

# Human Papillomavirus Vaccine Effectiveness and Herd Protection in Young Women

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## abstract

**BACKGROUND:** Clinical trials of the 4-valent human papillomavirus (HPV) vaccine demonstrate high efficacy, but surveillance studies are essential to examine the long-term impact of vaccine introduction on HPV prevalence in community settings. The aims of this study were to determine during the 11 years after vaccine introduction the prevalence of (1) vaccine-type HPV in adolescent and young adult women who were vaccinated (to assess vaccine effectiveness) and (2) vaccine-type HPV in women who were unvaccinated (to assess herd protection).

**METHODS:** Young women 13 to 26 years of age were recruited from hospital-based and community health clinics for 4 surveillance studies from 2006 to 2017. We determined the proportion of vaccinated and unvaccinated women who were positive for vaccine-type HPV across the studies, and the odds of positivity for vaccine-type HPV using logistic regression; all analyses were propensity score–adjusted to control for between-wave differences in participant characteristics.

**RESULTS:** Vaccination rates increased from 0% to 84.3% (97% of study participants received the 4-valent vaccine). Among women who were vaccinated, 4-valent vaccine–type HPV detection decreased from 35% to 6.7% (80.9% decline; odds ratio 0.13, 95% confidence interval 0.08 to 0.22). Among women who were unvaccinated, 4-valent vaccine–type HPV detection decreased from 32.4% to 19.4% (40% decline; odds ratio 0.50, 95% confidence interval 0.26 to 0.97). Estimated vaccine effectiveness was 90.6% in wave 3 and 80.1% in wave 4.

**CONCLUSIONS:** In this study in which trends in HPV in a US community >10 years after 4-valent HPV vaccine introduction and after 9-valent vaccine introduction were examined, we found evidence of vaccine effectiveness and herd protection. Further research is needed to examine trends in 9-valent vaccine–type HPV after higher rates of vaccination are achieved.

