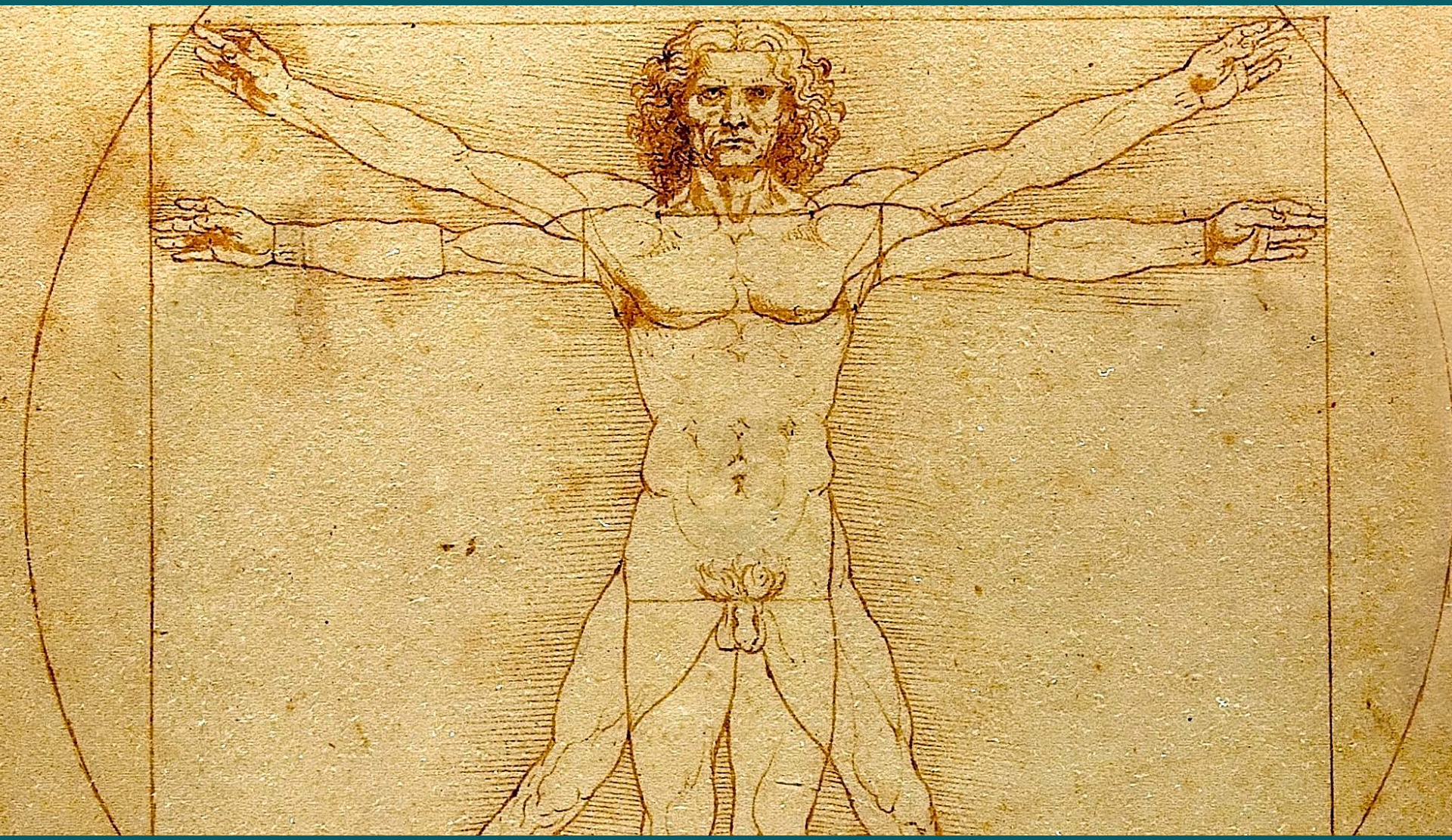
Men's Health: from the Prostate to the Brain

island health



a place of mind

Vancouver Coastal Health Research Institute

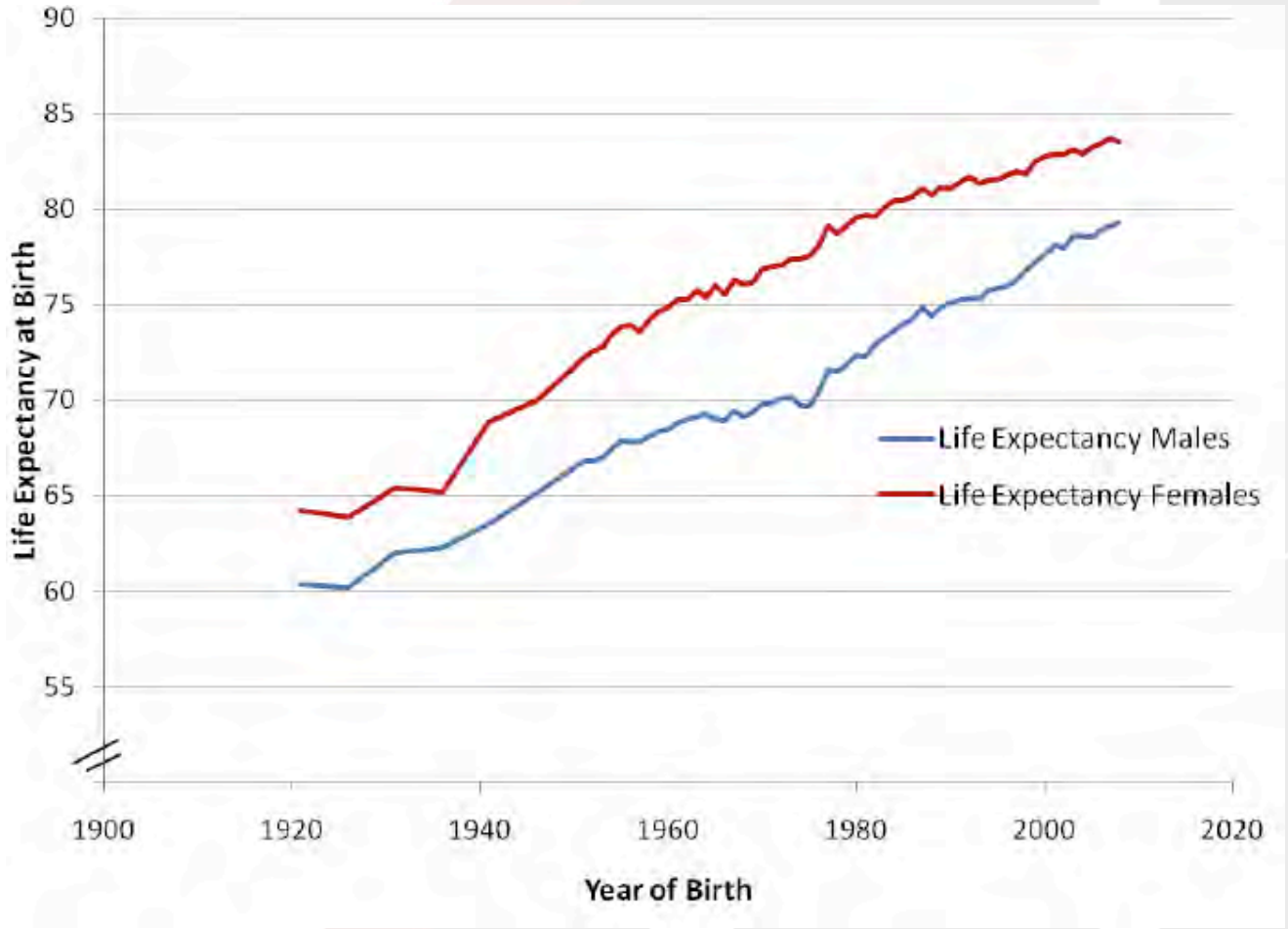
Men's Health: From the Prostate…

Michael E. Cox, PhD
Dept. Urologic Sciences, University of British Columbia
The Vancouver Prostate Centre, Vancouver Coastal Health Research Institute

Department of UROLOGIC SCIENCES UBC

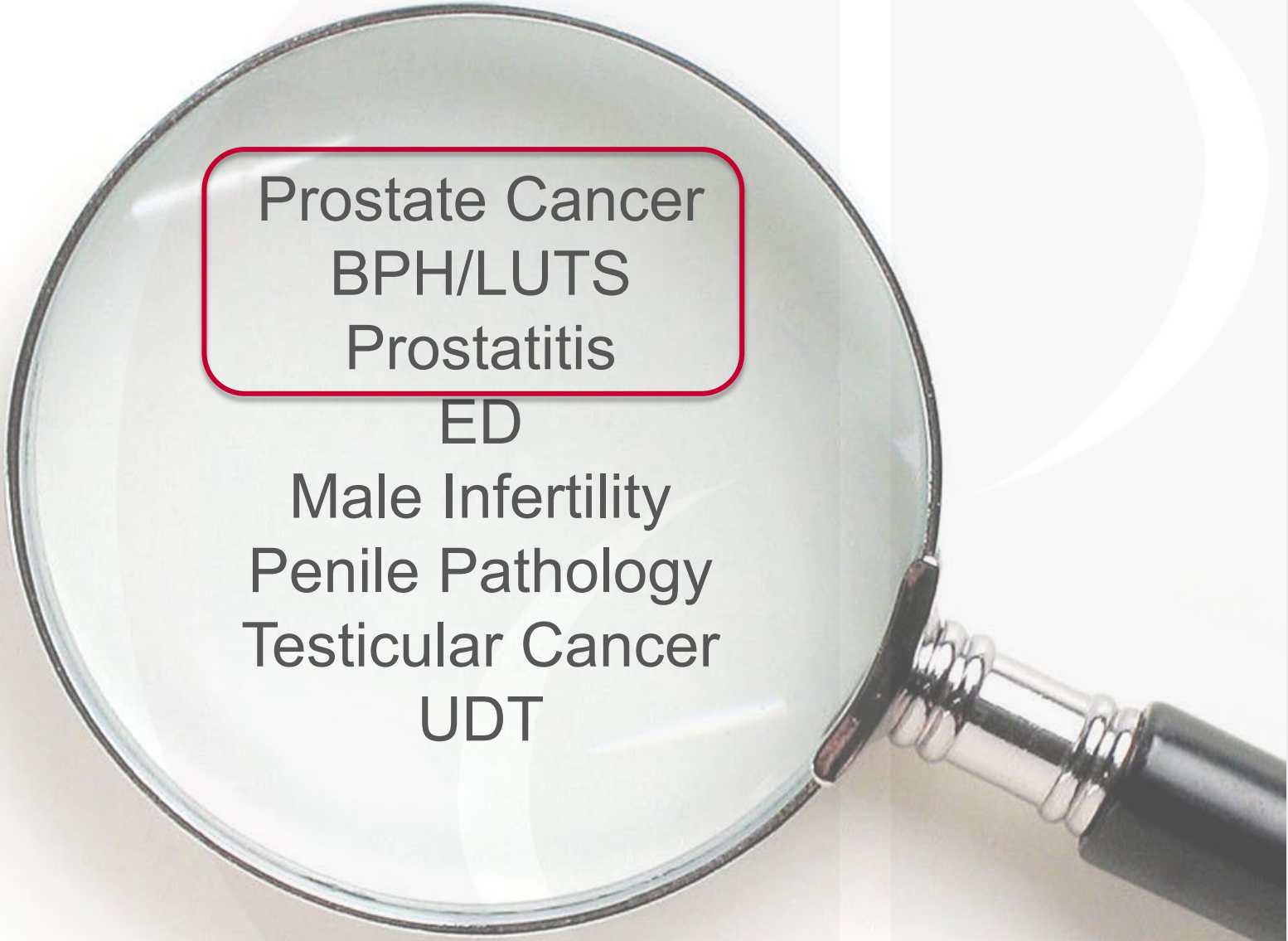
VANCOUVER PROSTATE CENTRE
A UBC & VGH Centre of Excellence

The Life Expectancy Discrepancy



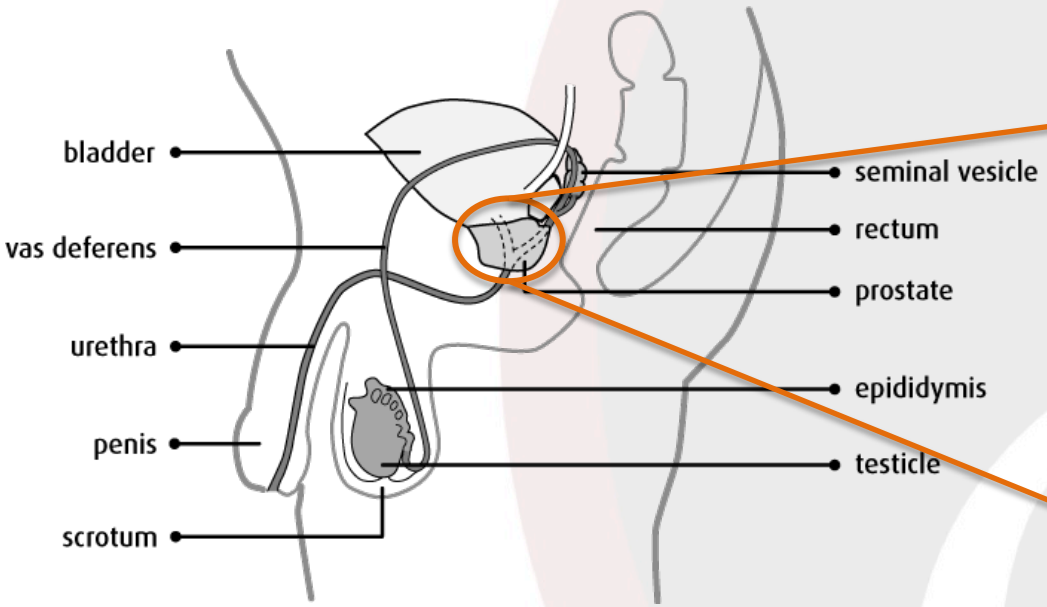
Canadian Men are:
79% more likely to die from heart disease,
57% more likely to die from type 2 diabetes
40% more likely to die from cancer
4 times more likely to commit suicide.

Urology: a Lens into Men's Health

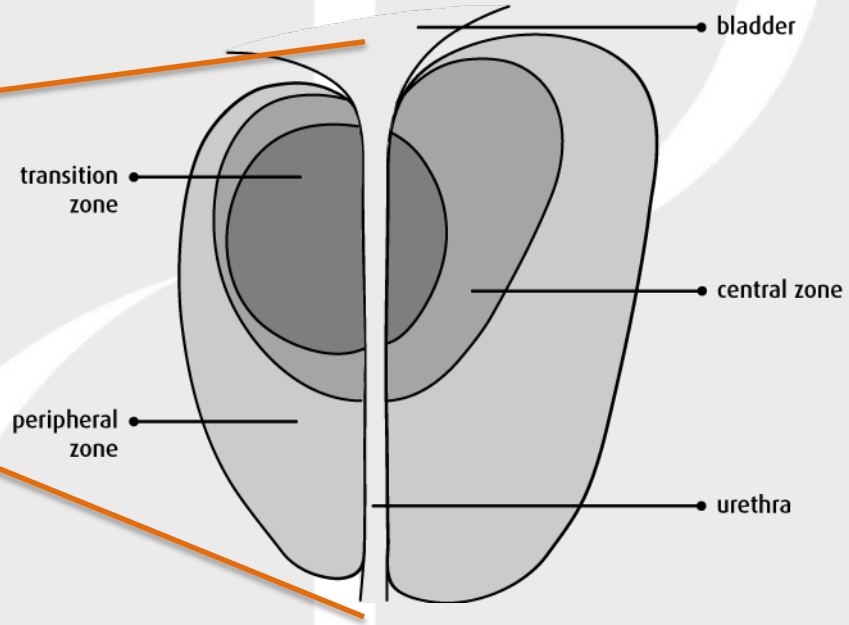


What Is The Prostate Gland?

