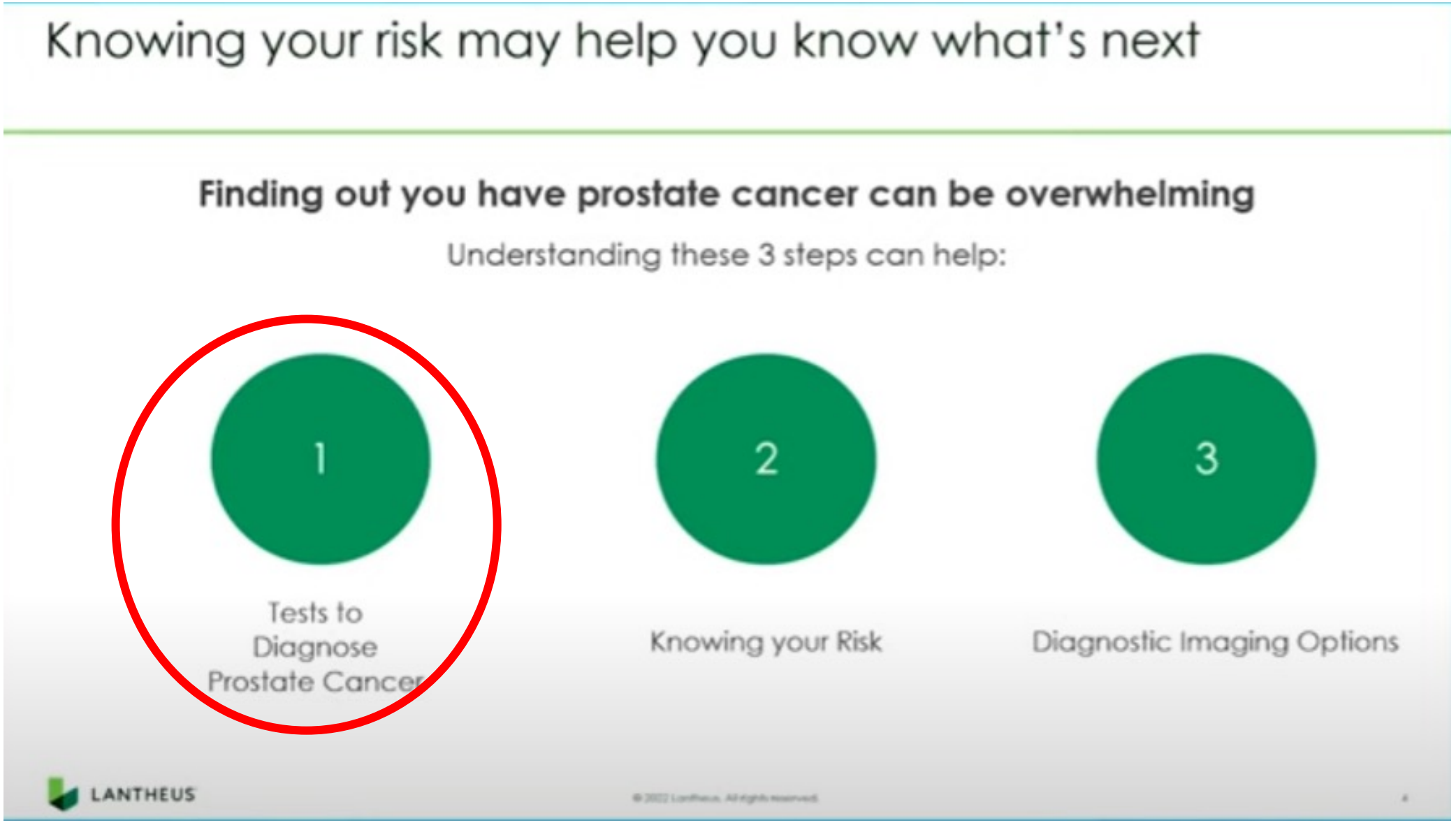
No strong evidence to support Lycopene, selenium, Vitamin E