## Prostate Cancer

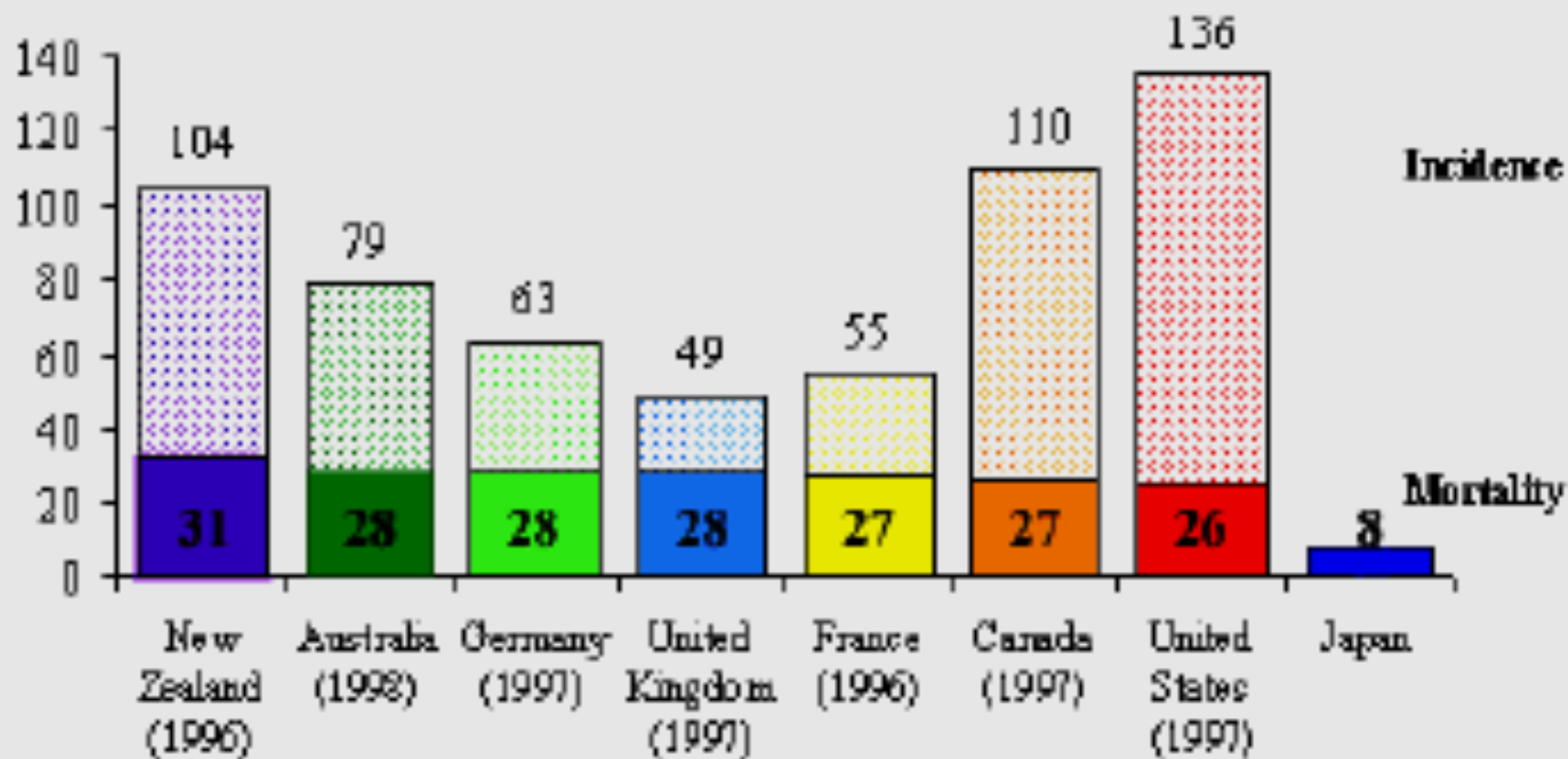
### Estimated Deaths

|                                |         |      | Males                                                                              | Females                                                                             |                                |         |      |
|--------------------------------|---------|------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|--------------------------------|---------|------|
| Lung & bronchus                | 83,550  | 26%  |  |  | Lung & bronchus                | 70,500  | 25%  |
| Prostate                       | 29,430  | 9%   |                                                                                    |                                                                                     | Breast                         | 40,920  | 14%  |
| Colon & rectum                 | 27,390  | 8%   |                                                                                    |                                                                                     | Colon & rectum                 | 23,240  | 8%   |
| Pancreas                       | 23,020  | 7%   |                                                                                    |                                                                                     | Pancreas                       | 21,310  | 7%   |
| Liver & intrahepatic bile duct | 20,540  | 6%   |                                                                                    |                                                                                     | Ovary                          | 14,070  | 5%   |
| Leukemia                       | 14,270  | 4%   |                                                                                    |                                                                                     | Uterine corpus                 | 11,350  | 4%   |
| Esophagus                      | 12,850  | 4%   |                                                                                    |                                                                                     | Leukemia                       | 10,100  | 4%   |
| Urinary bladder                | 12,520  | 4%   |                                                                                    |                                                                                     | Liver & intrahepatic bile duct | 9,660   | 3%   |
| Non-Hodgkin lymphoma           | 11,510  | 4%   |                                                                                    |                                                                                     | Non-Hodgkin lymphoma           | 8,400   | 3%   |
| Kidney & renal pelvis          | 10,010  | 3%   |                                                                                    |                                                                                     | Brain & other nervous system   | 7,340   | 3%   |
| All Sites                      | 323,630 | 100% |                                                                                    |                                                                                     | All Sites                      | 286,010 | 100% |

The 10 leading cancer types for estimated deaths in the United States in 2018. (American Cancer Society)