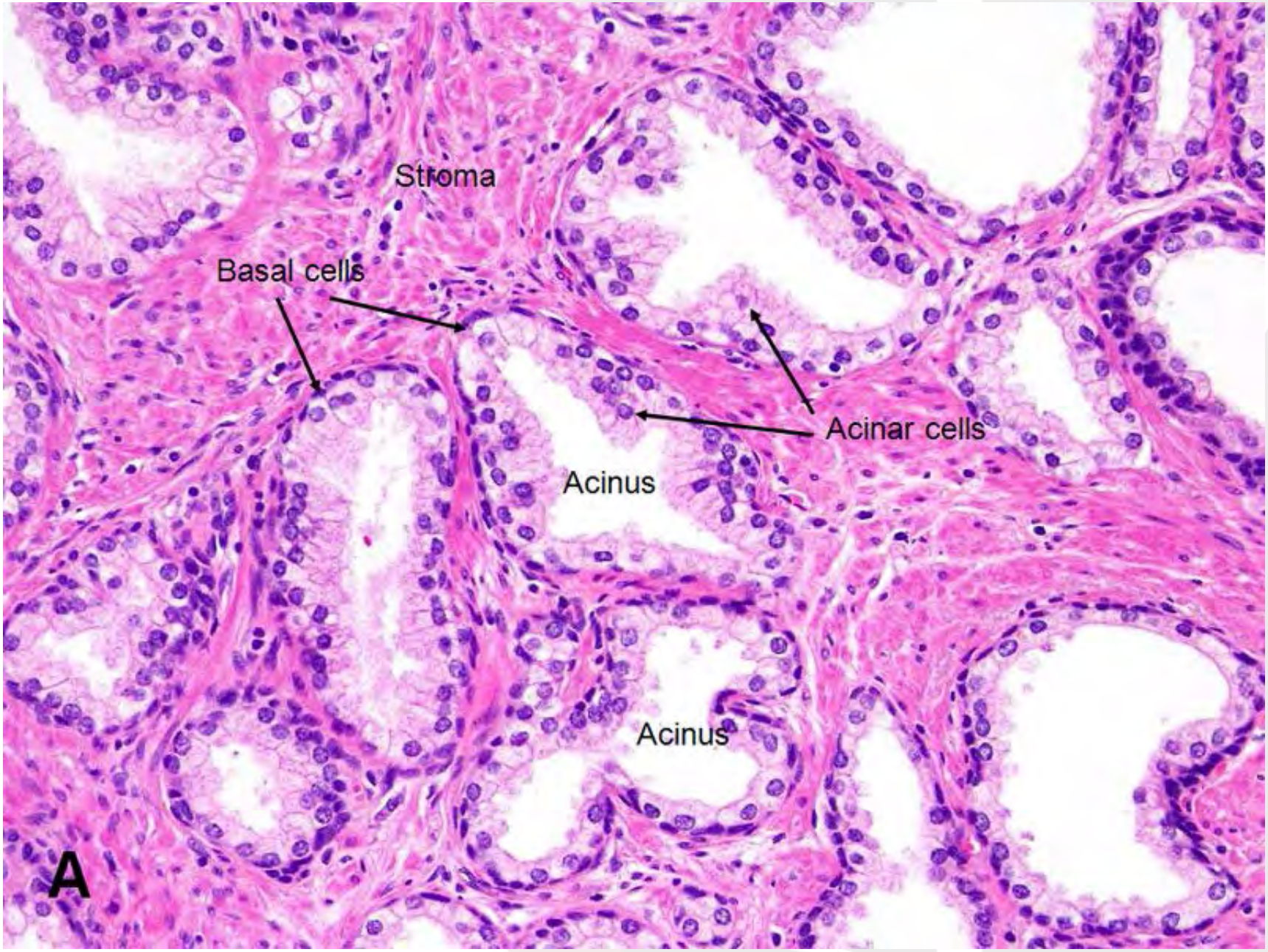
Male Reproductive System



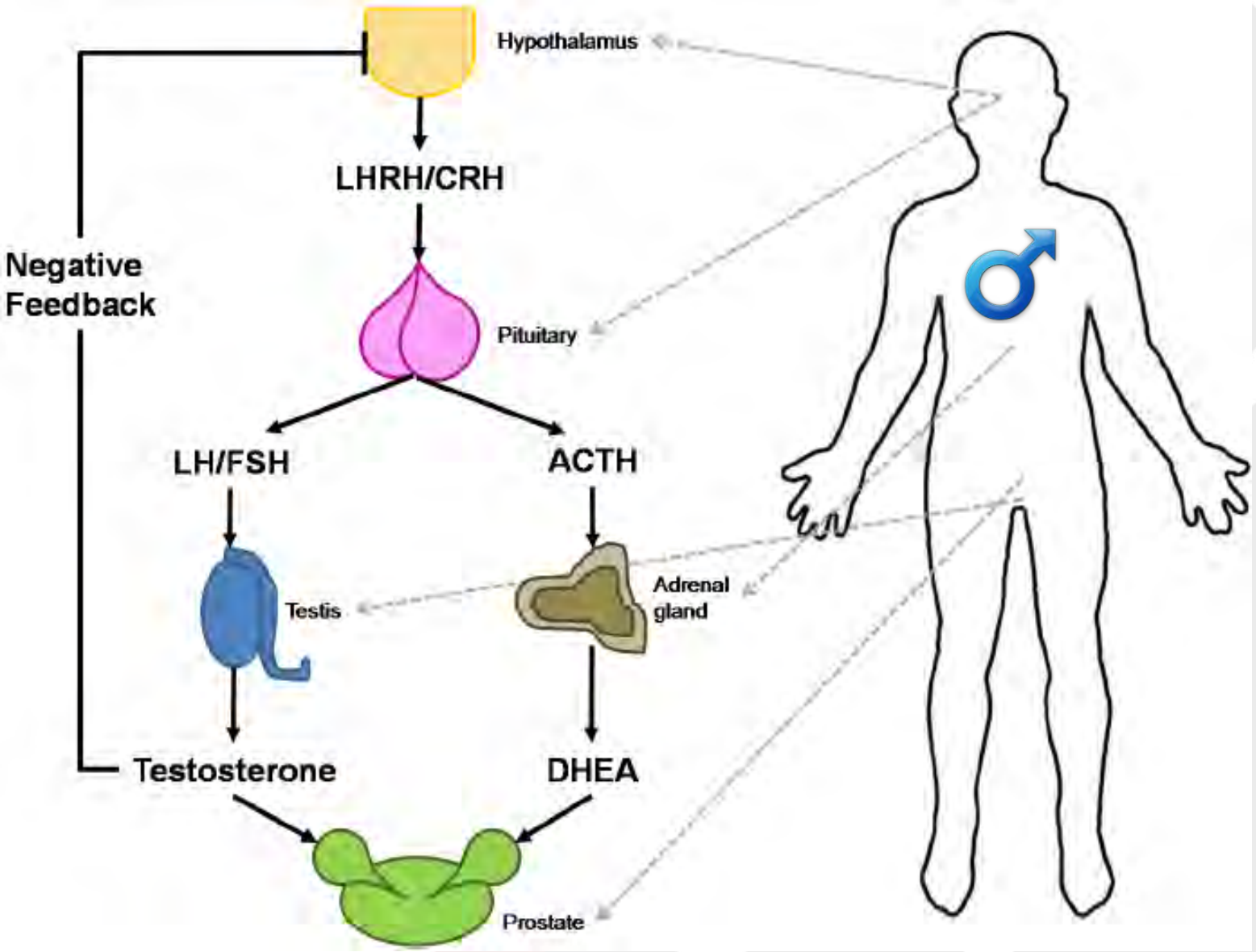
Prostate Zones



Prostate Histology

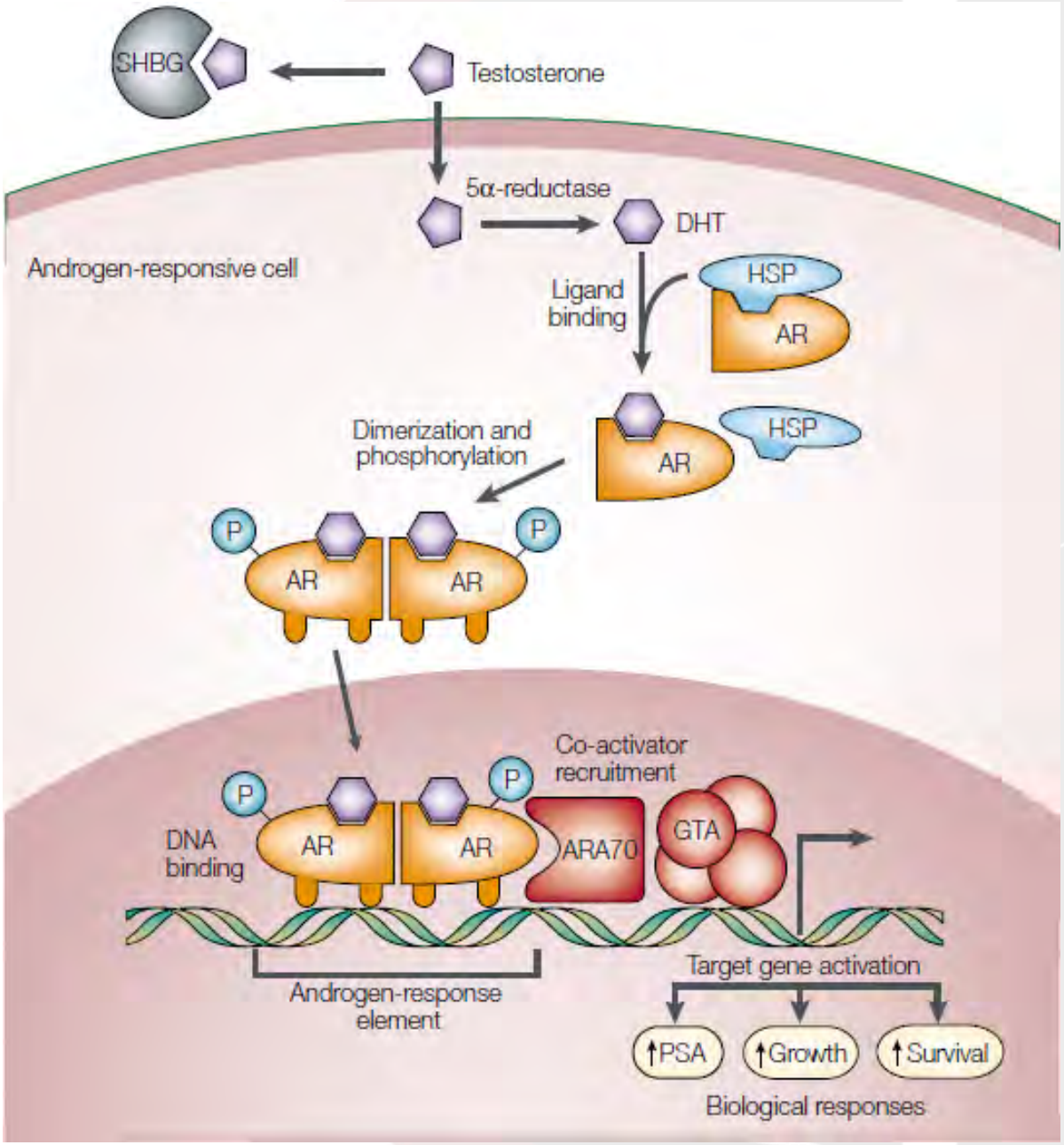


Androgens Control Prostate Development

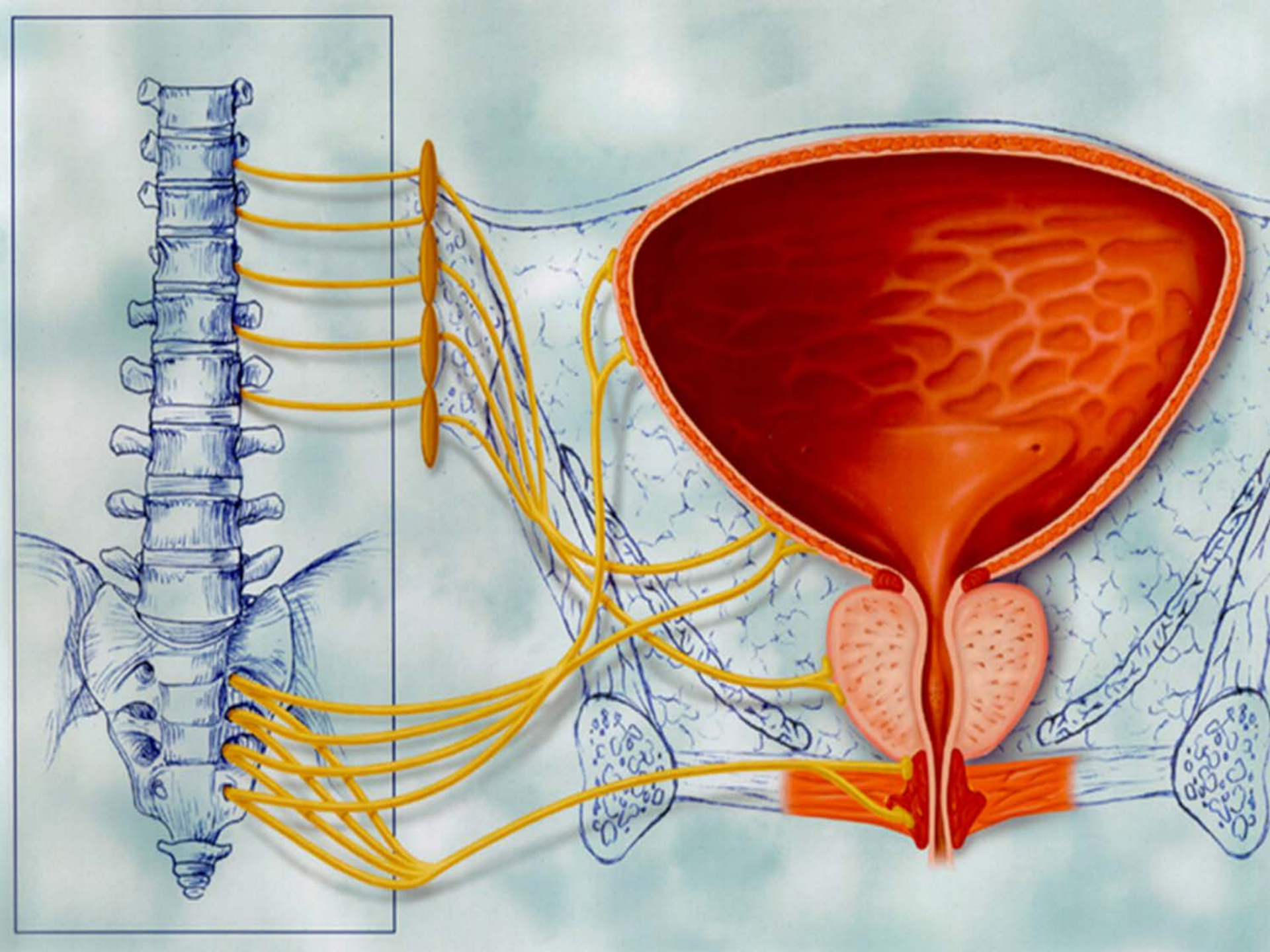


Locke J. MSc Thesis 2009

Androgens: Mechanism of Action



Feldman & Feldman, Nat Rev Cancer, 2001



The Prostate Gland & the Ageing Male:

"Gram-for-gram the most diseased organ in the body"

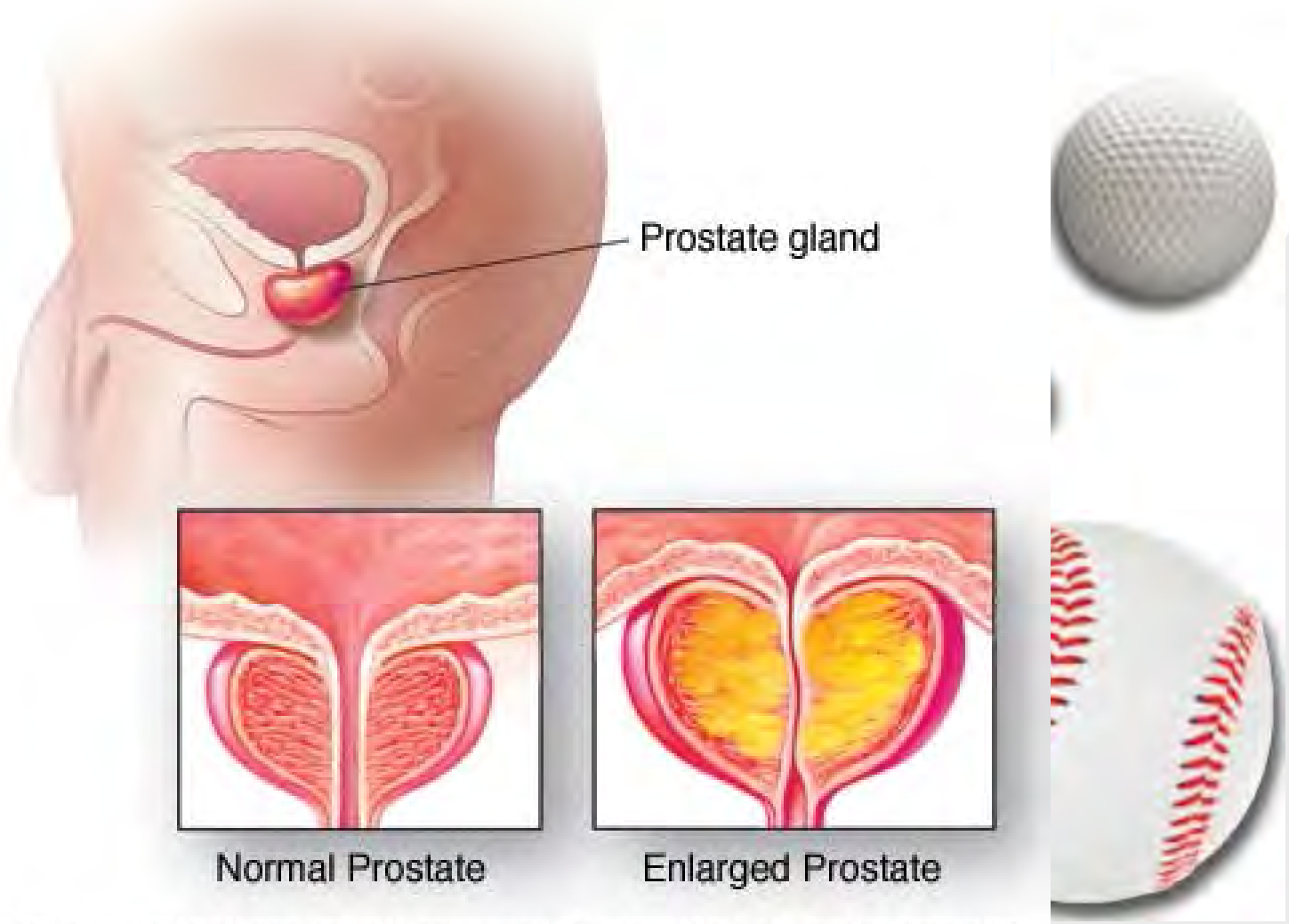
stromoglandular hyperplasia

AGE 20-

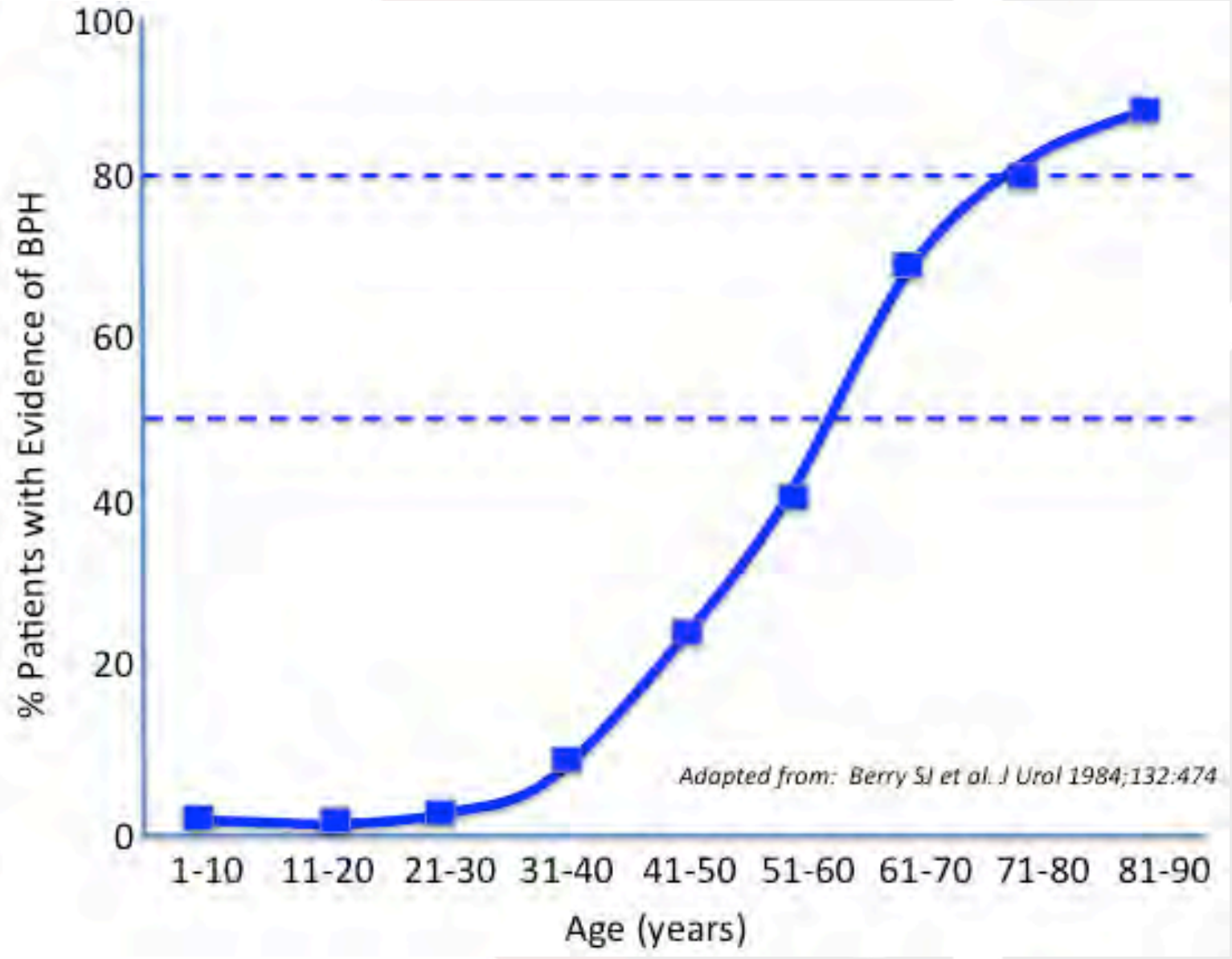
Most healthy
have a prost
the size of a

AGE 50-

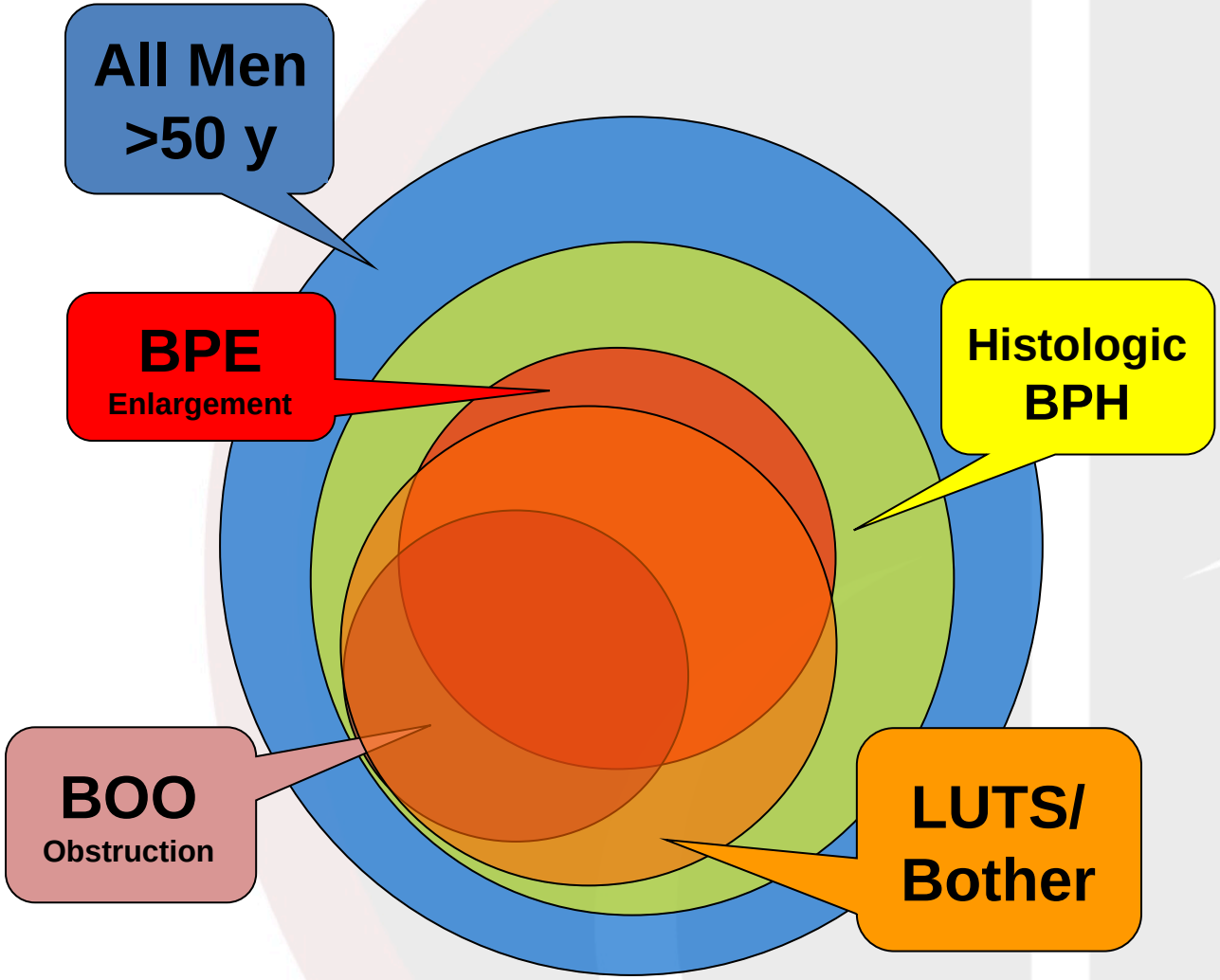
Over 50% of m
affected. A swo
of an orange. It
increasingly PA
making it difficu
urinate, and se
function is notic
impaired.