SCREENING: EARLY DETECTION OF PROSTATE CANCER: AUA/SUO GUIDELINE 2023

1. Clinicians should engage in shared decision-making (SDM) with people for whom prostate cancer screening would be appropriate and proceed based on a person's values and preferences. (*Clinical Principle*)
2. When screening for prostate cancer, clinicians should use PSA as the first screening test. (*Strong Recommendation; Evidence Level: Grade A*)
3. For people with a newly elevated PSA, clinicians should repeat the PSA prior to a secondary biomarker, imaging, or biopsy. (*Expert Opinion*)
4. Clinicians may begin prostate cancer screening and offer a baseline PSA test to people between ages 45 to 50 years. (*Conditional Recommendation; Evidence Level: Grade B*)
5. Clinicians should offer prostate cancer screening beginning at age 40 to 45 years for people at increased risk of developing prostate cancer based on the following factors: Black ancestry, germline mutations, strong family history of prostate cancer. (*Strong Recommendation; Evidence Level: Grade B*)
6. Clinicians should offer regular prostate cancer screening every 2 to 4 years to people aged 50 to 69 years. (*Strong Recommendation; Evidence Level: Grade A*)
7. Clinicians may personalize the re-screening interval, or decide to discontinue screening, based on patient preference, age, PSA, prostate cancer risk, life expectancy, and general health following SDM. (*Conditional Recommendation; Evidence Level: Grade B*)
8. Clinicians may use digital rectal exam (DRE) alongside PSA to establish risk of clinically significant prostate cancer. (*Conditional Recommendation; Evidence Level: Grade C*)
9. For people undergoing prostate cancer screening, clinicians should not use PSA velocity as the sole indication for a secondary biomarker, imaging, or biopsy. (*Strong Recommendation; Evidence Level: Grade B*)
10. Clinicians and patients may use validated risk calculators to inform the SDM process regarding prostate biopsy. (*Conditional Recommendation; Evidence Level: Grade B*)
11. When the risk of clinically significant prostate cancer is sufficiently low based on available clinical, laboratory, and imaging data, clinicians and patients may forgo near-term prostate biopsy. (*Clinical Principle*)

- Shared Decision Making
- PSA is 1st screening test
  - Repeat if elevated
- Start 45-50yo
  - 40-45yo if increased risk
    - Family hx, genetic mutations, back ancestry
- Offer screening every 2-4 years 50-69yo
- Don't solely rely on PSA velocity
  - May use calculators, DRE, family history
- If low risk for clinically significant prostate cancer, may forgo biopsy

PROSTATE CANCER JOURNEY



PSA & PROSTATE CANCER SCREENING: DO I HAVE CLINICALLY SIGNIFICANT PROSTATE CANCER?

PSA

Protein enzyme called ***prostate-specific*** antigen (PSA), which liquefies the semen, essentially freeing it from the seminal coagulum. PSA also gets credit for neutralizing the cervix's blocking enzyme, which allows sperm to freely enter the uterus and, hopefully, penetrate the egg.

The half-life of PSA is 2 to 3 days.

BPH (ENLARGED PROSTATE)

50% 50-year-olds have BPH related lower tract urinary symptoms (LUTS).

Benefits

- Simple blood draw
  - No DRE, fasting, holding urination, etc.
- Early detection