# Geographical Incidence and Mortality

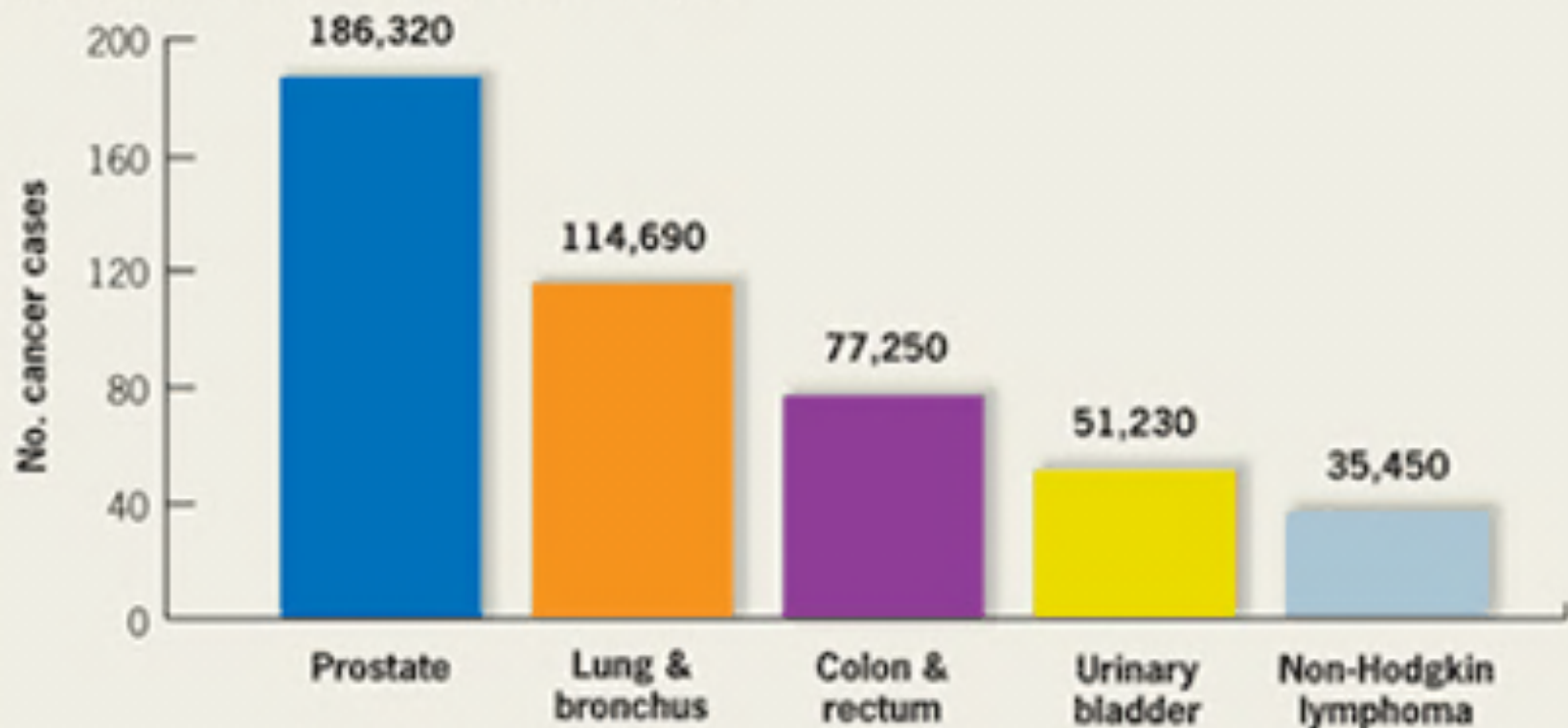
Chart V-1  
Prostate Cancer Incidence and Mortality  
per 100,000 Males per Year