Benign Prostatic Hyperplasia (BPH): the Most Common Neoplasia



BPH and Associated Syndromes



May be associated with

Lower Urinary Track Syndrome
Benign Prostatic Enlargement
Bladder Outlet Obstruction

Medical Treatments for BPH Symptoms

Pharmacology

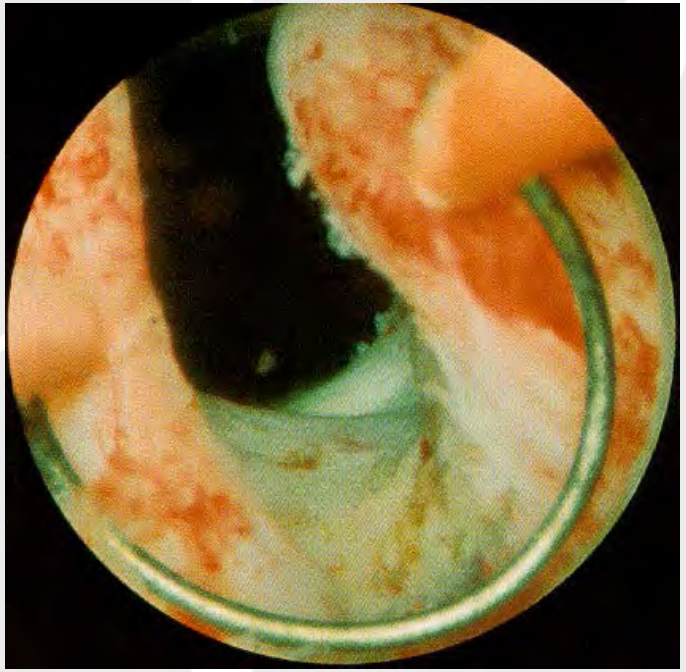
5α-Reductase Inhibitors:

Stop Disease Progression

Alpha-Blockers:

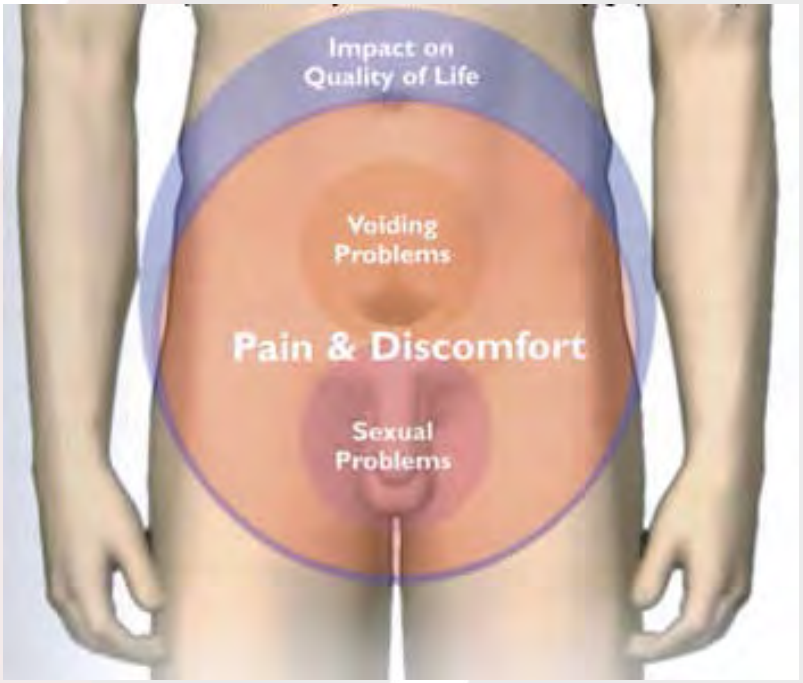
Rapidly Relieve Symptoms

Surgery



Prostatitis: the Enigmatic Disease

Most common urologic diagnosis in men < 50, 3rd most common in men > 50.



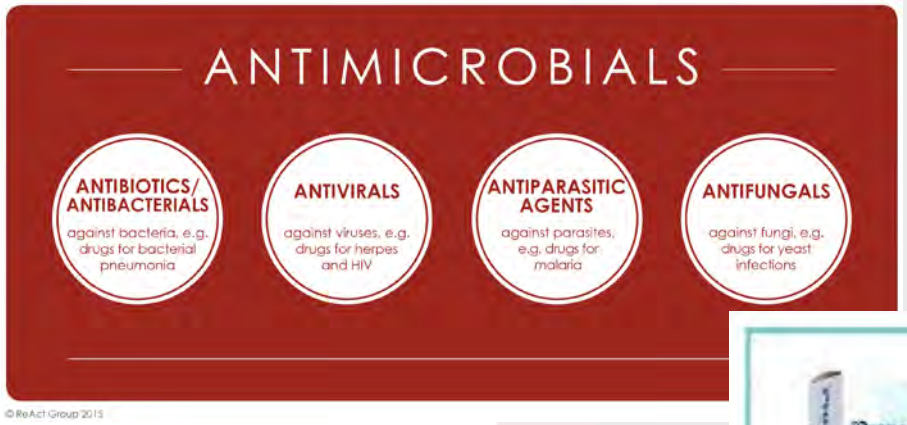
Cat I: Acute Bacterial Prostatitis
Cat II: Chronic Bacterial Prostatitis
Cat III: Chronic Pelvic Pain Syndrome
90%
Cat IIIA: Inflammatory CPPS
Cat IIIB: Non-inflammatory CPPS
Cat IV: Asymptomatic Inflammatory Prostatitis

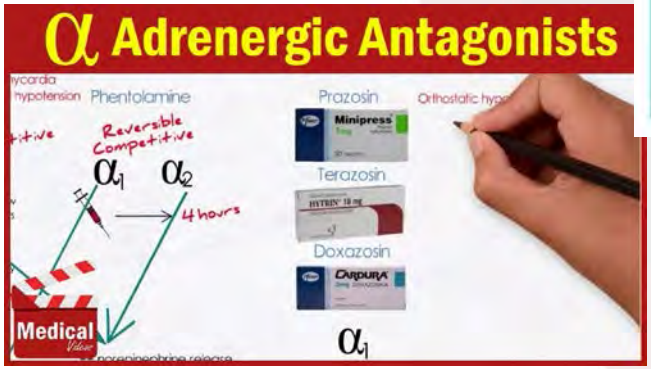
http://hopeforprostate.blogspot.ca/

Prostatitis/CPPS Management

Goals:

- Target the infectious agent,
- Reduce inflammation,
- Improve urodynamics.





Canadian Cancer Rates by Site

Incidence

Males
103,100
New cases

Prostate	20.7%
Colorectal	14.5%
Lung and bronchus	14.0%
Bladder	6.5%
Non-Hodgkin lymphoma	4.5%
Kidney and renal pelvis	4.1%
Melanoma	3.9%
Leukemia	3.5%
Oral	3.1%
Pancreas	2.7%
Stomach	2.1%
Liver	1.8%
Esophagus	1.7%
Brain/CNS	1.6%
Multiple myeloma	1.6%
Thyroid	1.6%
Testis	1.1%
Larynx	0.9%
Hodgkin lymphoma	0.6%
Breast	0.2%
All other cancers	9.3%

Females
103,200
New cases

Breast	25.5%
Lung and bronchus	13.8%
Colorectal	11.5%
Uterus (body, NOS)	7.1%
Thyroid	5.2%
Non-Hodgkin lymphoma	3.6%
Melanoma	3.2%
Ovary	2.7%
Pancreas	2.6%
Leukemia	2.5%
Kidney and renal pelvis	2.3%
Bladder	2.1%
Cervix	1.5%
Oral	1.4%
Brain/CNS	1.3%
Stomach	1.3%
Multiple myeloma	1.2%
Liver	0.6%
Esophagus	0.5%
Hodgkin lymphoma	0.4%
Larynx	0.2%
All other cancers	9.6%

Mortality

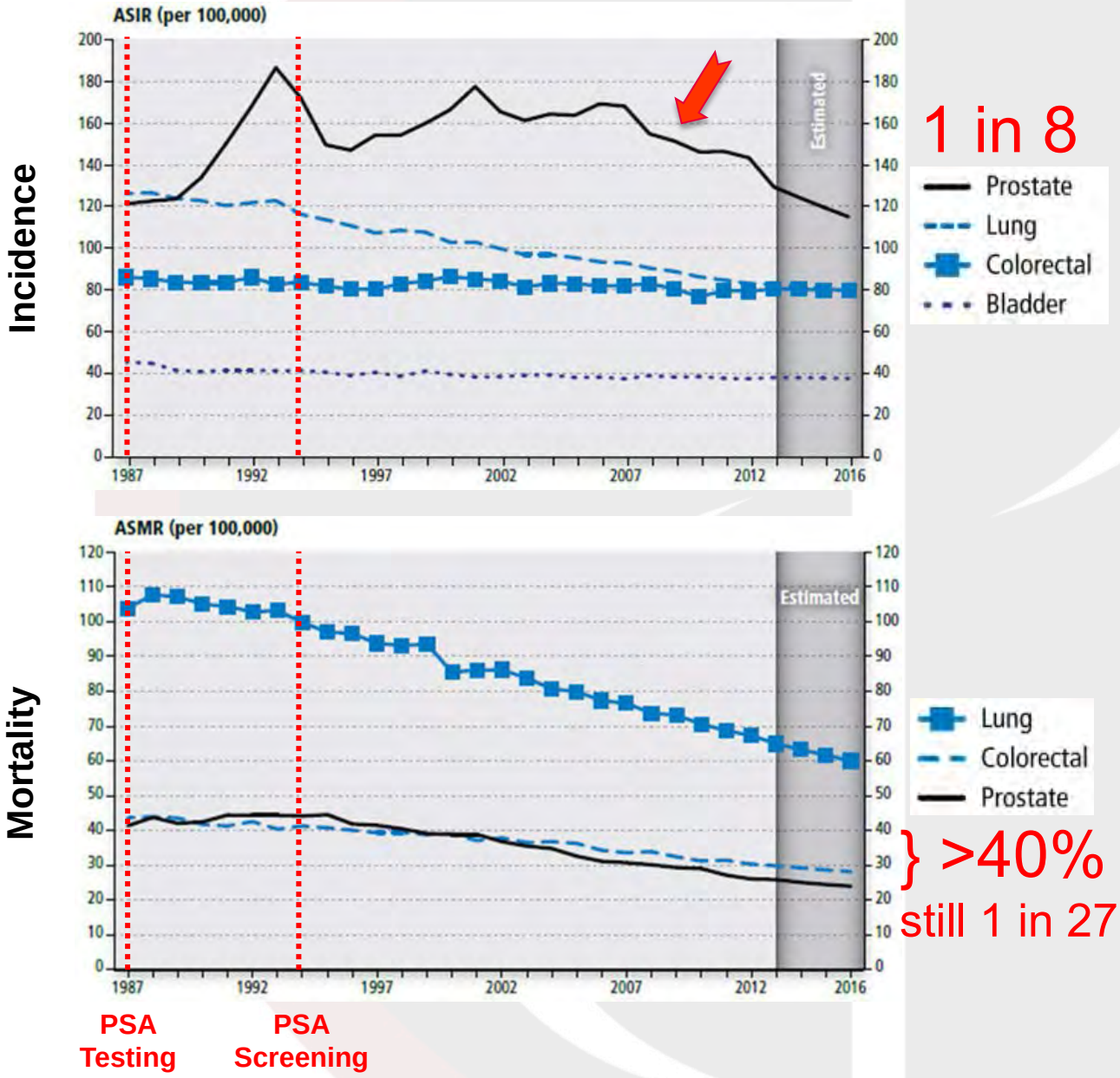
Males
42,600
Deaths

Lung and bronchus	26.1%
Colorectal	12.0%
Prostate	9.6%
Pancreas	5.6%
Bladder	4.0%
Esophagus	3.9%
Leukemia	3.9%
Non-Hodgkin lymphoma	3.5%
Brain/CNS	3.2%
Stomach	2.9%
Kidney and renal pelvis	2.8%
Liver*	2.2%
Oral	2.0%
Multiple myeloma	1.9%
Melanoma	1.9%
Larynx	0.8%
Thyroid	0.2%
Hodgkin lymphoma	0.2%
Breast	0.1%
Testis	0.1%
All other cancers	12.9%

Females
38,200
Deaths

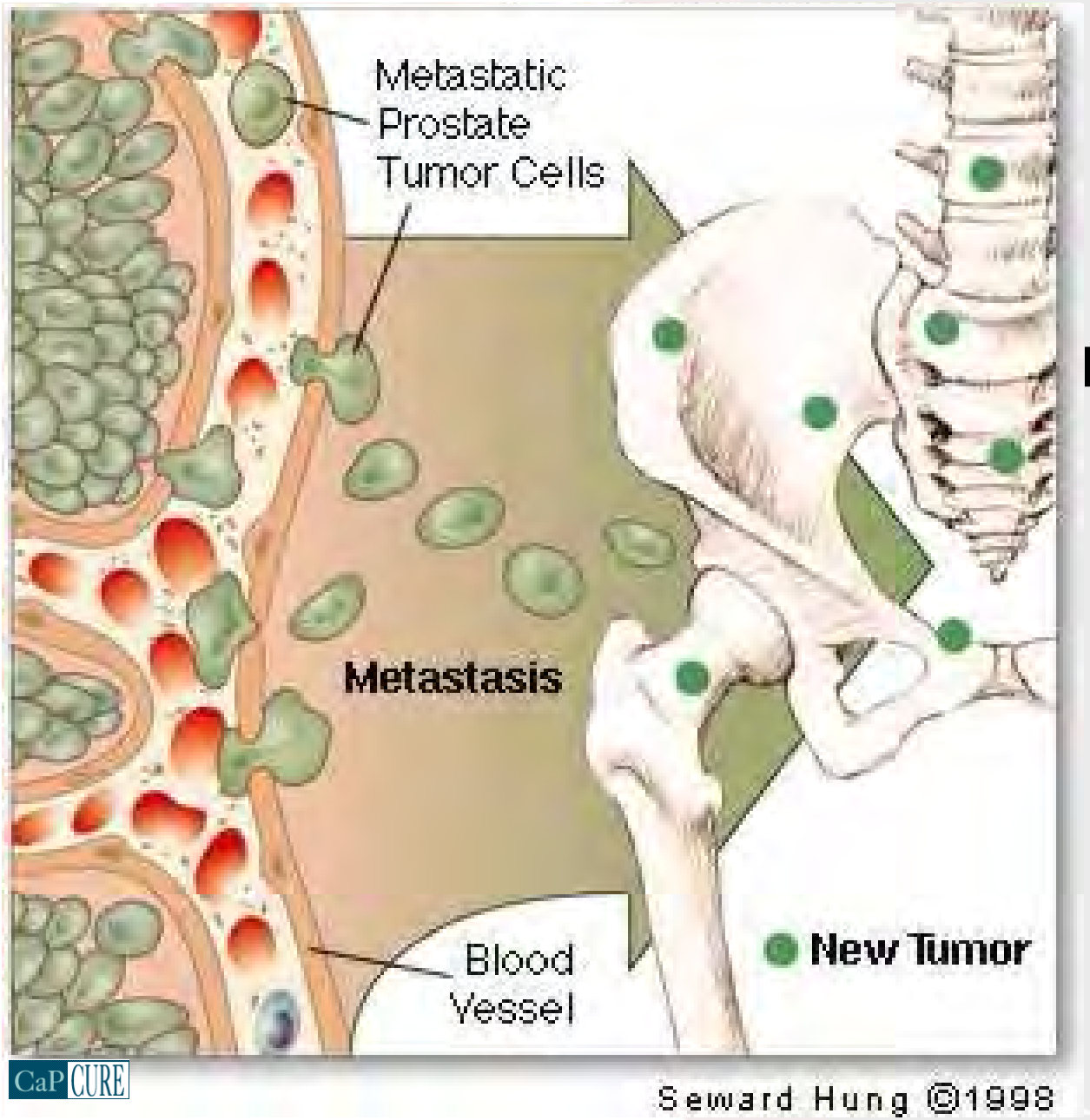
Lung and bronchus	26.2%
Breast	13.1%
Colorectal	11.3%
Pancreas	6.3%
Ovary	4.7%
Leukemia	3.3%
Non-Hodgkin lymphoma	3.1%
Uterus (body, NOS)	3.0%
Brain/CNS	2.7%
Stomach	2.1%
Bladder	1.8%
Kidney and renal pelvis	1.8%
Multiple myeloma	1.7%
Esophagus	1.3%
Melanoma	1.2%
Cervix	1.0%
Oral	1.0%
Liver*	0.7%
Thyroid	0.3%
Larynx	0.2%
Hodgkin lymphoma	0.2%
All other cancers	12.8%

Male Cancer Incidence & Mortality Rates 1987-2016



Canadian Cancer Statistics 2016

Prostate Cancer Development & Progression



Normal Prostate

↓

Histological Cancer

↓

Local Disease

↓

Metastatic Disease

CaP CURE

Risk Factors for Prostate Cancer

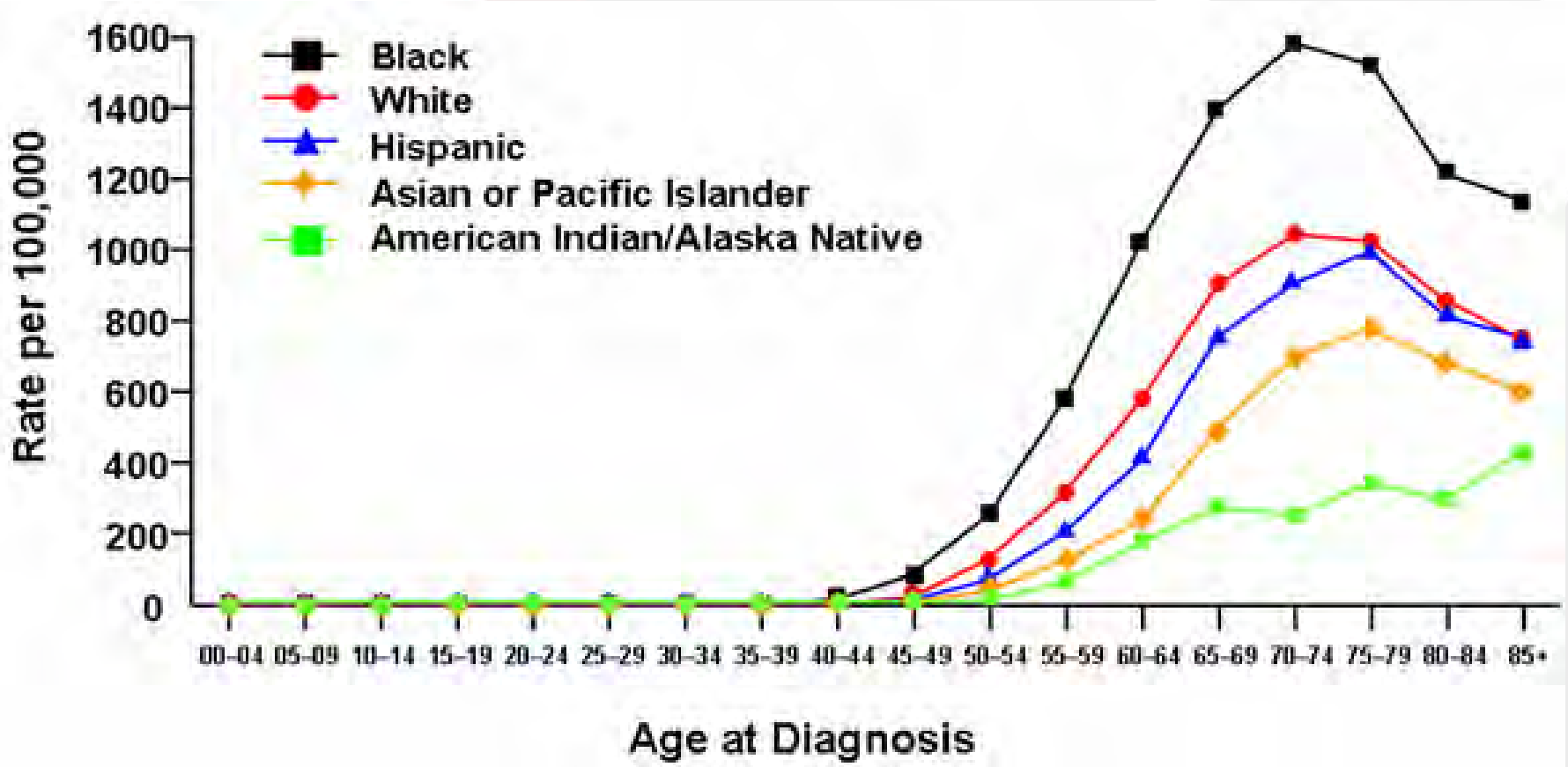
Unmodifiable(Beyond Your Control):

- Age
- Race
- Family History

Modifiable (Lifestyle):