Limitations

- Not specific
  - Detects clinically insignificant cancer, anxiety provoking
  - *Cycling, sex,* prostatitis

sensitive

- Misses aggressive cancer

SCREENING/RISK FACTOR ASSESSMENT

PROSTATE CANCER BIOMARKERS: URINE-BASED

Test	Biomarker Component	Patient Selection	Result	Key Test Characteristic	Clinical Use
ExoDx Prostate Intelliscore	PCA3, ERG, SPDEF, mRNA	Pre-biopsy	Risk of clinically significant PCa (csPCa) on biopsy	NPV = 91%	Rule out need for a biopsy
miR	Small non-coding mRNAs	Pre- and Post-biopsy	Risk of PCa and csPCa on biopsy	Specificity = 96% AUC = 0.98 – 0.99	PCa risk stratification
MPS MyProstateScore	PCA3, TMPRSS2:ERG, PSA	Pre-biopsy	Risk of csPCa on biopsy	NPV = 98%	Rule out csPCa on biopsy
PCA3	PCA3	Negative prior biopsy	Risk of PCa on biopsy	NPV = 88%	Rule out need for a repeat biopsy
SelectMDx	HOXC6, DLX1 mRNA	Pre-biopsy	Risk of csPCa on biopsy	AUC = 0.90	Select patients for biopsy

Parker WP, Borza T, Isharwal S, Vemulakonda V. Prostate Cancer Screening, Diagnosis and Risk Stratification. Prostate Cancer Screening, Diagnosis and Risk Stratification - Oncology - Adult | Urology Core Curriculum (auanet.org)