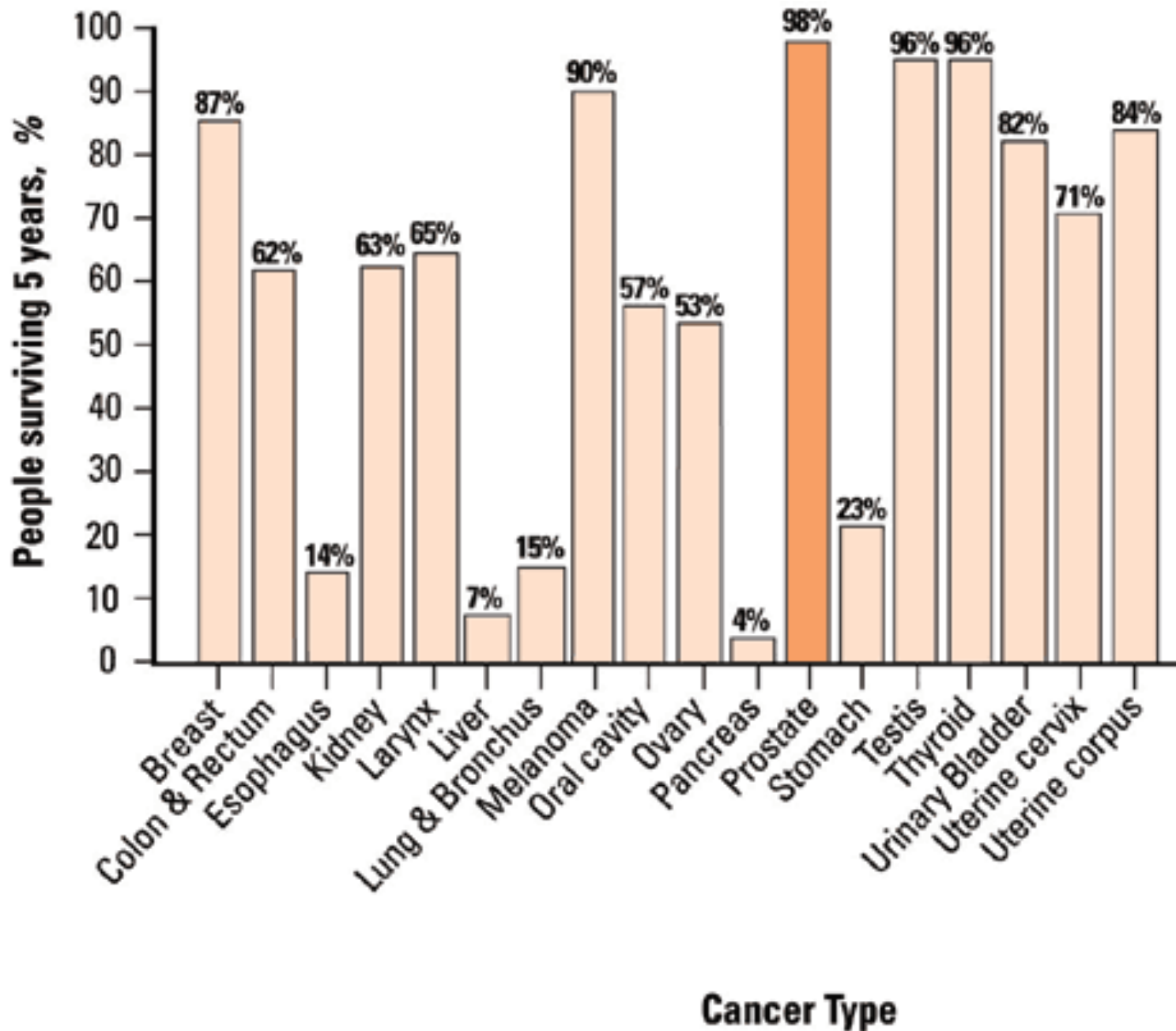
# The Most Common Cancer in Men

## Prostate Cancer Still No. 1

Prostate cancer remains the most commonly diagnosed malignancy among men in the United States. It accounted for one quarter of the 745,180 estimated new cancers diagnosed in men in 2008, according to the American Cancer Society. The top five cancers in American men are shown here.



# Prostate Cancer 5 year Survival



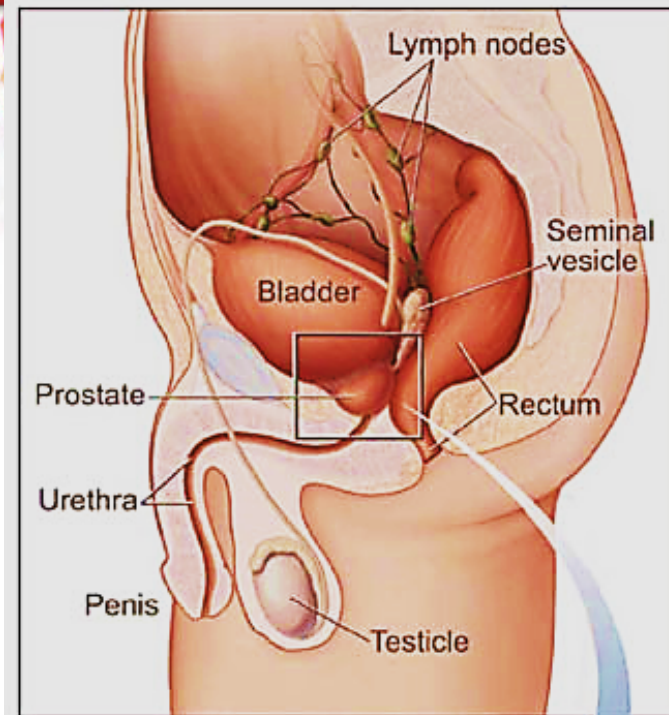
# What is Prostate Cancer?

## ❑ Definition of prostate cancer:

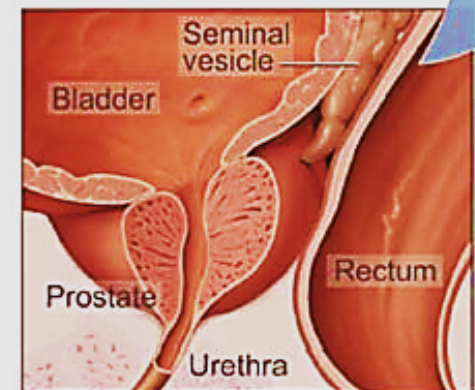
Cancer that forms in tissues of the prostate (a gland in the male reproductive system found below the bladder and in front of the rectum). Prostate cancer usually occurs in older men.

## ❑ Estimated new cases and deaths from prostate cancer in the United States in 2010:

**New cases: 217,730**  
**Deaths: 32,050**



This shows the prostate and nearby organs.