- Geography
- Diet
- Exercise

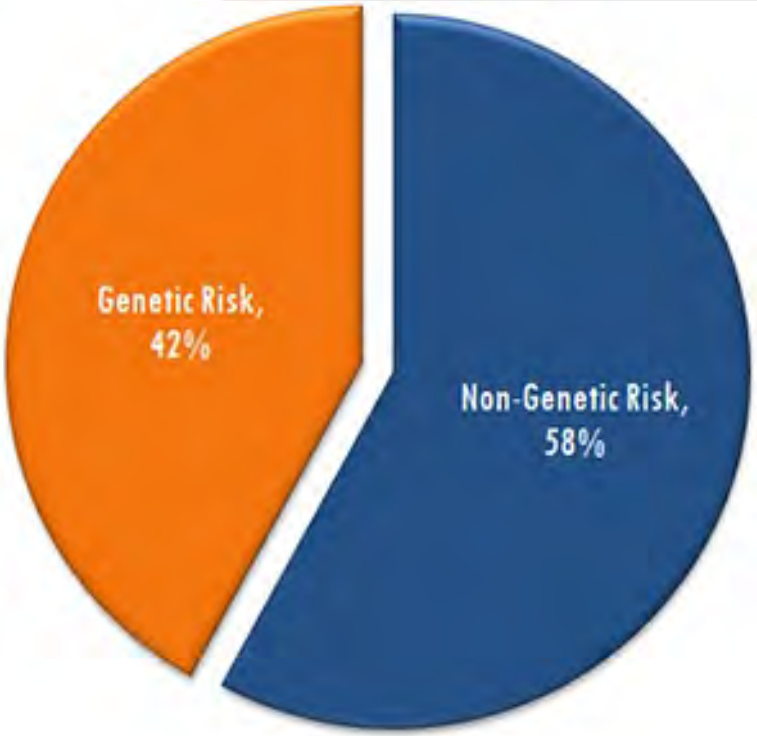
Prostate Cancer: Risk of Diagnosis by Age & Race

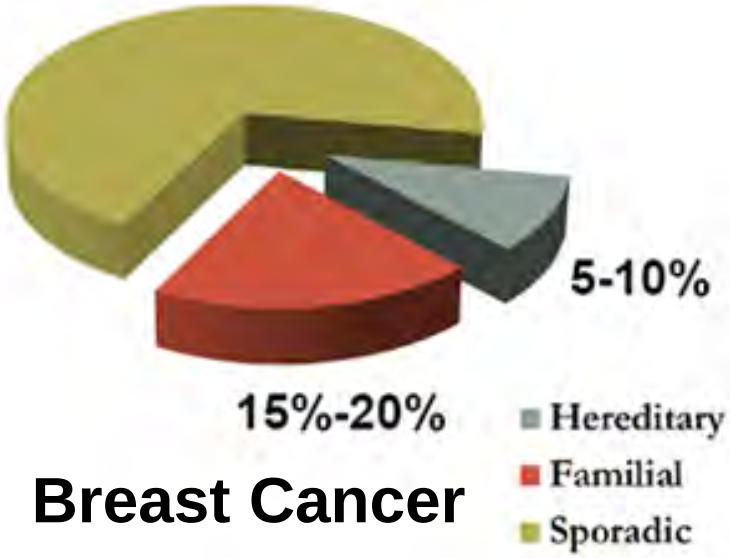


Of all cancers, PCa incidence increases most dramatically with age

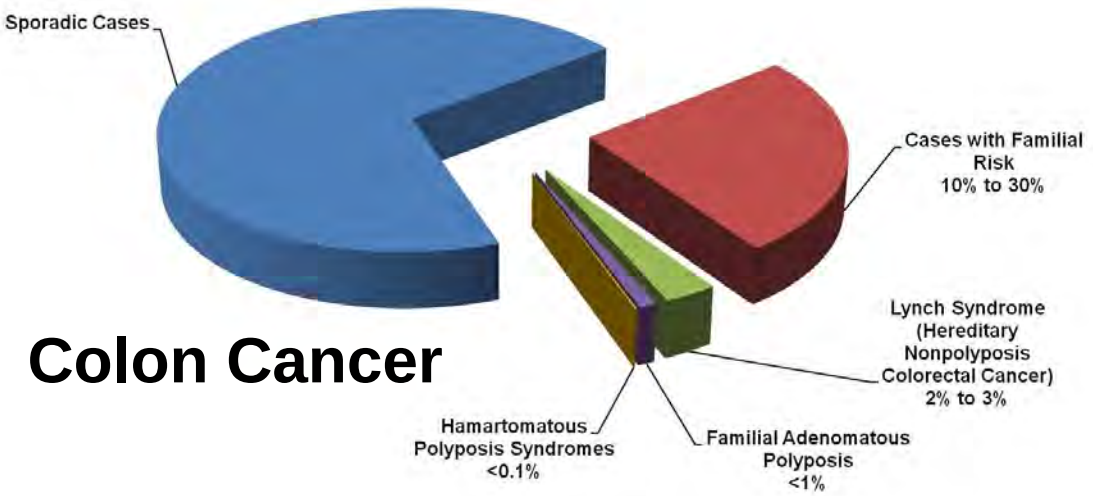
Prostate cancer ethnic group SEER Stat Fact Sheets. http://seer.cancer.gov/statfacts/html/prost.html.

Prostate Cancer: Family History vs Environment



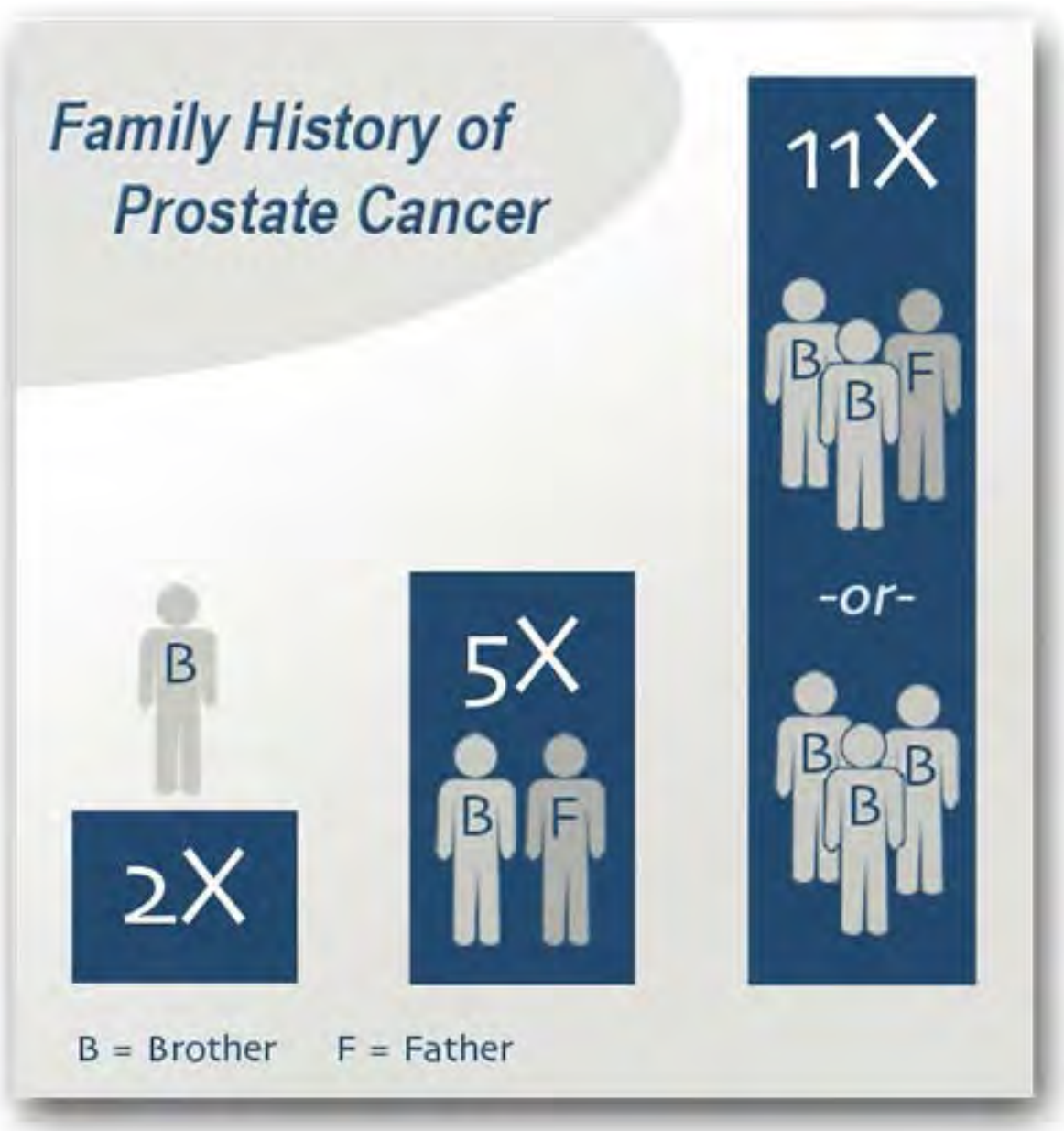


Breast Cancer

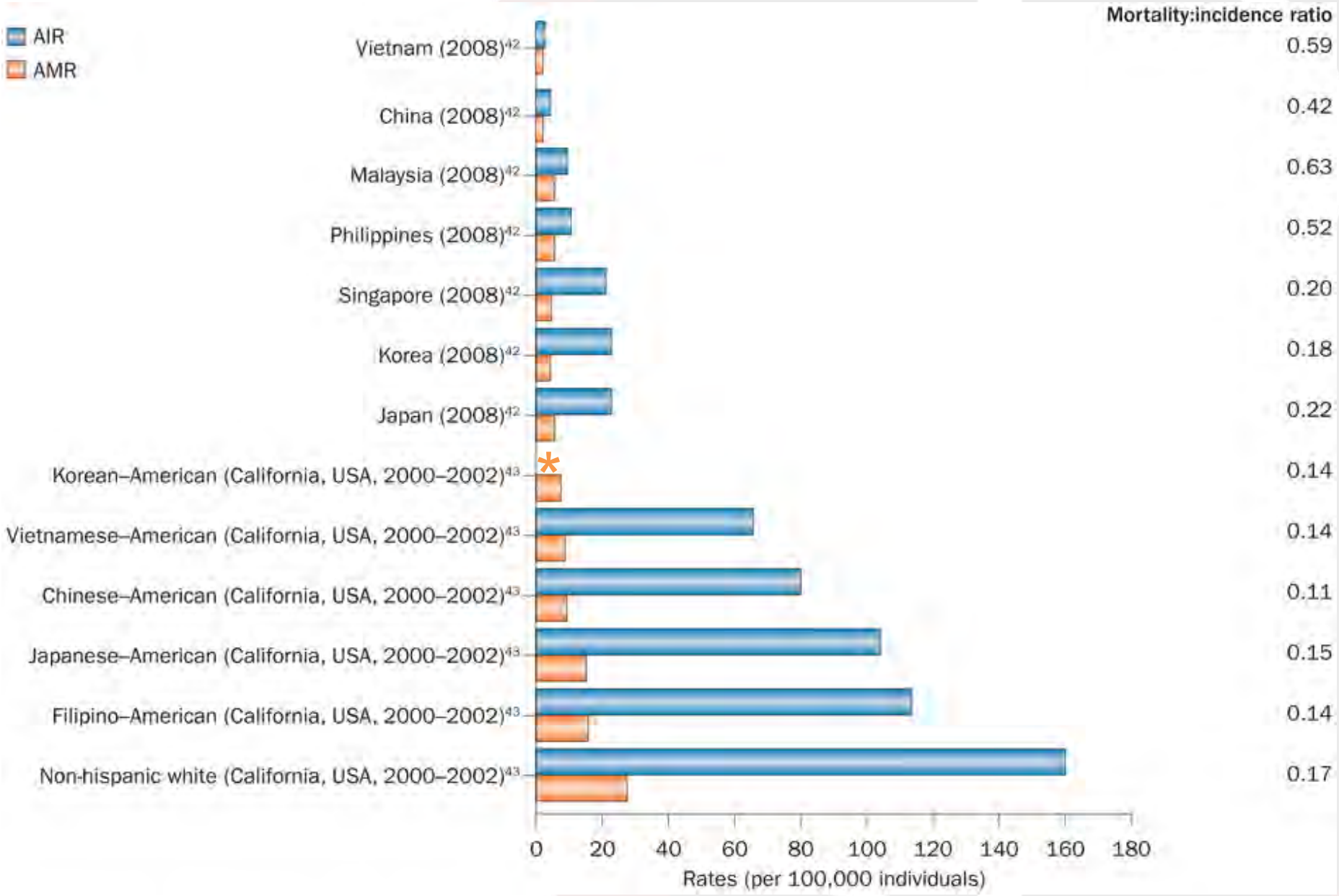


Colon Cancer

Prostate Cancer: Family History Risk



Prostate Cancer: Role of Geography?



Ito, Nature Rev. Urology, 2014

Dietary Factors Impacting Prostate Cancer Risk

Table 1. Factor-loading matrix for two dietary patterns identified from post-diagnostic FFQ among men with prostate cancer ($n = 926$) in the PHS[a]

Food group	Prudent dietary pattern	Western dietary pattern
Legumes	0.55	—
Dark-yellow vegetables	0.55	—
Green, leafy vegetables	0.54	—
Other vegetables	0.54	—
Fruit	0.51	—
Cruciferous vegetables	0.51	—
Tomatoes	0.49	—
Whole grains	0.44	—
Garlic	0.40	—
Soy products	0.36	—
Fish	0.32	—
Oil and vinegar dressing	0.31	—
Processed meats	—	0.66
Red meats	—	0.60
Eggs	—	0.48
Snacks	—	0.46
High-fat dairy products	—	0.45
Potatoes	—	0.44
French fries	—	0.42
Butter	—	0.39
Sweets and desserts	—	0.35
Refined grains	—	0.33

[a]Food groups with loading factors less than 0.3 for both dietary patterns were not listed in the table, and included fruit juice, poultry, condiments, nuts, tea, low-fat dairy products, pizza, organ, cold breakfast cereal, wine, margarine, mayonnaise, low-energy drink, beer, coffee, high-energy drink, and liquor.

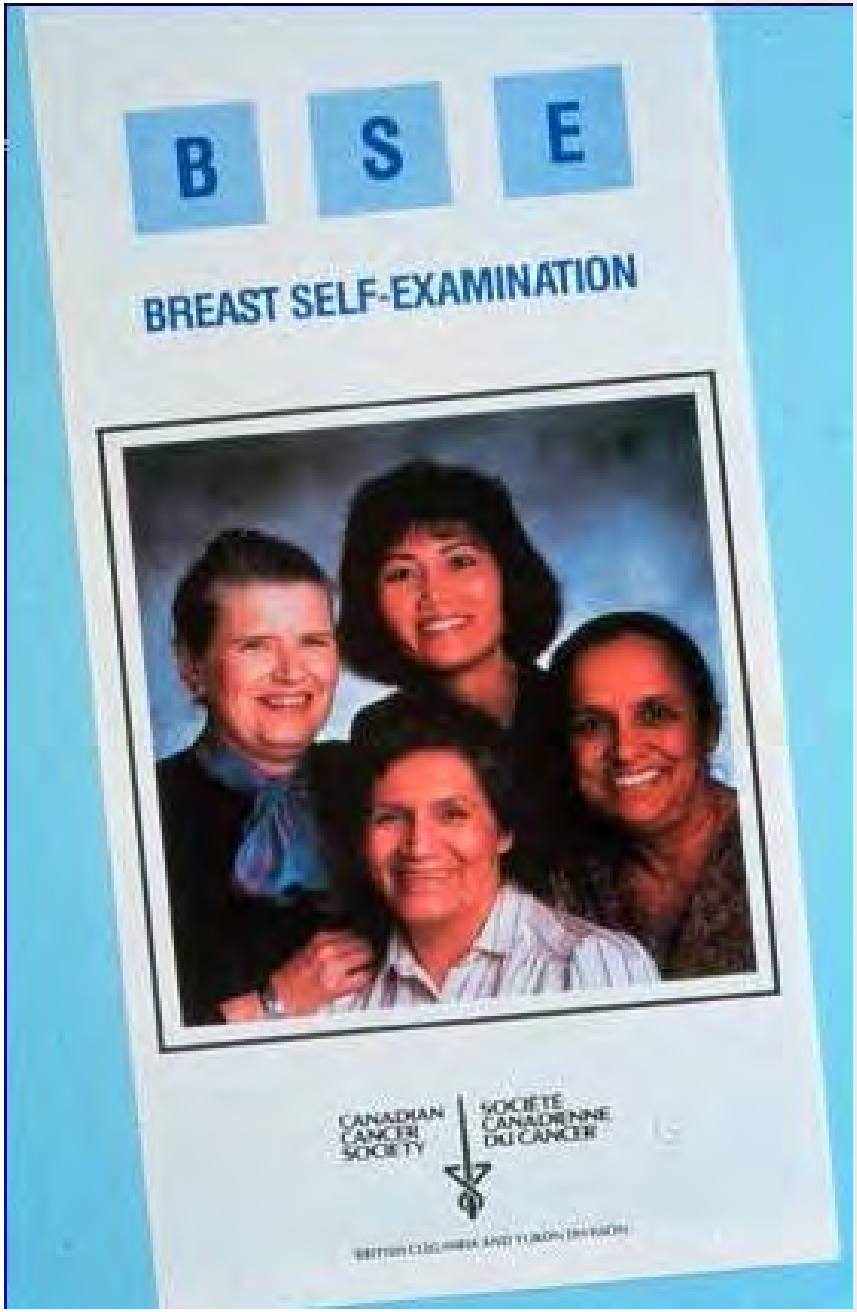
Yang, Cancer Prevention Res. 2015

Prostate Cancer Symptoms

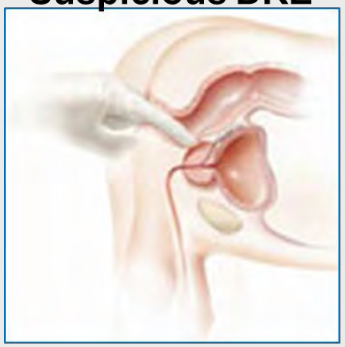
- Need to urinate frequently, especially at night
- Difficulty starting or holding back urination
- Weak or interrupted urine
- Painful or burning urination
- Erectile difficulties
- Painful ejaculation
- Blood in urine or semen
- Frequent pain or stiffness in the lower back, hips, or upper thighs

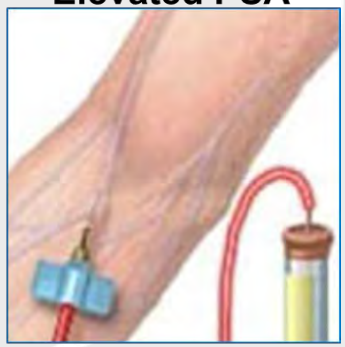
symptoms not typically helpful !

Early Detection Saves Lives!!