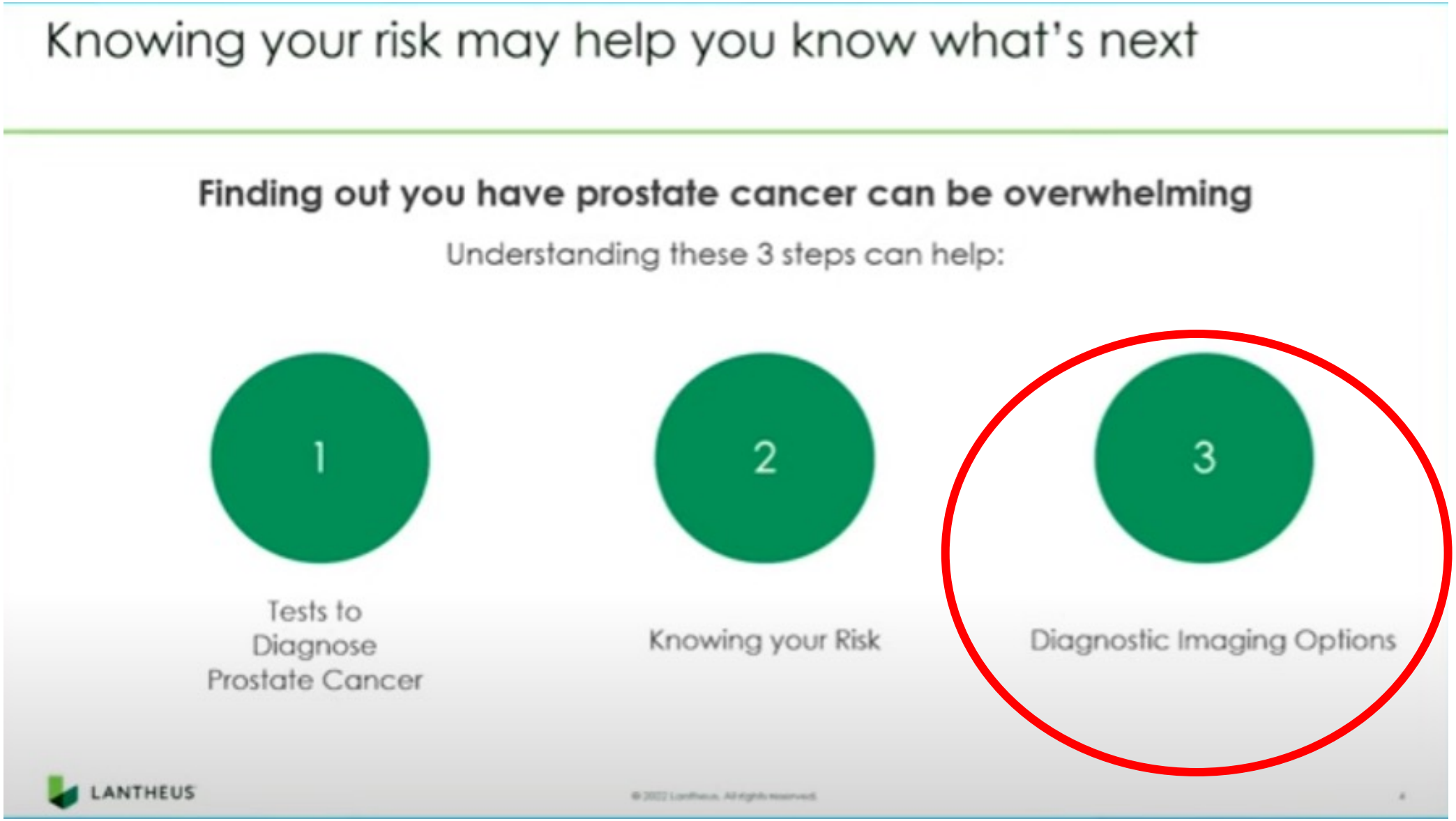
RISK FACTOR ASSESSMENT

PROSTATE CANCER BIOMARKERS: BLOOD-BASED

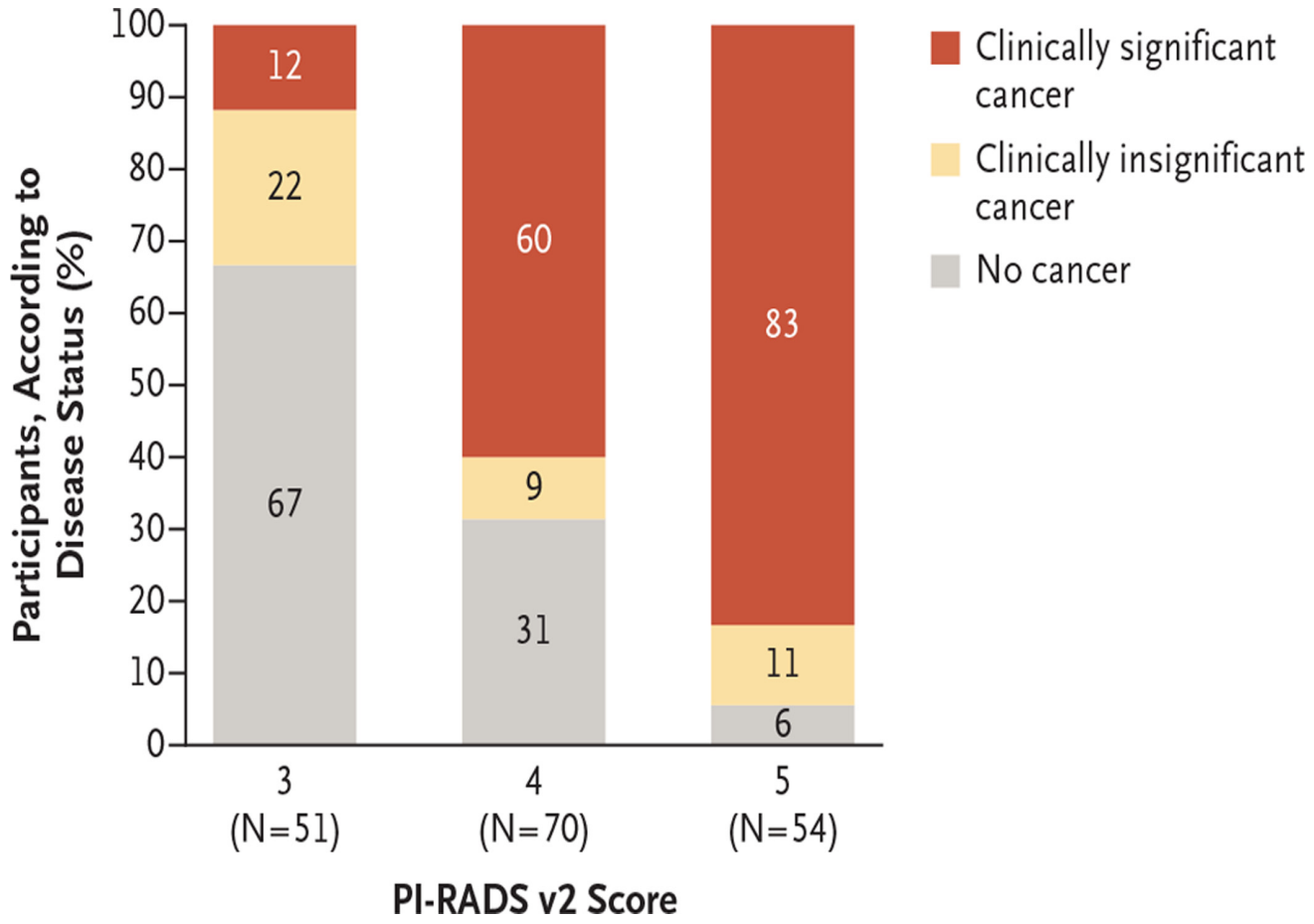
Test	Biomarker Component	Patient Selection	Result	Key Test Characteristic	Clinical Use
PHI (Prostate Health Index)	p2PSA, fPSA, PSA	Pre-biopsy	Risk of csPCa on biopsy	AUC = 0.71	Rule out need for a biopsy
4K Score	PSA, fPSA, iPSA, hk2	Pre-biopsy	Risk of csPCa on biopsy	AUC = 0.82	Rule out need for a biopsy