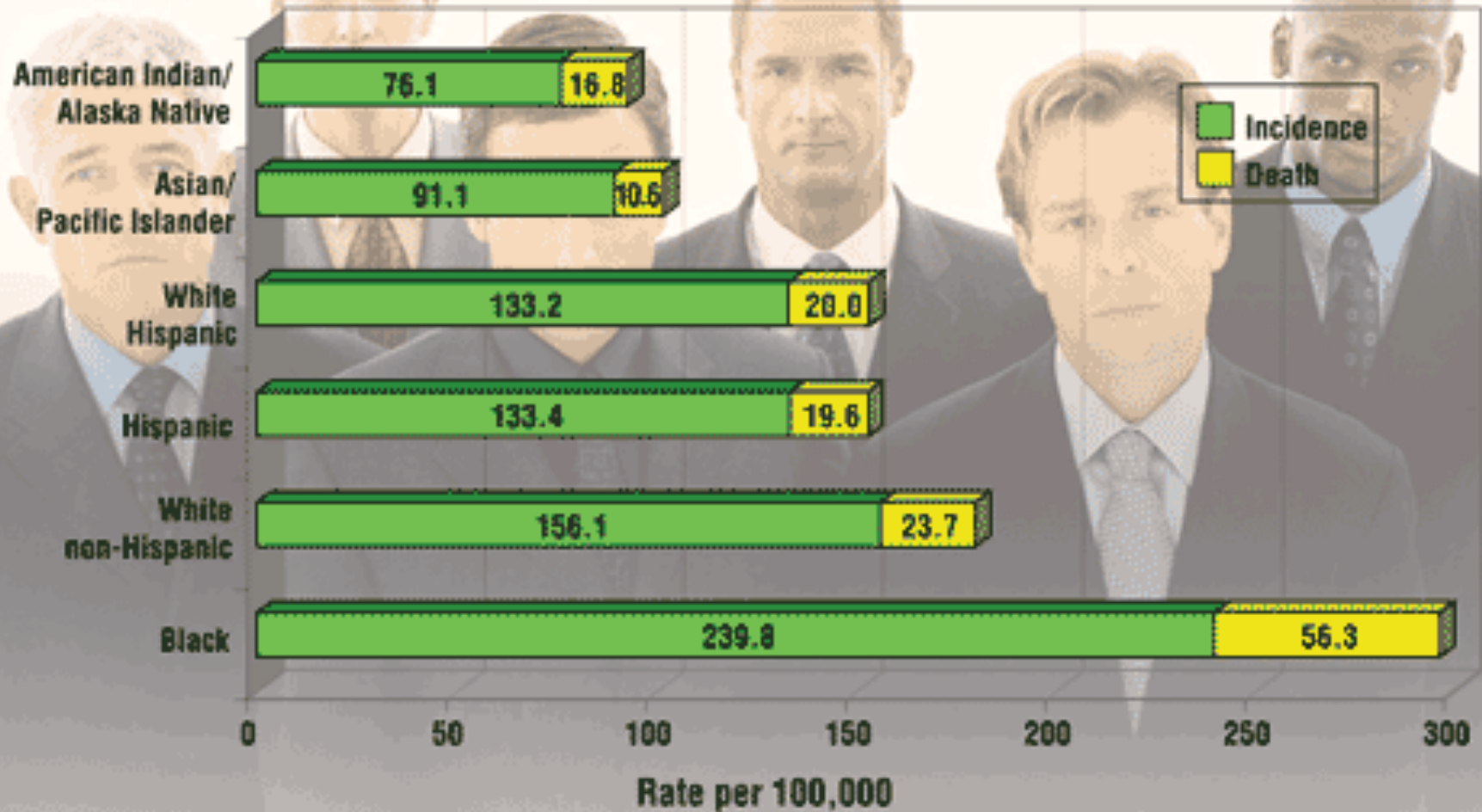
This shows the inside of the prostate, urethra, rectum, and bladder.

# Prostate Cancer Symptoms

- ☐ Early prostate cancer usually has no or few symptoms and as a result is often not diagnosed until a later stage.
- ✓ Weak or interrupted urine flow
- ✓ Frequent urination
- ✓ Difficulty urinating
- ✓ Blood in the urine or semen
- ✓ Pain or burning on urination
- ✓ Impotence
- ☐ Prostate cancer most frequently metastasize to the bones, causing bone pain.