Suspicious DRE &/or Elevated PSA

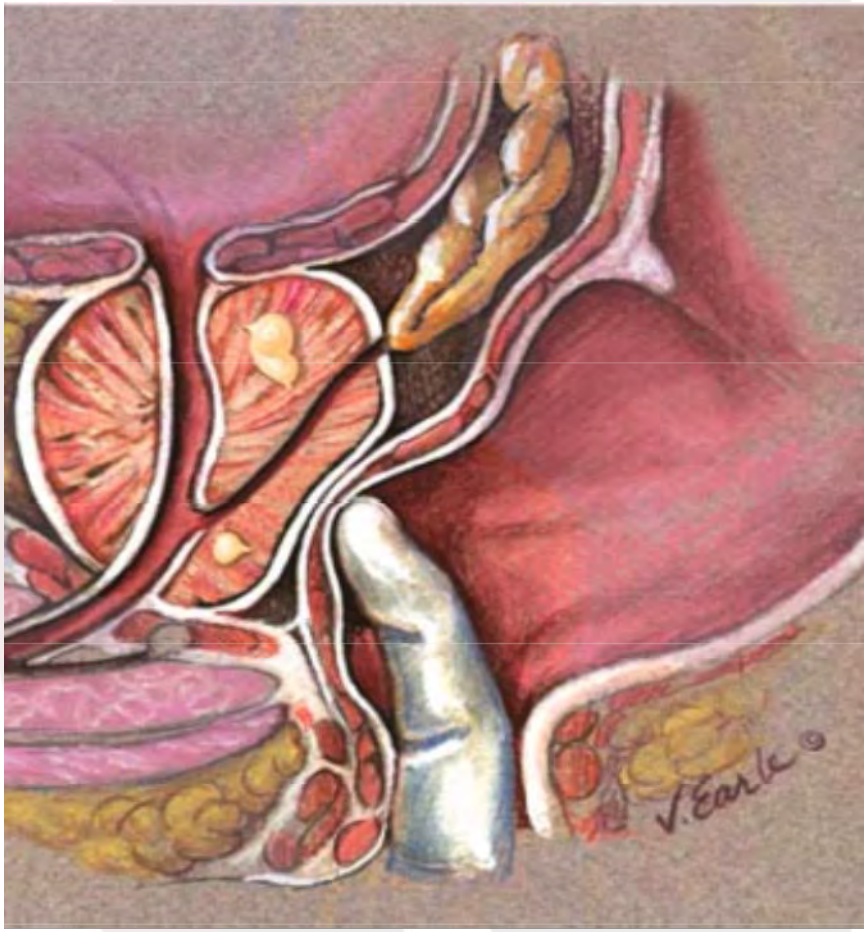




Prostate Biopsy

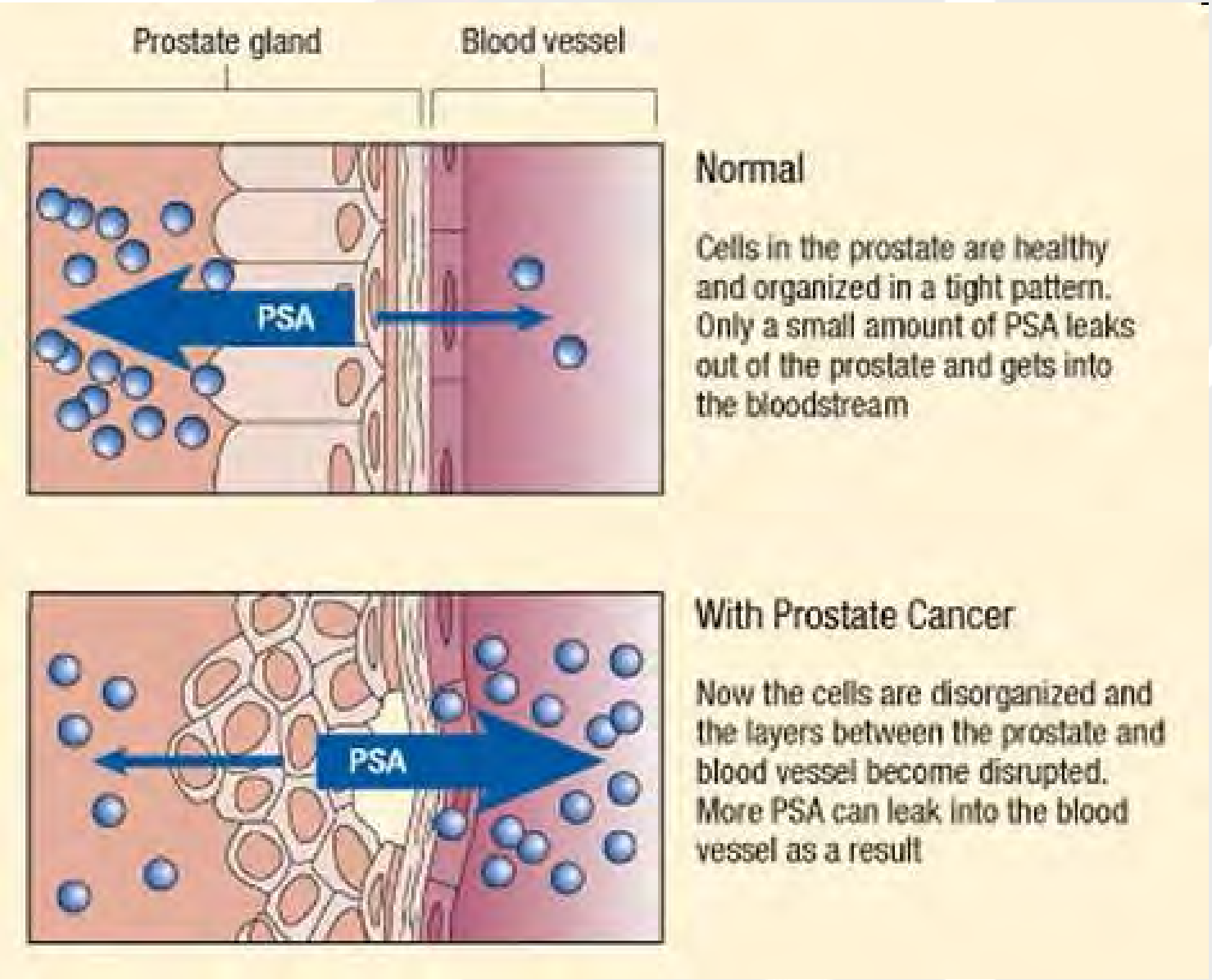
PCA3.org

Digital Rectal Examination (DRE)



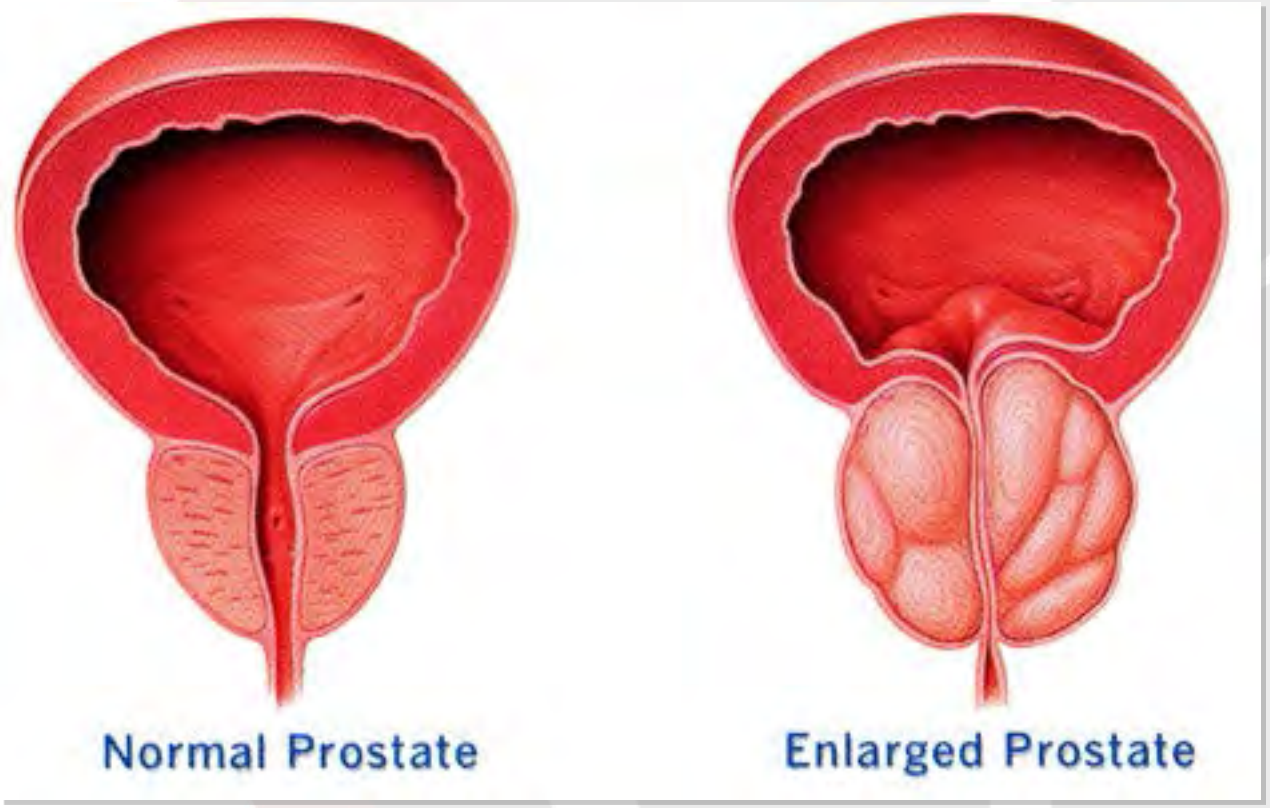
Prostate Specific Antigen (PSA)

liquefies semen and releases progressively motile sperm.



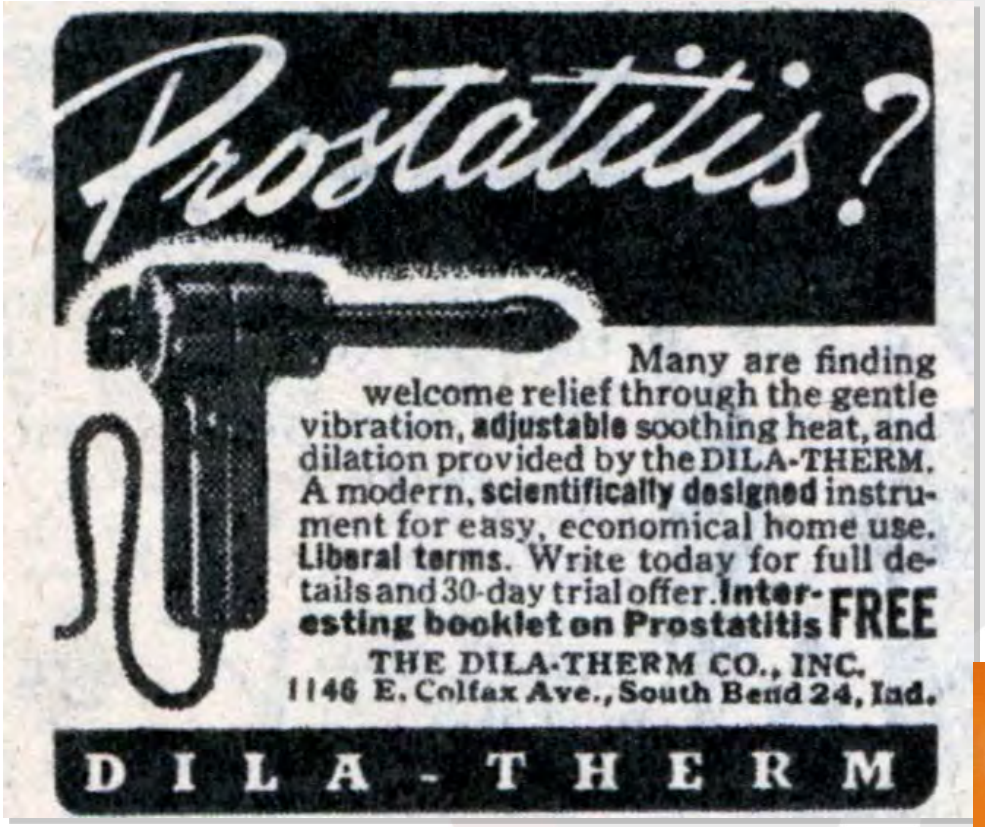
Tumor Markers, p.198-9 (2002)

Things that can elevate serum PSA levels



Things that can elevate serum PSA levels

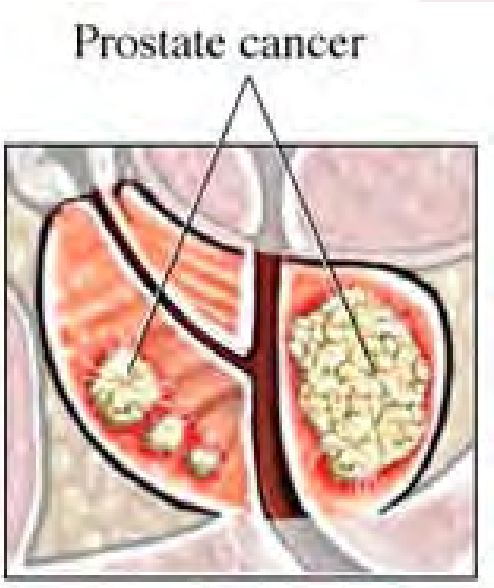
Things that can elevate serum PSA levels

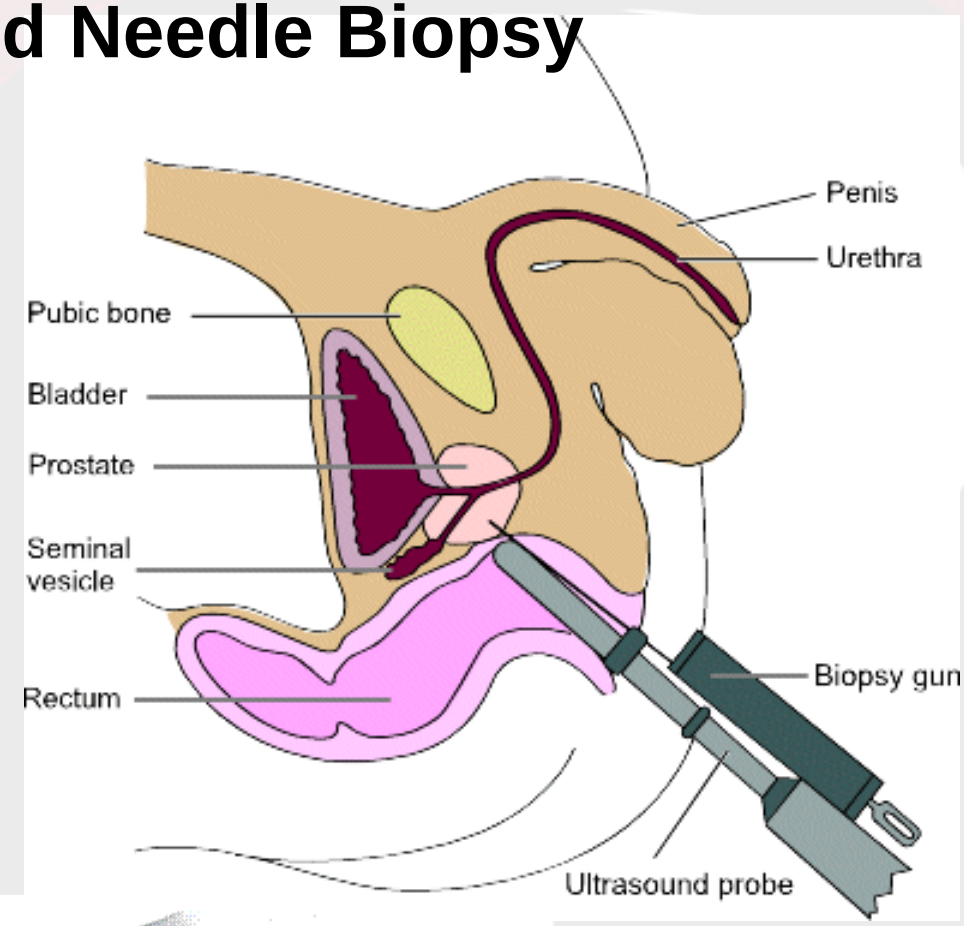


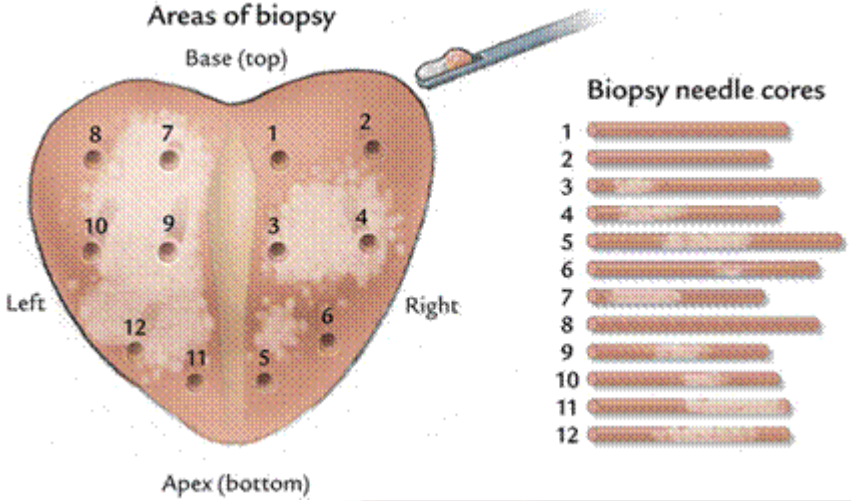
Use of PSA as a Tumor Marker

1. Early detection
2. Staging once PCa is diagnosed
3. Post-treatment assessment and management

TRUS-Guided Needle Biopsy



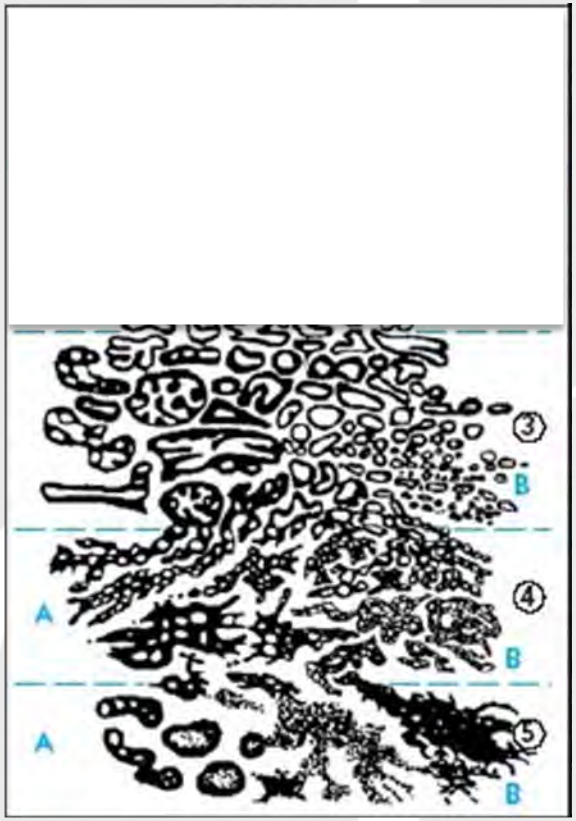




Gleason Grading

Donald F. Gleason

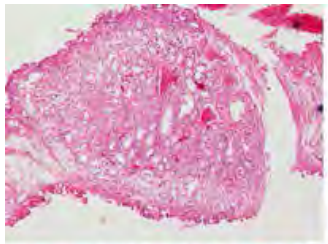
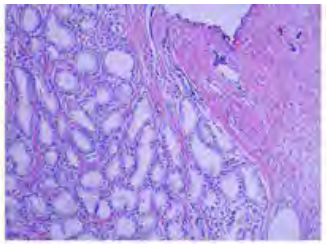
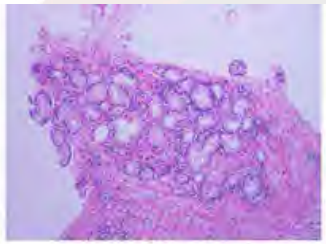
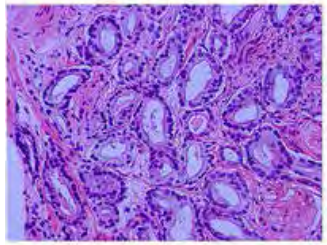
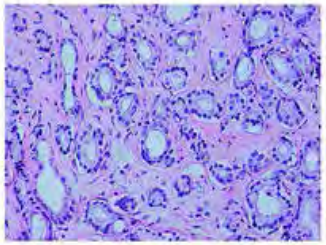
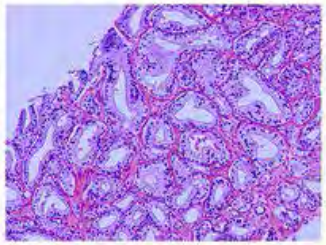
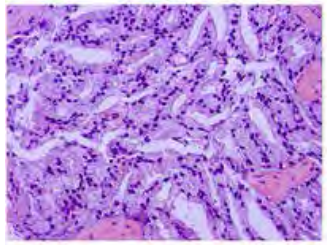
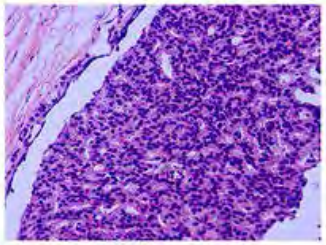
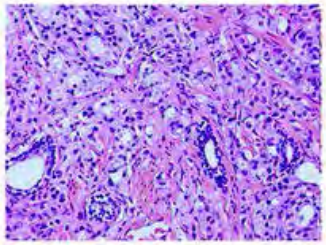
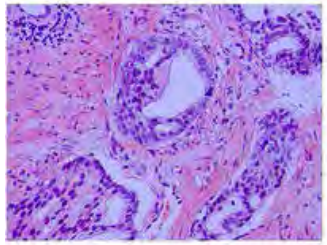
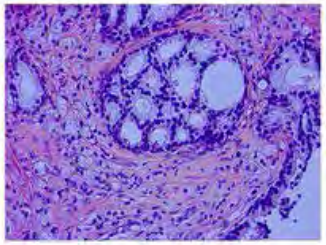
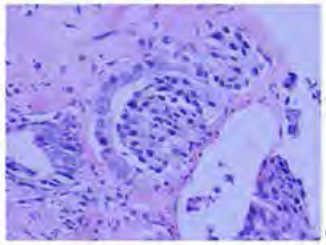
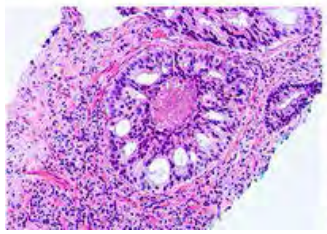
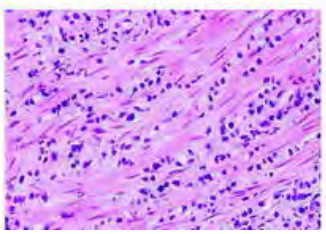
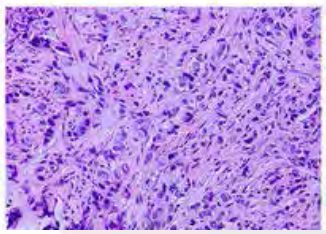
Grade	Description
Grade 1	Small, uniform glands with minimal nuclear changes
Grade 2	Medium-sized acini, still separated by stroma but more closely arranged.
Grade 3	The most common finding in prostate cancer biopsies. Marked variation in glandular size and organization, infiltration of stromal and neighboring tissues.
Grade 4	Markedly atypical cells with extensive infiltration into surrounding tissues.
Grade 5	Sheets of undifferentiated cancer cells.