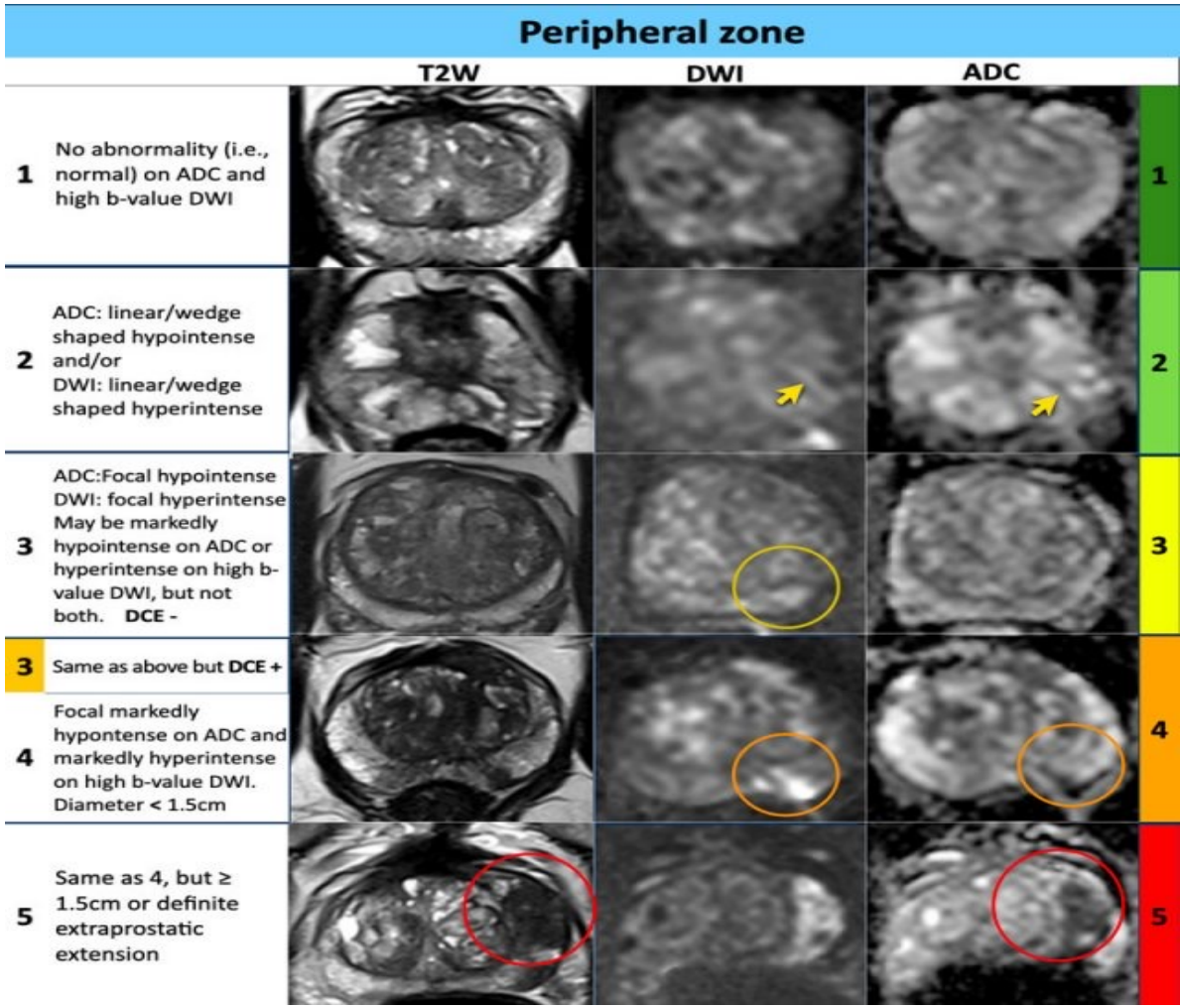
Parker WP, Borza T, Isharwal S, Vemulakonda V. Prostate Cancer Screening, Diagnosis and Risk Stratification. Prostate Cancer Screening, Diagnosis and Risk Stratification - Oncology - Adult | Urology Core Curriculum (auanet.org)