# Prostate Cancer Incidence and Mortality by Race in the US

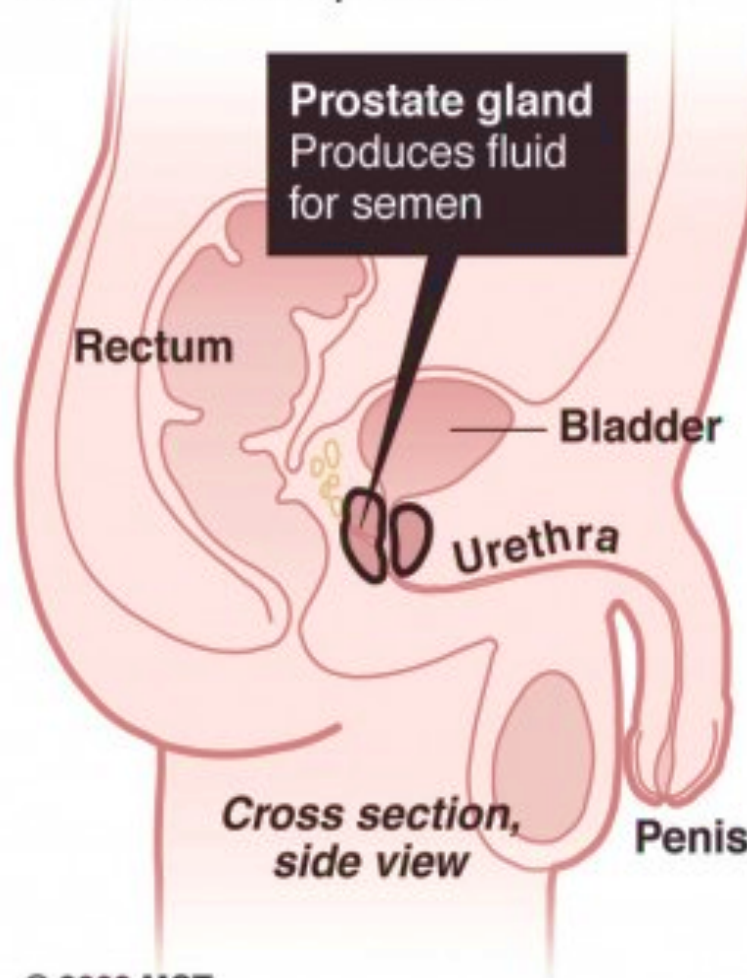
Incidence and Mortality Rates, 2006



# Common Risk Factors and Symptoms

## Prostate cancer

*The second most common malignancy in men, after skin cancer, is cancer of the prostate.*



© 2009 MCT

Source: U.S. National Cancer Institute

### Common symptoms

**Early stages** Often none

**Later stages** Difficulty urinating, blood in semen, painful ejaculation, lower back pain

### Screening

**Common tests** Manual exam by physician and PSA blood test

### Cancer risk factors

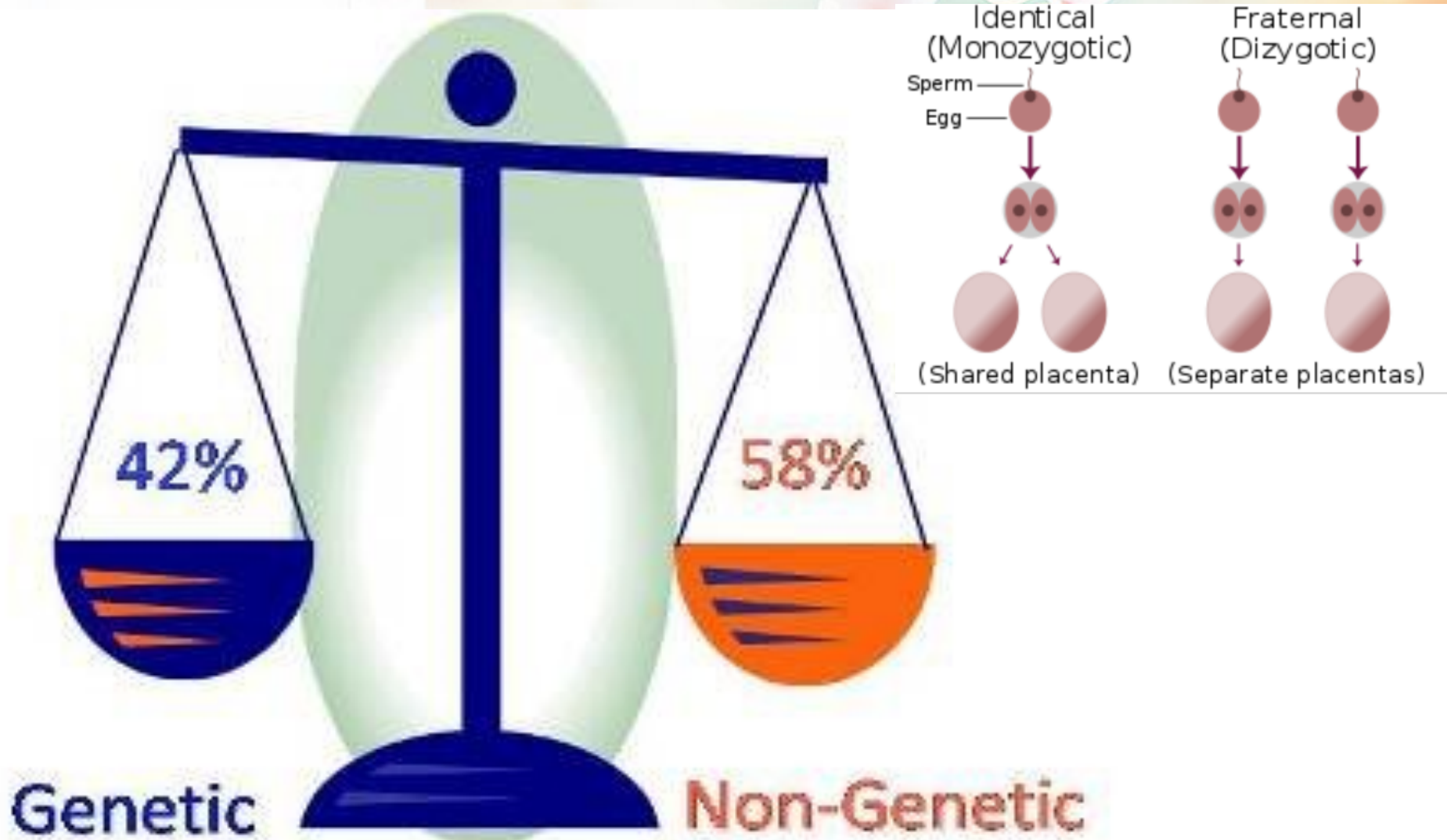
**Heredity** About 15% of men with prostate cancer have a father or brother with it