Gleason Score = most frequent grade + 2nd most frequent grade

Gleason, Cancer Chemother. Rep. 1966.

A Contemporary Prostate Cancer Grading System

Gleason patterns 1–3
distinct, discrete, individual glands

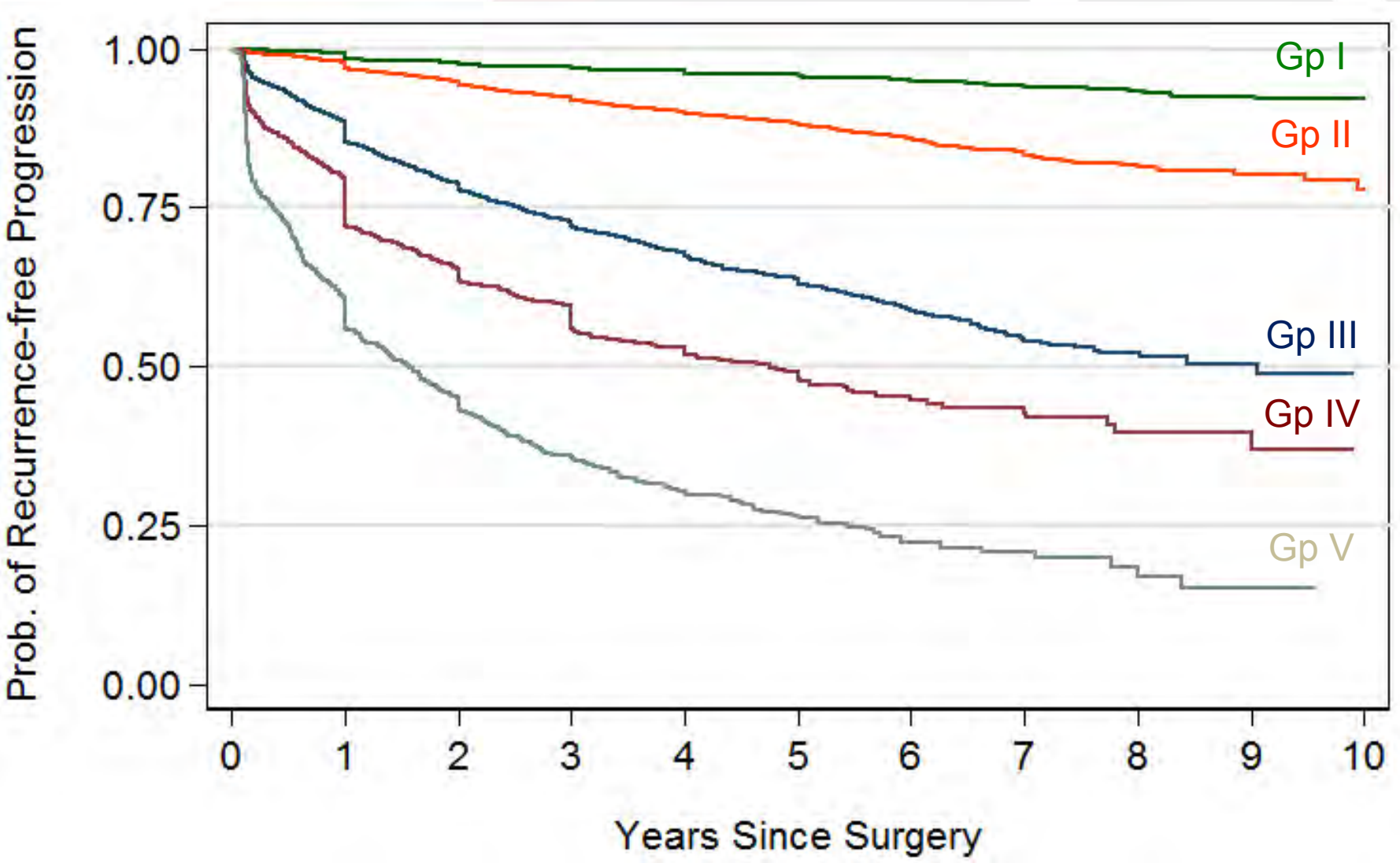
Gleason pattern 4
fused, cribriform, or poorly-formed glands, or glomerularion

Gleason pattern 5
comedo necrosis, cords, sheets, solid nests, single cells

Gleason score ≤6	Grade group I
Gleason score 3+4=7	Grade group II
Gleason score 4+3=7	Grade group III
Gleason score 4+4=8 3+5=8 5+3=8	Grade group IV
Gleason score 4+5=9 5+4=9 5+5=10	Grade group V

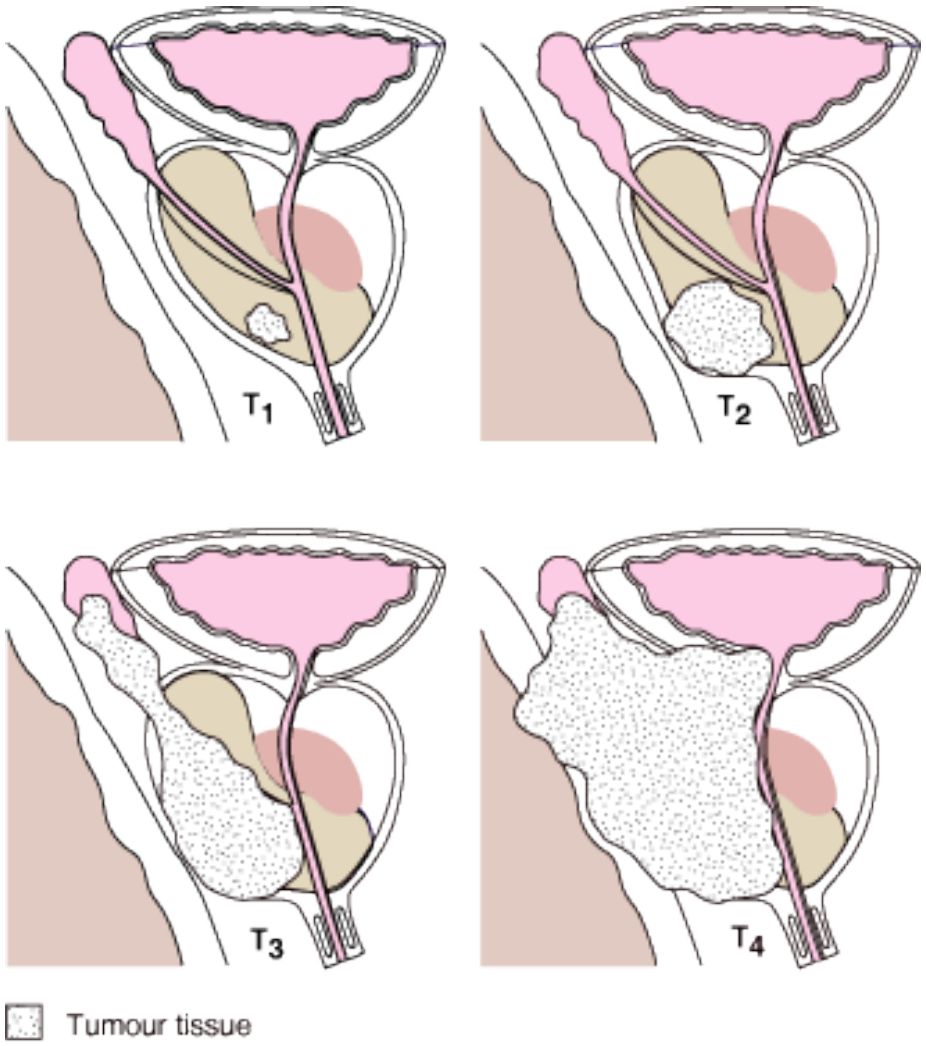
Epstein, Eur. Urol. 2015

A Contemporary Prostate Cancer Grading System



Epstein, Eur. Urol. 2015

TNM Staging Prostate Cancer: Tumor



T_1 Clinically unapparent tumor not palpable or visible by imaging

- **T1a:** Tumor incidental, found in ≤ 5% of resected tissue
- **T1b:** Tumor incidental, found in >5% of resected tissue
- **T1c:** Tumor identified by needle biopsy (because of high PSA)

T_2 Tumor confined within the prostate gland

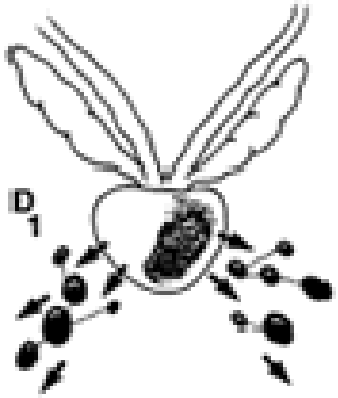
- **T2a**: Tumor involves one lobe
- **T2b**: Tumor involves both lobes

T_3 Tumor extends through prostatic capsule

- **T3a**: Extracapsular extensions (unilateral or bilateral)
- **T3b**: Tumor invades seminal vesicles

T_4 Tumor invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles and/or pelvic wall

TNM Staging Prostate Cancer: Lymph Node Status



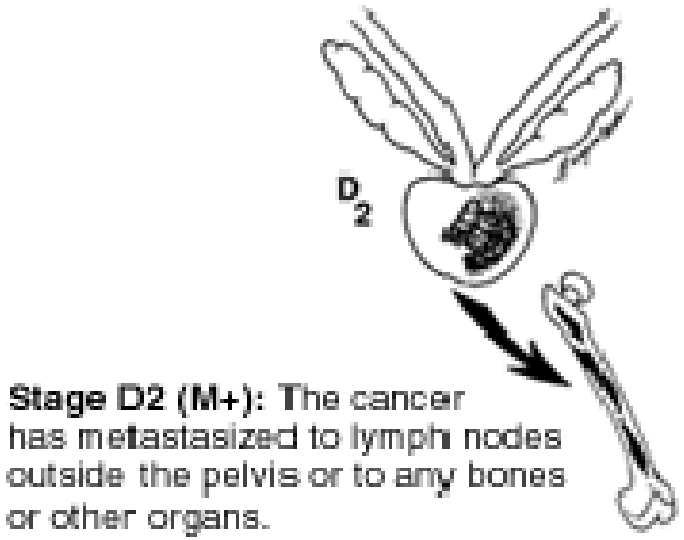
Stage D1 (N+): The cancer has metastasized to the lymph nodes (only in the pelvic area).

Nx: Regional lymph nodes have not been assessed

N0: No regional lymph node metastasis

N1: Regional lymph node metastasis

TNM Staging Prostate Cancer: Distant Metastasis



Stage D2 (M+): The cancer has metastasized to lymph nodes outside the pelvis or to any bones or other organs.

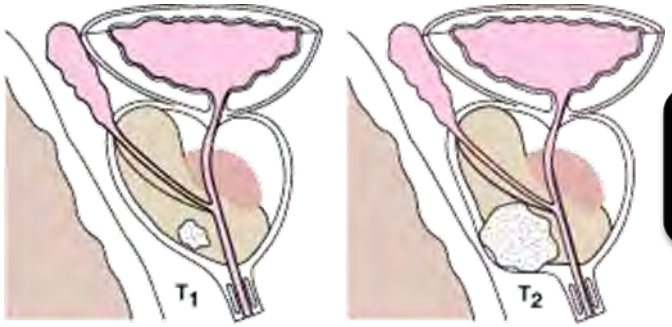
Mx: Distant metastasis has not been assessed

M0: No distant metastasis

M1: Distant metastasis

- **M1a**: Non-regional lymph nodes
- **M1b**: Bone
- **M1c:** Other sites

Primary Treatment Options



Localized disease

- Curative intent (radical therapy)
  - Radiotherapy
    - External beam therapy
    - Brachytherapy
  - Surgery
    - Open prostatectomy
    - Laparoscopy prostatectomy
    - Robotic Laparoscopy prostatectomy
- Active surveillance
  - Monitor the course of the disease PSA every 6 months

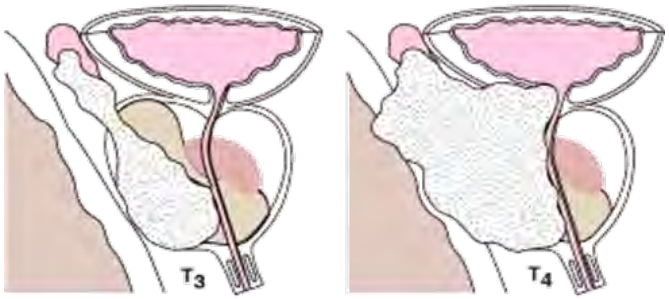
High cure rates in low-intermediate risk diseases

~ 50% impotence rates
10% urgency incontinence

~ 50% impotence rates
5 - 10% stress incontinence

Prostate cancer treatment inconsistencies found in Canada
CBC News **Nov 02, 2015**

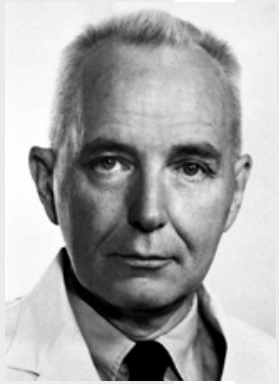
Primary Treatment Options



Disseminated disease

Surgery/ radiotherapy	Hormone therapy	Chemotherapy	Target Therapy
First line	First line	Second line	Second/Third line

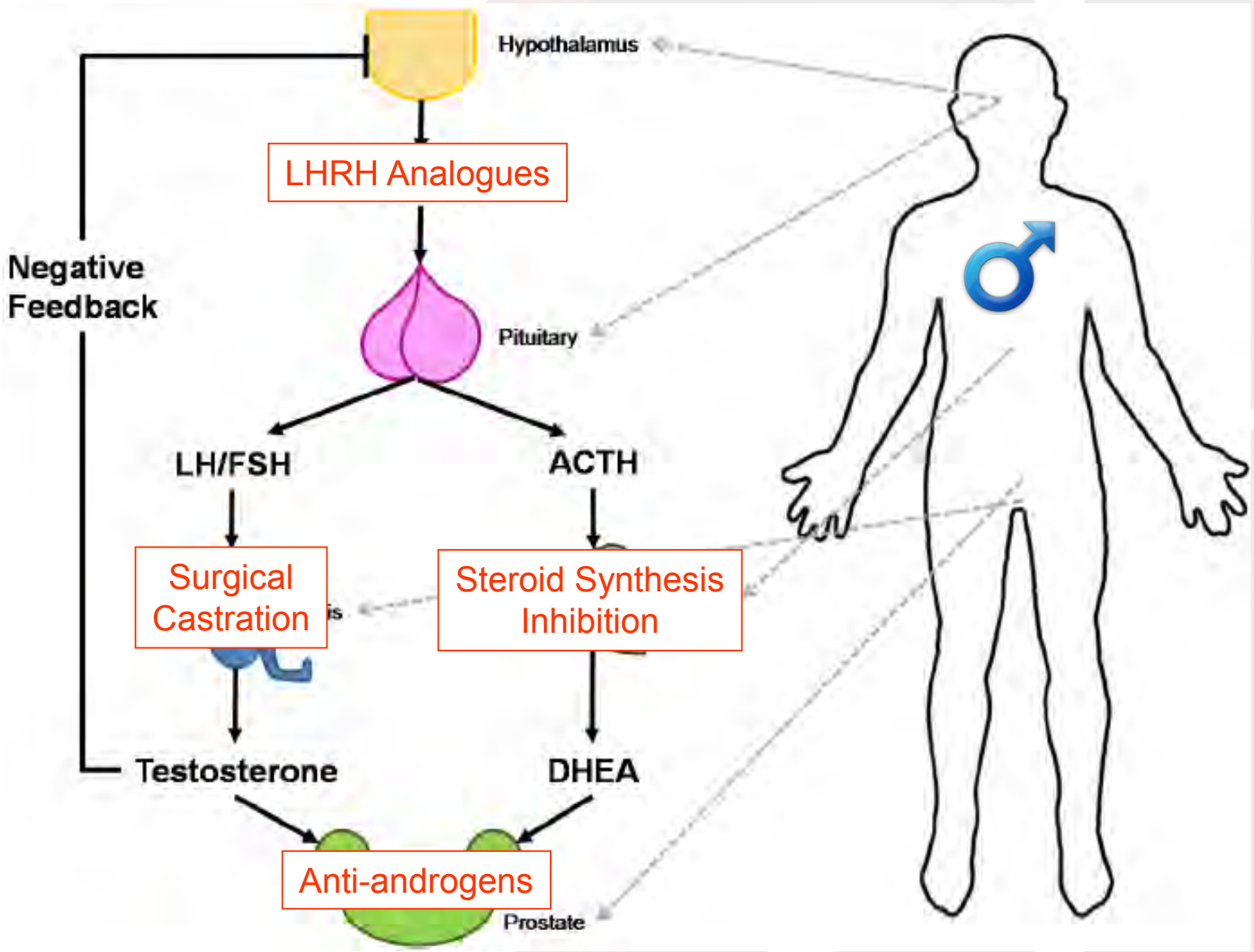
Androgens Regulate Prostate Cancer



Charles B. Huggins
Nobel Prize, 1966

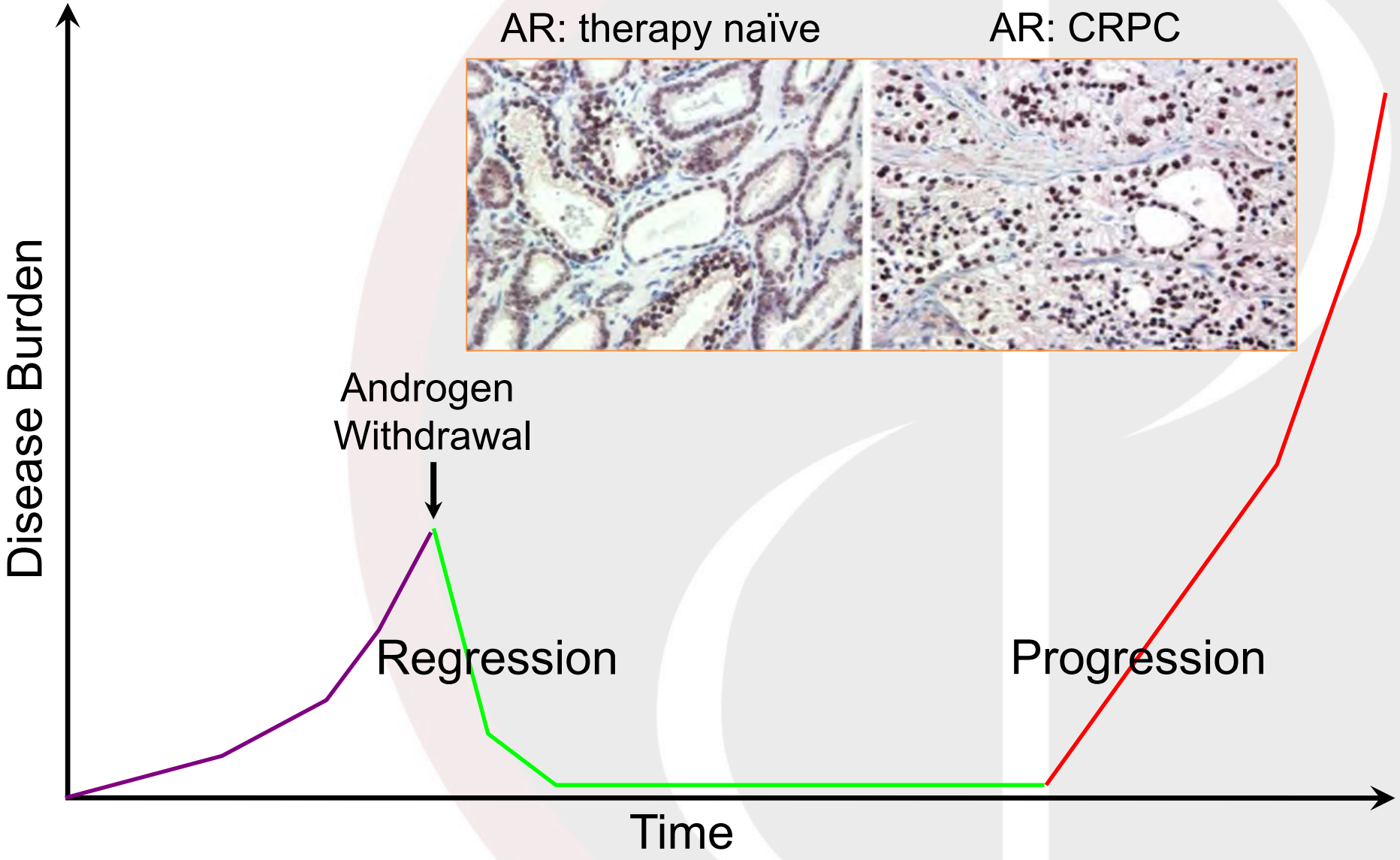
Established the androgen pathway as the 1st credentialized therapeutic target in prostate cancer

Androgen Pathway Targeting



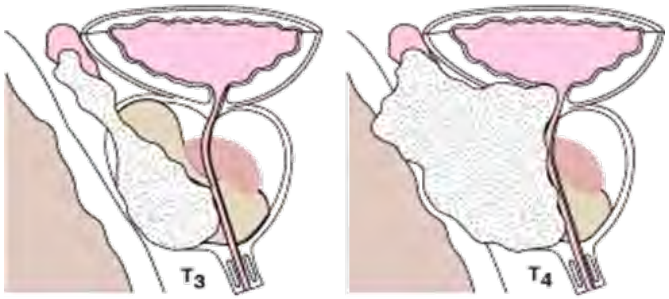
Locke J. MSc Thesis 2009

Castration-resistant Progression of Prostate Cancer



AR retention is a characteristic of prostate cancers, and it continues to play a pivotal role in maintaining the castration-resistant phenotype.