PROSTATE CANCER JOURNEY



RISK FACTOR ASSESSMENT: IMAGING





Kasivisvanathan V, Rannikko AS, Borghi M, et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med. 2018 May 10;378(19):1767-1777

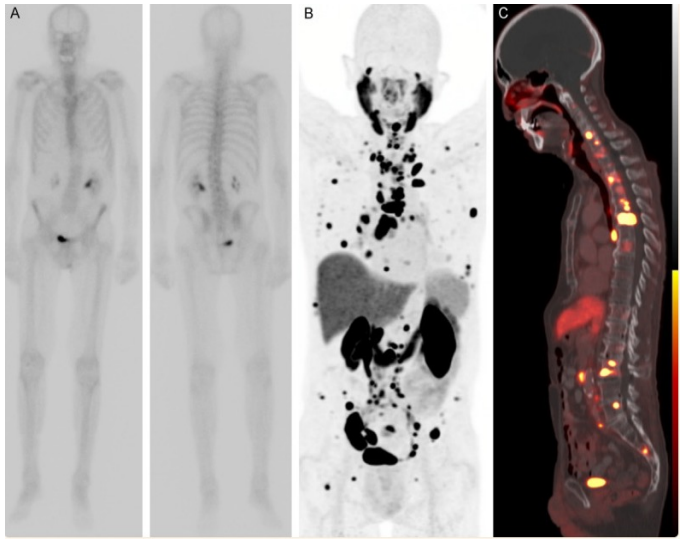
The Radiology Assistant : Prostate Cancer - PI-RADS v2.1