**Race** Incidence highest among men of African descent

**Age** Risk increases with age; 98% of cases are in men 55 and older

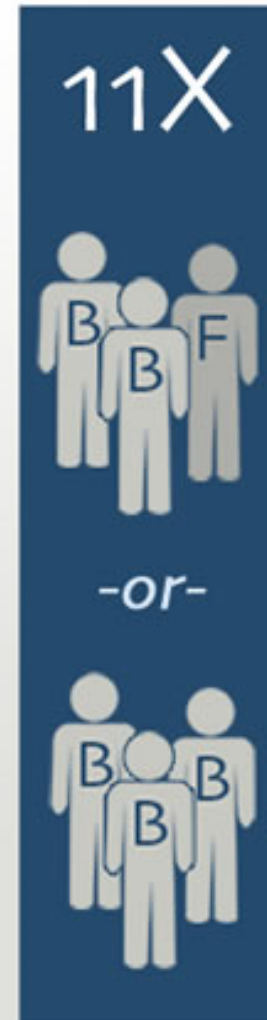
# Prostate Cancer Risk Factors

## Twin studies



# Family History and Prostate Cancer

## *Family History of Prostate Cancer*



B = Brother    F = Father

# Early baldness doubles risk of prostate cancer ...



## Early Balding Found to Double Prostate Cancer Risk

By: **JENNIE SMITH**, Skin & Allergy News Digital Network

02/15/11

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### VITALS

**Major Finding:** The men with prostate cancer were twice as likely to have had male pattern baldness at age 20 (OR 2.01).

**Data Source:** Men with a diagnosis of prostate cancer ( $n = 388$ ), recruited from radiation oncology clinics in three French institutions.

**Disclosures:** Neither Dr. Hassa nor his coauthors declared conflicts of interest.

### RELATED NEWS:

Men with prostate cancer are twice as likely to have had male pattern baldness starting at age 20, according to results of a study that found no increased risk among men who began balding in their 30s or 40s.

The findings, published Feb. 16 in *Annals of Oncology* (doi:10.1093/annonc/mdq695), suggest that men with early baldness may benefit from routine prostate cancer screening or preventive measures that could include the systematic use of 5-alpha reductase inhibitors, the researchers wrote.

For their research, Dr. Michael Yassa, who was a radiation oncology fellow at the Georges Pompidou European Hospital in Paris at the time of the study, and his associates studied 388 men with a diagnosis of prostate cancer, recruited from radiation oncology clinics in three French institutions. The study also included 281 matched controls with no history of cancer or hormonal pathologies, but with family histories similar to those of the cases. The mean age of the subjects was 67.2, and the controls, 66.4.