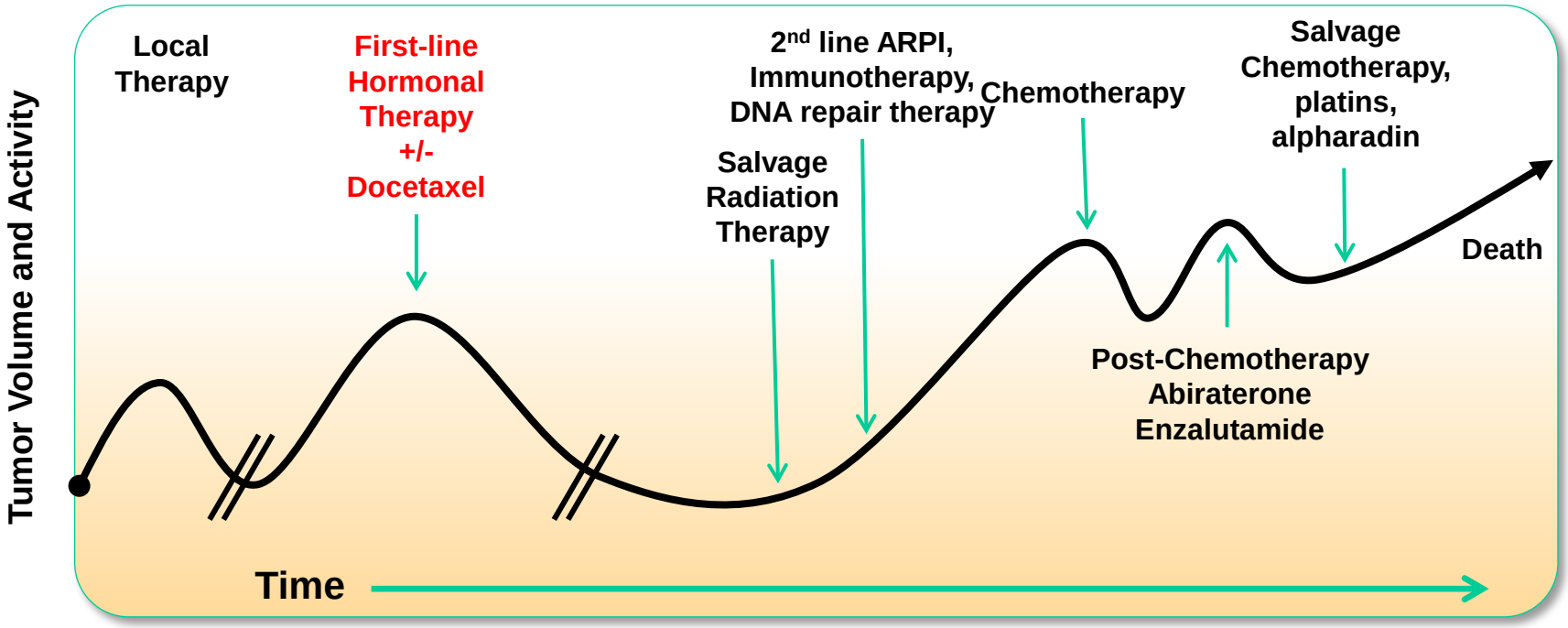
Secondary Treatment Options



Disseminated disease

- Surgery/ radiotherapy — First line
- Hormone therapy — First line
- Chemotherapy — Second line
- Target Therapy — Second/Third line

Prostate Cancer: Targeting Clinical States

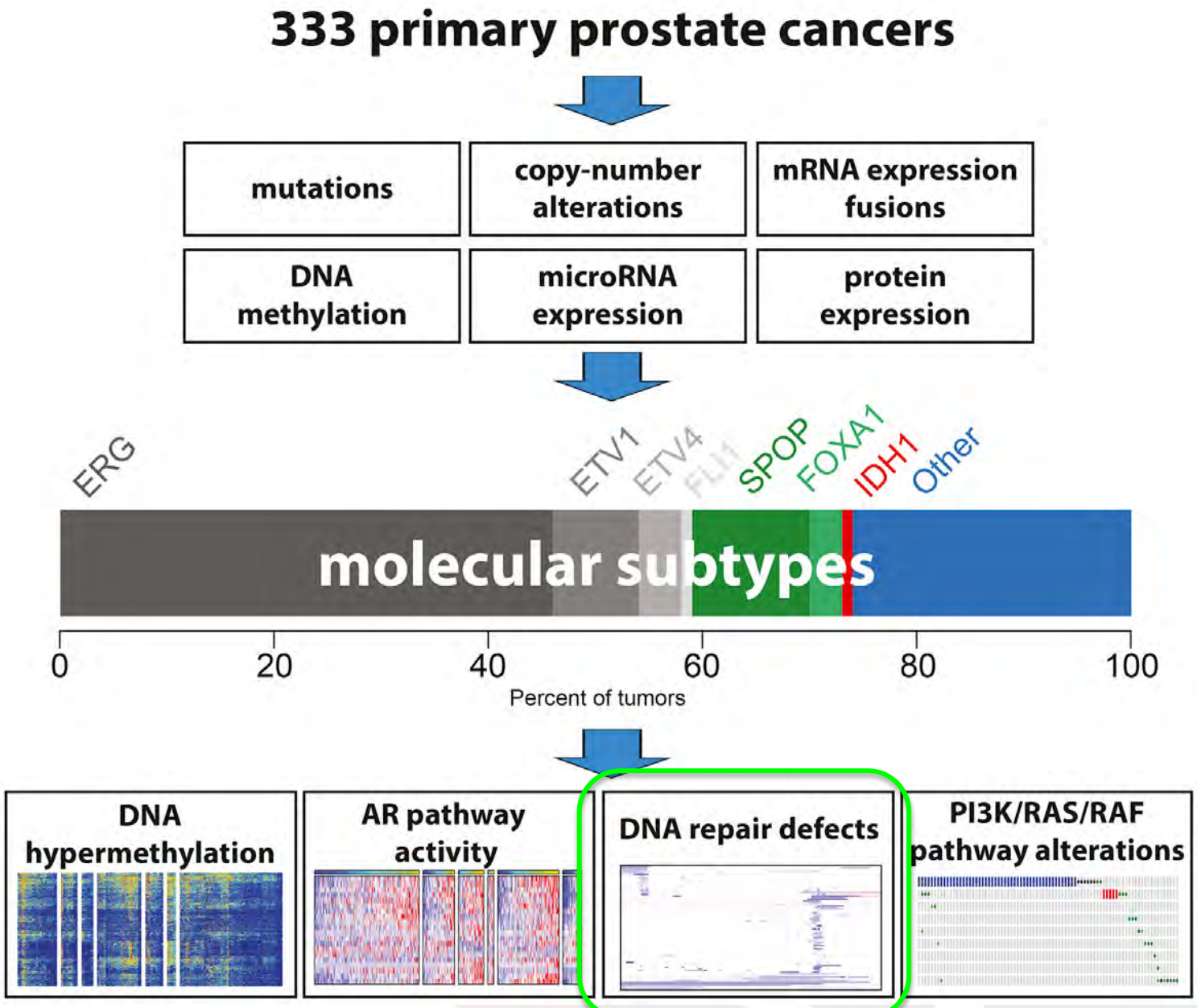


<u>Current Therapies for Advanced Prostate Cancer</u>:
Enzalutamide (Xtandi), Apalutamide (Erleada), Nilutamide (Nilandron/Anandrone) anti-androgens
Abiratarone (Zytida), a CYP 17 inhibitor with anti-androgen activity

Alpharadin (Xofigo), Radium 223
Sipuleucel-T (Provenge), immunotherapy
Cabazitaxel (Jevtana), a second line taxane for MDR PCa
Olaparib (Lynparza), Rucaparib (Rubraca), PARP inhibitors

Modified from Christopher Evans

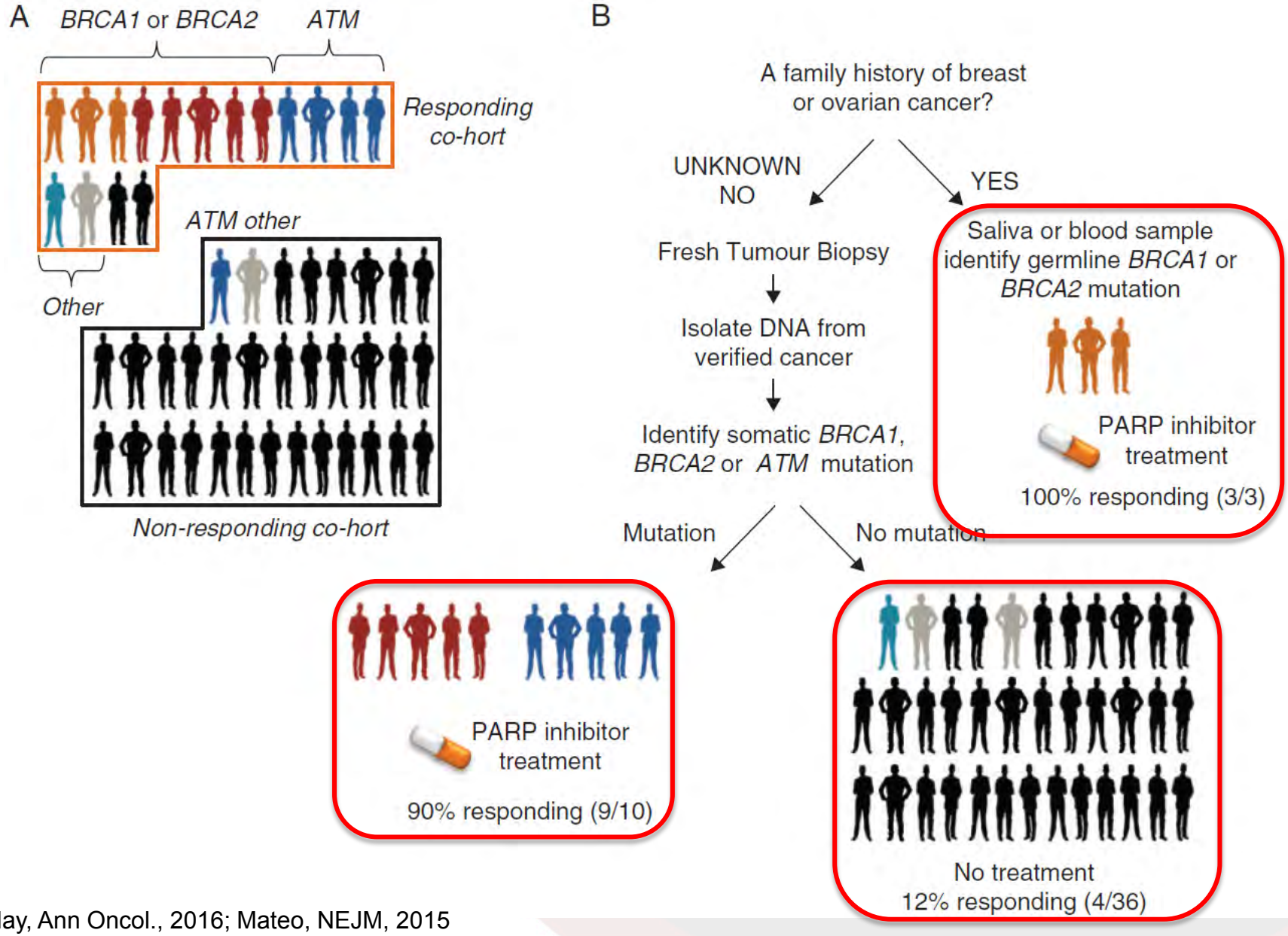
Molecular Taxonomy of Primary PCa



The Cancer Genome Atlas Research Network, Cell 2015

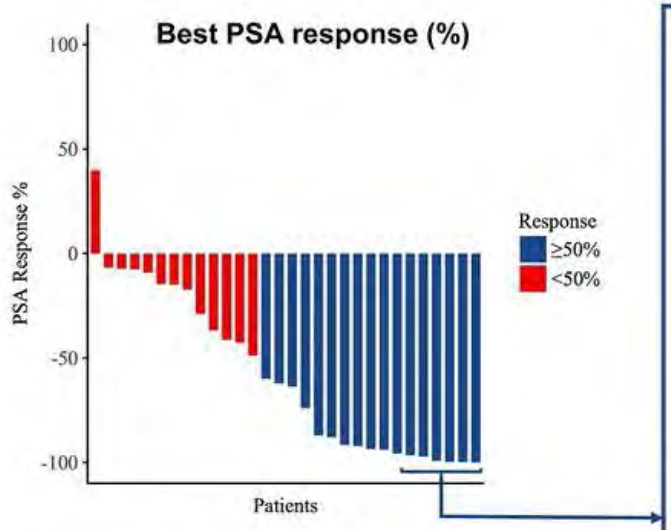
Olaparib

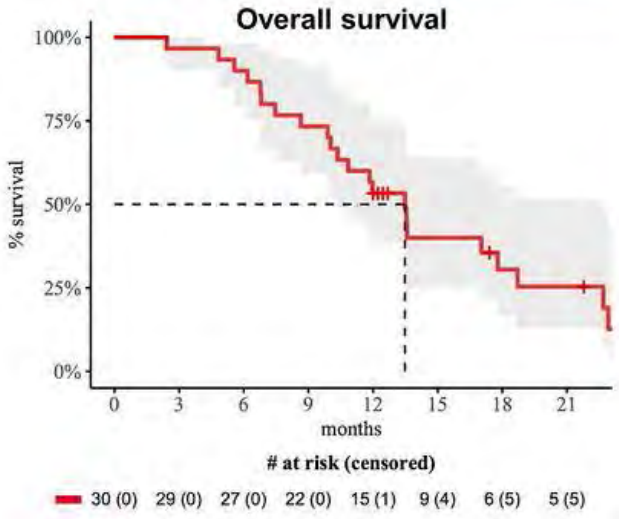
FDA Breakthrough Therapy Designation for CRPC

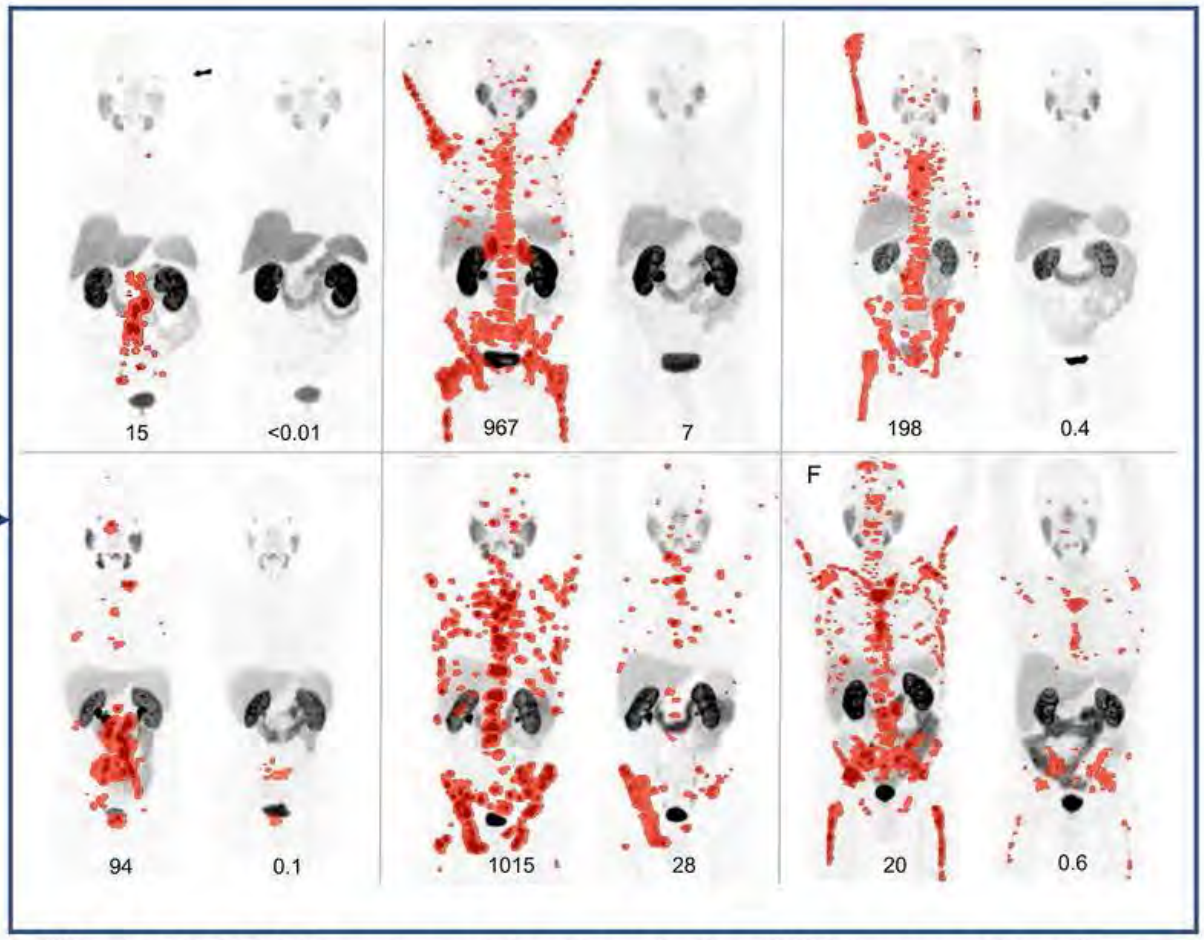


Helleday, Ann Oncol., 2016; Mateo, NEJM, 2015

PSMA-targeted “Theranostics”



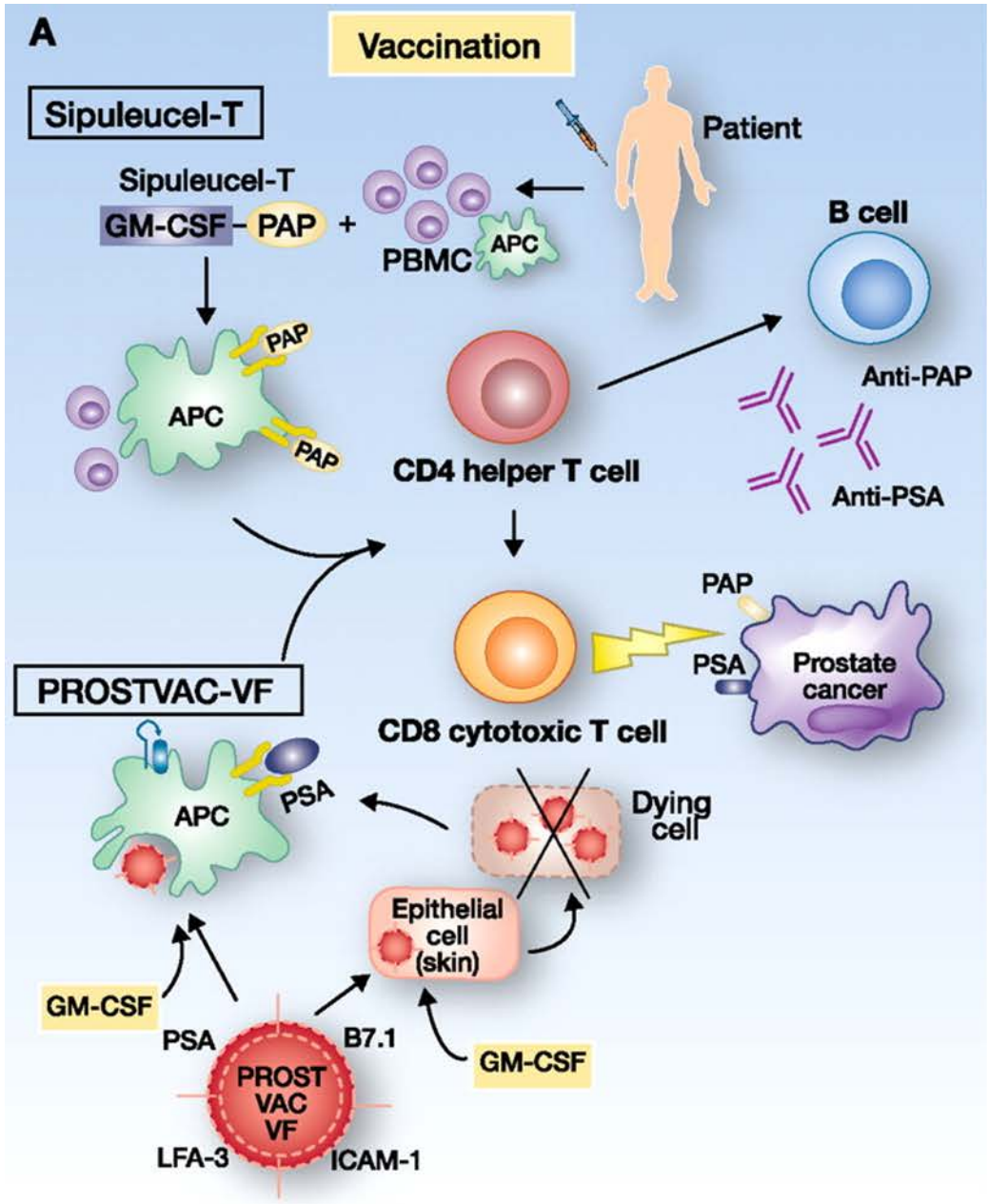




^{68}Ga-PSMA11 PET maximum intensity projection (MIP) images at baseline and 3 months after ^{177}Lu-PSMA617 in 6 patients with PSA decline >98%. Any disease with SUVmax over 3 in red.