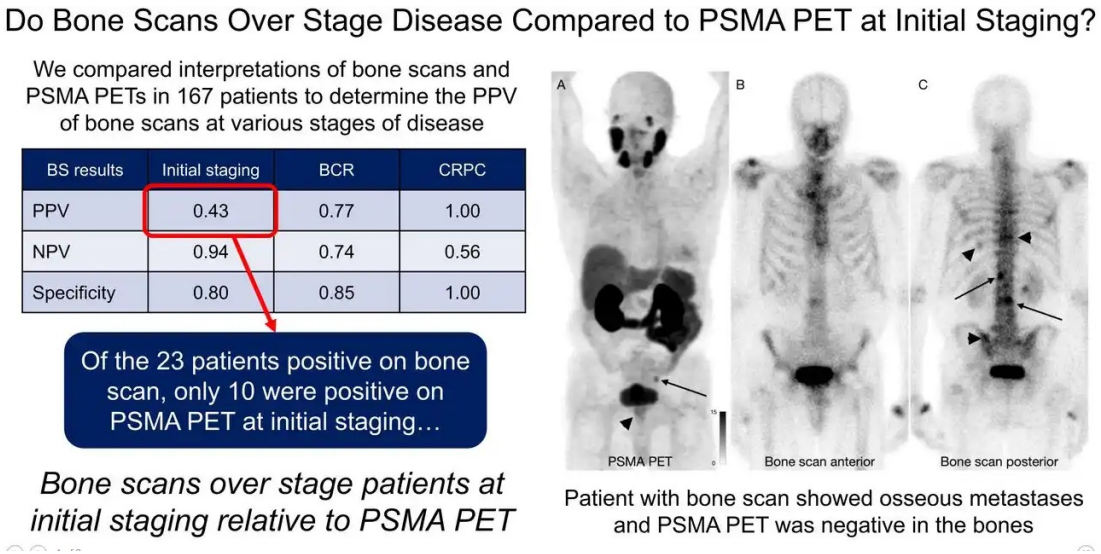
IMAGING

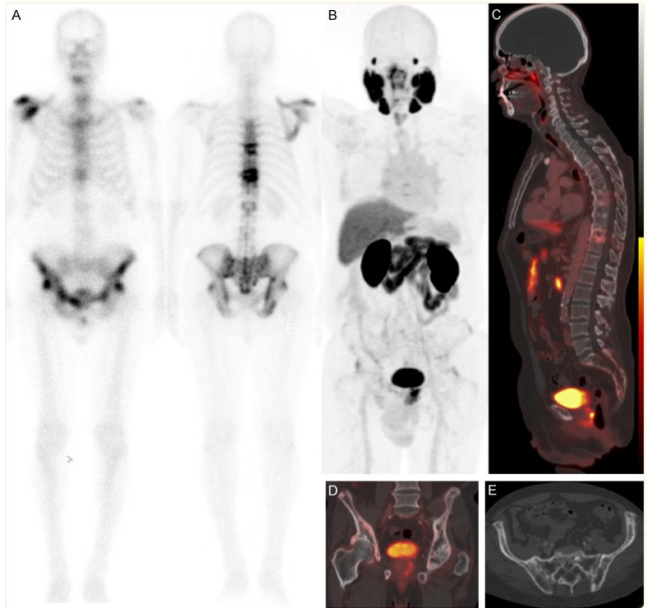
- DEXA BONE DENSITY SCAN *not for cancer staging/evaluation*
- CT SCAN WITH CONTRAST
  - Soft tissue, bone
- mpMRI PROSTATE/PELVIS WITH/WITHOUT CONTRAST
  - Soft tissue, bone

Tracer

- T99 BONE SCAN
  - Bone only
- F18 FDG PET/CT
- AXUMIN F18 PET/CT
- PSMA PET/CT
  - Bone, soft tissue
    - POSLUMA
    - PYLARIFY
    - 68GALLIUM



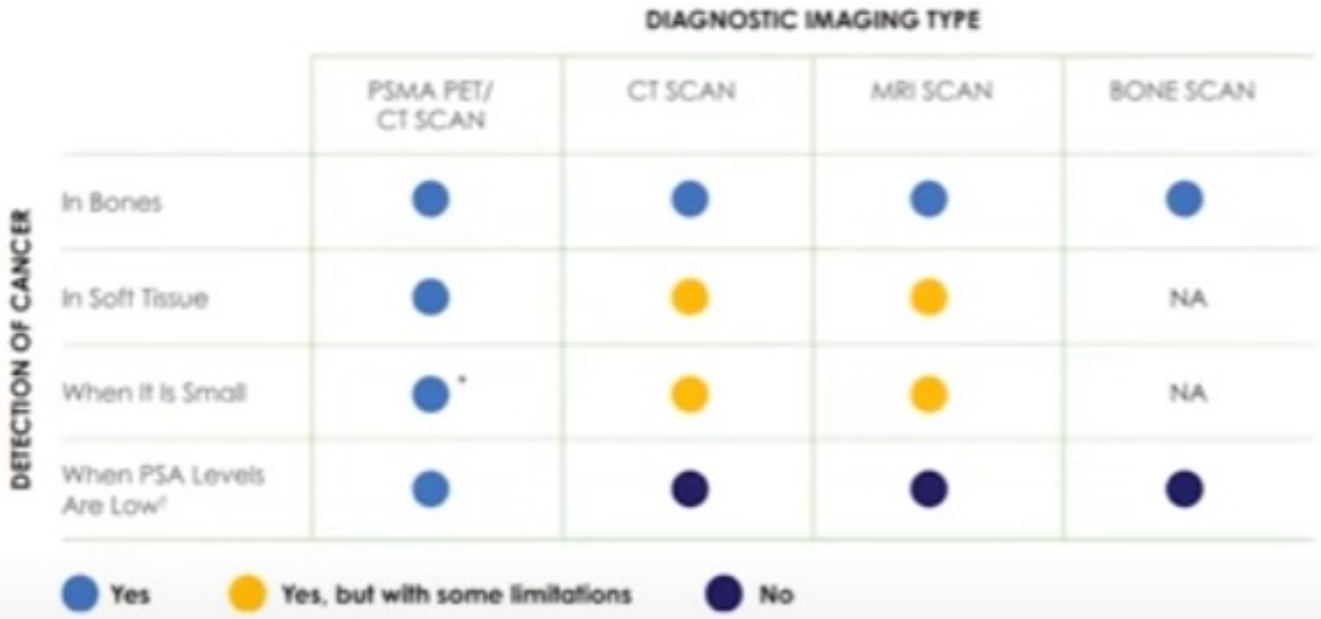




IMAGING

Not all prostate cancer diagnostic imaging is the same: different options have different benefits

How does each diagnostic imaging option perform when detecting cancer?



*Although a PET scan has some limitations when finding very small tumors, it can find smaller tumors compared to CT or MRI.

[1]PSA <2ng/mL

LANTHEUS

THE PUZZLE: DO I HAVE PROSTATE CANCER THAT WILL TRY TO KILL ME IN THE NEXT 5-10 YEARS?

QUESTION & ANSWER

JOIN US FOR THE NEXT SUPPORT GROUP (SUBJECT TO CHANGE)

- ~~May 2024: Intro to Prostate Cancer: Risk factors, screening, biomarkers, staging, imaging~~
- Aug 2024: Stress Management & Self-Care with prostate cancer or terminal cancer
- Nov 2024: Urinary Leakage & Pelvic Floor Therapy
- Feb 2025: Erection Treatments
- May 2025: Financial Toxicity & Resources
- Aug 2025: Testosterone Lowering treatments & side-effect management
- Nov 2025: The Immune System and Prostate Cancer
- Feb 2026: Stigma & Myths vs benefits of Chemotherapy/Palliative/Hospice care

PLEASE COMPLETE THE SURVEY AND LET US KNOW HOW WE ARE DOING

THANK YOU, WE ARE HERE FOR YOU!

https://www.unitedurology.com/arizona-urology-specialists-tucson/patient-resources/patient-portal/