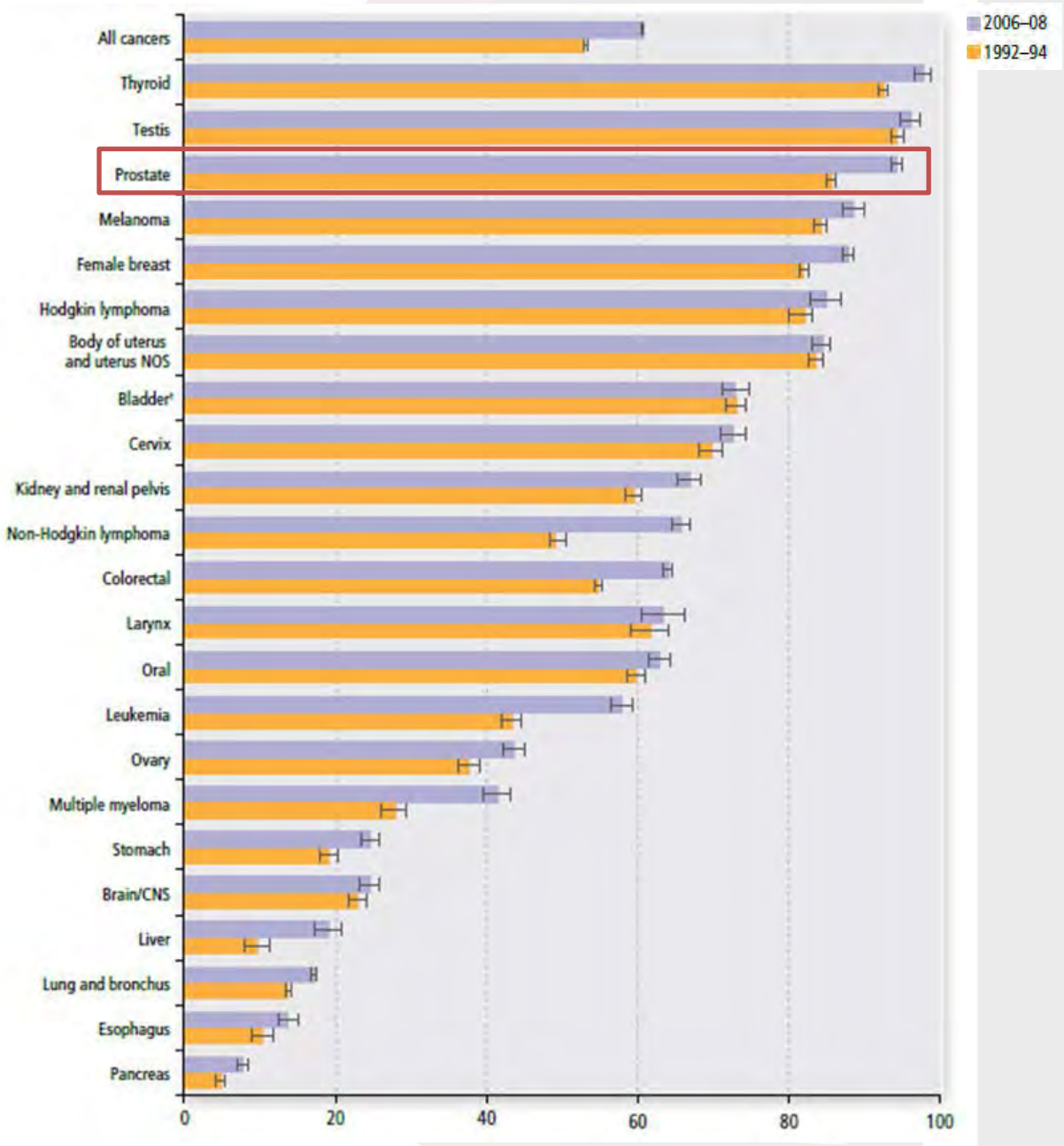
Hofman et al. Lancet 2018; J Nucl Med 2018

Prostate Cancer Immunotherapy



May et al., Clin. Cancer Res. 2012; De Bono et al., J. Clin. Oncol. 2018; Tasuku Honjo and James Allison, Nobel Prize Medicine 2018.

5 Year Net Cancer Survival



Prostate Health and the Aging Man

RECOGNIZE the Common Underlying Risk Factors:

- Smoking
- Diet
- Exercise
- Obesity
- Illicit Drugs
- Occupational
- High BP
- Lipids
- Diabetes

CANADIAN MEN'S HEALTH FOUNDATION

Campaigns and Resources

DONTCHANGEMUCH.ca
Where guys go to get healthy

Don't Change Much

Don't Change Much is a health resource inspiring men and their families to lead healthier lives. With reliable information and easy tips, we know every guy and their family can make small changes that will have a big impact on their health.

VISIT DONTCHANGEMUCH

YOUCHECK.CA
The helpful health tool for men

You Check

YouCheck is a world first helpful health tool for men – a health awareness tool built specifically for men. Take your first step in making small changes that lead to big time benefits over the long haul. It's free and 100% confidential.

GET YOUCHECKED

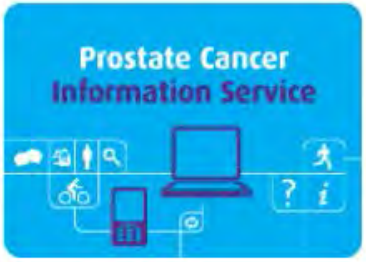
Canadian Men's Health Week

Join Canadians from coast to coast to coast in the goal of improving men's and family health in Canada. Canadians believe they're a pretty healthy nation. But weirdly, Canadian guys aren't that healthy. It's not because of genetics; it's a result of lifestyle.

CELEBRATE

Prostate Cancer Canada

About Us | Prostate Cancer | Research | Supporting You | Get Involved | Donate



PCC Spotlight

Dream car draw a win for all Ontarians affected by prostate cancer
February 22, 2019 – TORONTO, ON – A dream came true today for Harold Mutter (ticket #19273), the lucky winner of a 2018 Acura NSX valued at more than $235,000 - the prize for Prostate Cancer Canada's seventh Rock the Road Raffle.
More →

Researchers discover common markers of tumour hypoxia across 19 cancer types
Landmark pan-cancer study analyzes mutation signatures of low oxygen in more than 8,000 tumours
More →

Rock the Road Raffle returns with its most valuable car to date
A 2018 Acura NSX to be prized by Prostate Cancer Canada and TADA at the AutoShow
More →

→ Click here for news archive

Quick Links

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Like Us

Tom is dealing with prostate cancer. The waiting. The treatments. The side effects.
What would you do in his place? Watch these videos to map out a strategy that will work for you.

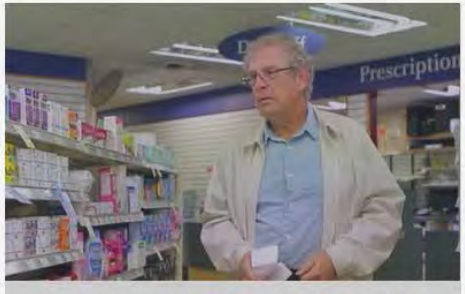
IF I WERE TOM

Get Started ▶ Choose Scene ↓

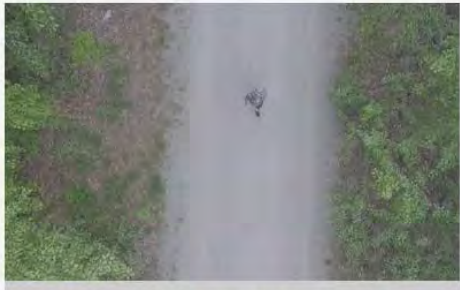
PCF BC

CUT TO THE CHASE

FIRST THINGS TO KNOW



TREATMENTS AND SIDE EFFECTS



LIVING WITH PROSTATE CANCER

"What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?"

Exercise and PCa

Harvard Health Professionals Study (JAMA 2011)

- Men over age 65 who exercised vigorously (more than 3 hours per week) had a 35% decrease in death rate from all causes and a 70% decrease in risk of developing high grade, advanced or fatal PCa

- No associations were shown in younger men ??

Exercise and PCa

Durham VA Study (Banez et al, Cancer, 2013)

n = 307 (164 white; 143 black)

- white men in their 60's who were moderately or highly active were 53% less likely to develop PCa

- no similar link seen in the black men ???

Physical Activity: Give me 30 minutes/day and I will give you…

- Physical health Mental Health
- Premature death= 30-50% -Depression
- Heart disease= 40-50%
- Stroke= 30-50%
- Type II diabetes= 30-40%
- Breast cancer= 20-30%
- Colon cancer…= 30-50%
- Osteoporosis= 40-50%
- ….(Manson J, Amend P. The 30-minute fitness solution, 2002.)

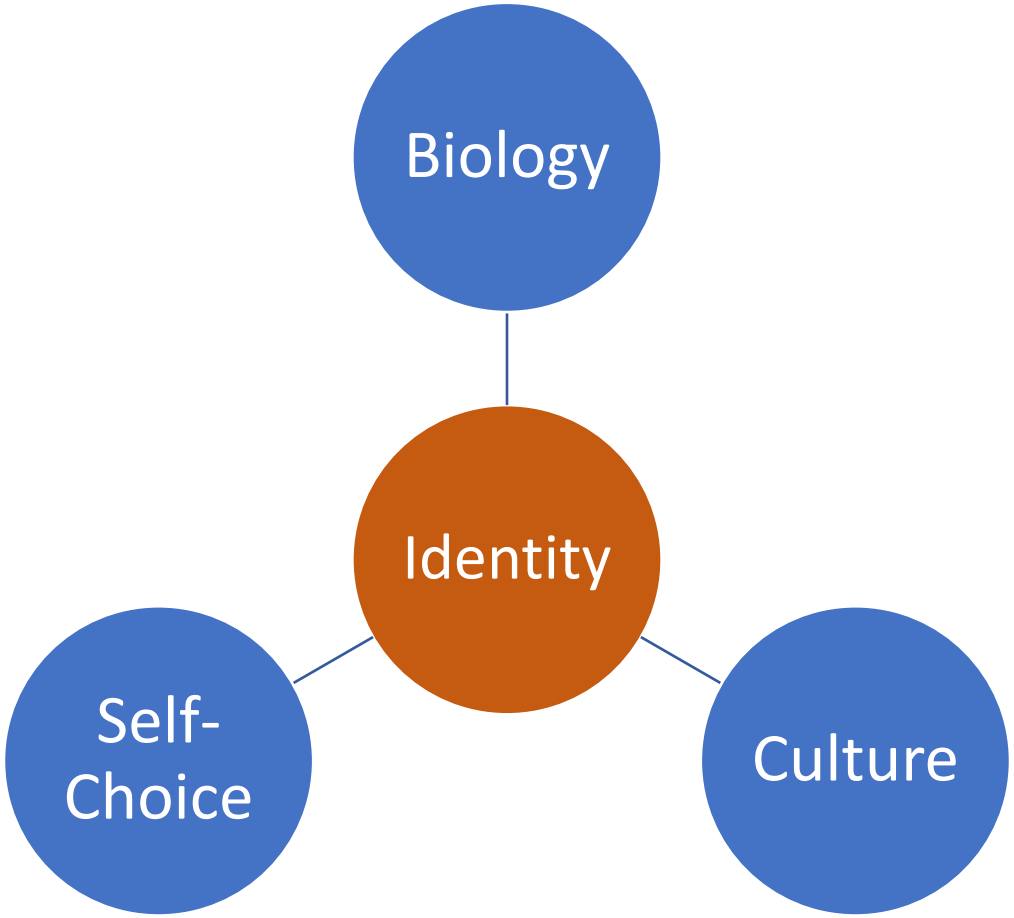
Critical issues in men's mental health

Dan Bilsker PhD

Clinical Assistant Prof.

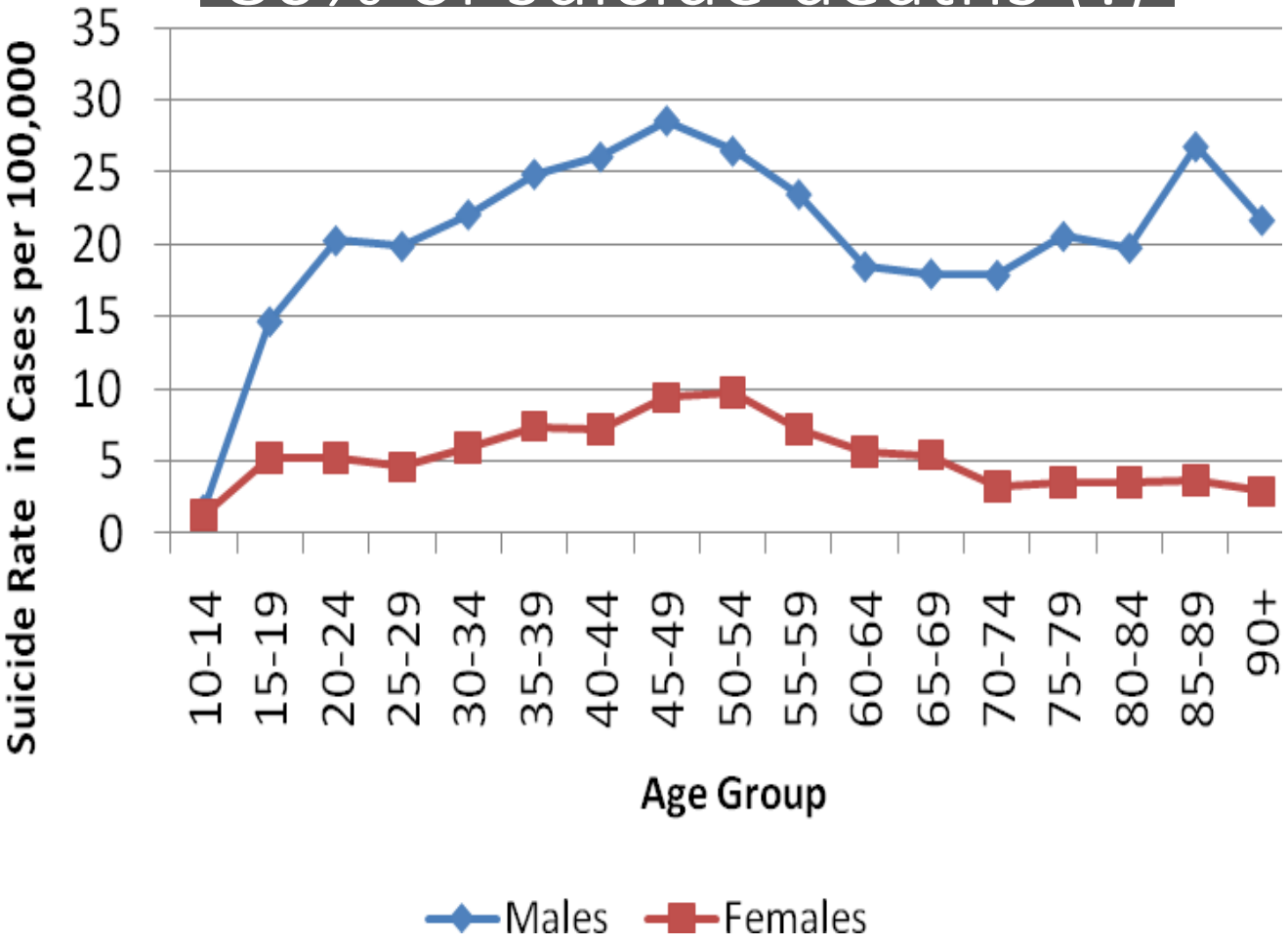
Dept. of Psychiatry, UBC

Sources of Male Identity



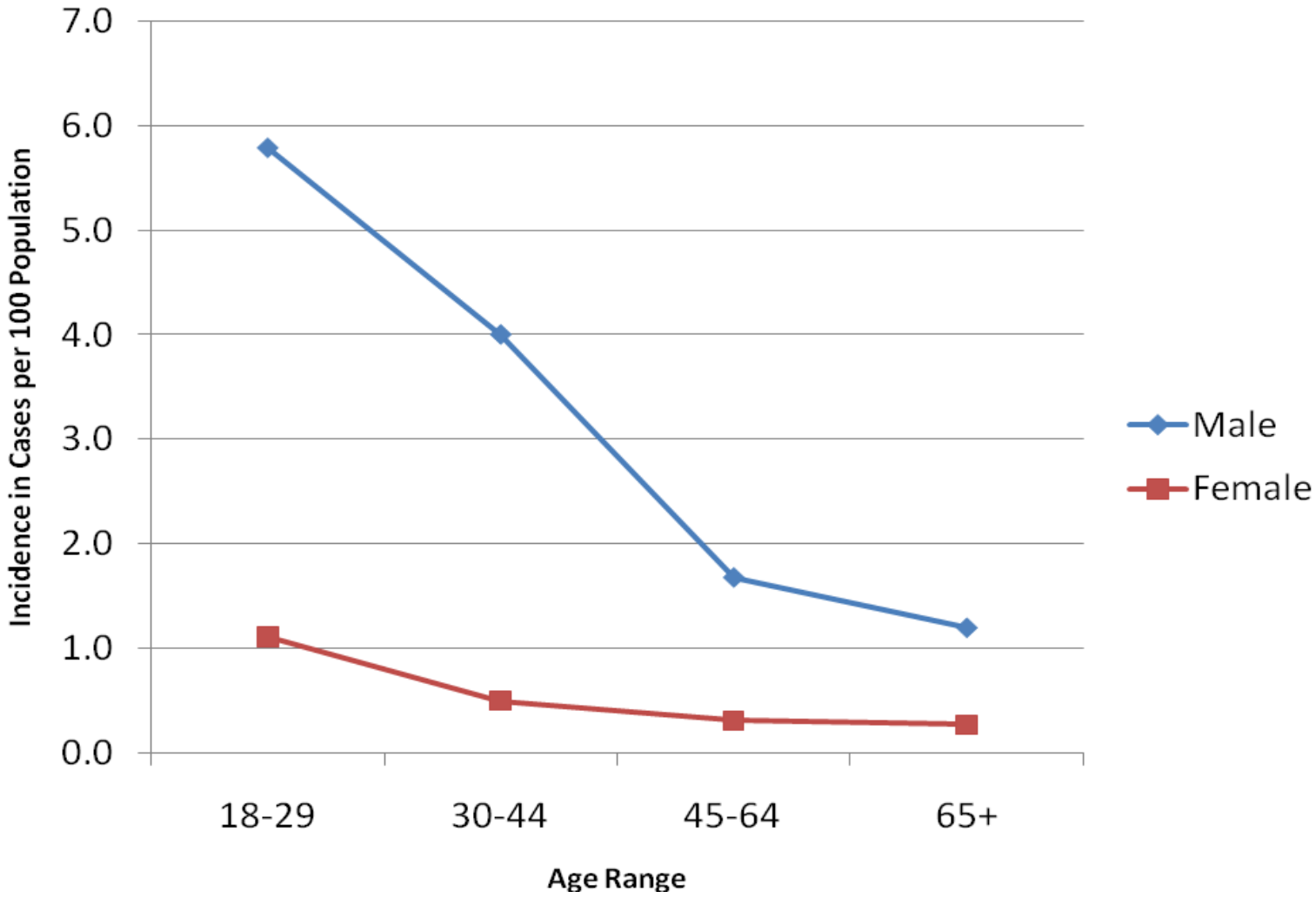
High incidence of male suicide

80% of suicide deaths (!)



Perplexing nature of male depression

Alcohol use disorder (80% men!)



Underutilization of psychological treatment

Men's coping with psychological suffering

Drink

Deny

Isolate

Get Angry

Clinical Responses

Reflect on your own assumptions

Don’t confuse affect with suffering

Refer to male-appropriate therapy

Monitor alcohol use

Population-Level Responses

Resist stigmatizing men	Provide targeted services
Fund Research	Enhance men's coping

Men's Resilient Coping

Balance	Self-Acceptance* REVERSE SCORED	Meaningful Work	Trusted Social Support	Physical Self-Care
• I make time for my personal and family life, even when the job is very demanding	• I'm disapproving and judgmental about my own flaws and inadequacies	• The work that I do fits well with my personal values and beliefs	• I have friends at work I can rely on to support me when I need it.	• I am careful to maintain a good level of physical fitness

Self-care tools

Tool	Search for
Antidepressant Skills Workbook	Same
Managing Anger (in Positive Coping with Health Conditions)	managing anger pchc
Rethinking Drinking	Same