All study participants were asked to report any personal history of prostate cancer and their fathers' histories of the same, and to describe their balding pattern at ages 20, 30, and 40 along with their

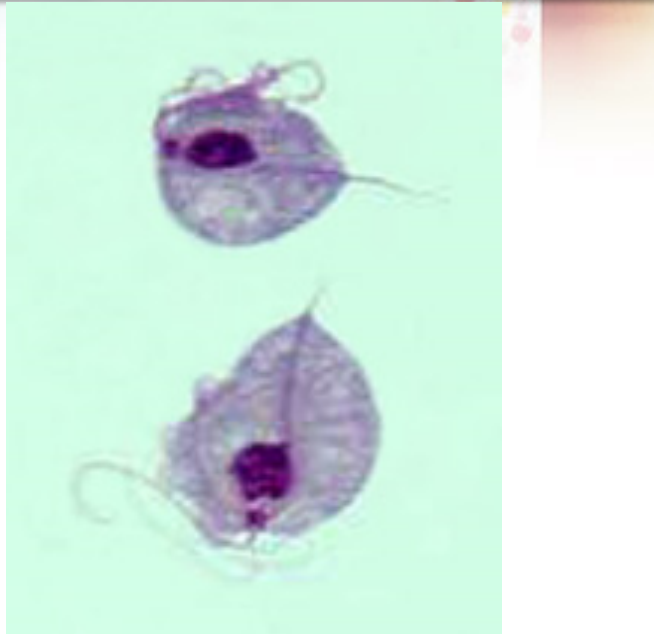


(c) Smobserver Wikipedia/ Creative Commons

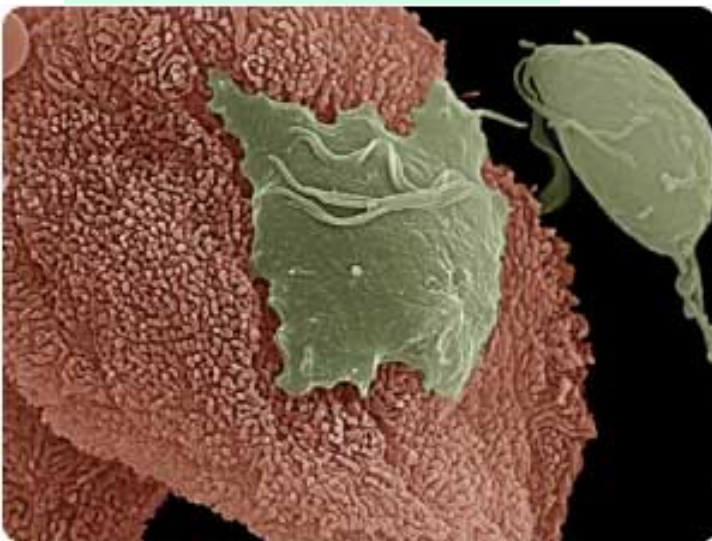
**Any balding present at age 20 was associated with an increased incidence of prostate cancer later in life.**

**Early-onset balding — a condition known as androgenic alopecia by age 20, doubled prostate cancer risk.**

# *Trichomonas vaginalis* Infection and Prostate Cancer Incidence and Mortality



- Men with antibodies to *T. vaginalis* were more than 2X as likely to develop tumors that spread outside the prostate and that ultimately led to metastases or prostate cancer-specific death.





## Report: Circumcision Linked to Lower Prostate Cancer Rate: A new report says that circumcised men have a 15 percent lower prostate cancer rate

   Comments 1  Share 3  +1 0  Tweet 0  Recommend 3

Jason Koebler  
U.S. News & World Report  
*March 13, 2012*

A new study released Monday has found that men who are circumcised before their first sexual encounter have a 15 percent lower incidence of **prostate cancer** than men who are uncircumcised or were circumcised after they first had sex.

Researchers say that because circumcised men are slightly less likely to contract herpes and human papillomavirus (**HPV**) than uncircumcised men, which previous studies have linked to a higher incidence of prostate cancer, circumcision might offer a level of protection against the disease.

[**CDC** Warns Untreatable **Gonorrhea** Is On the Way]

Janet Stanford, of the Fred Hutchinson **Cancer** Research Center and one of the authors of **the report**, which was published in the journal *Cancer*, says the study was a "natural extension" of ones that linked STDs to prostate cancer rates.

# BPH\*- chronic bacterial infection?

- **\*BPH benign prostate hyperplasia**

PLoS One. 2012;7(12):e51434. doi: 10.1371/journal.pone.0051434. Epub 2012 Dec 11.

## **Chronic prostatic infection and inflammation by *Propionibacterium acnes* in a rat prostate infection model.**

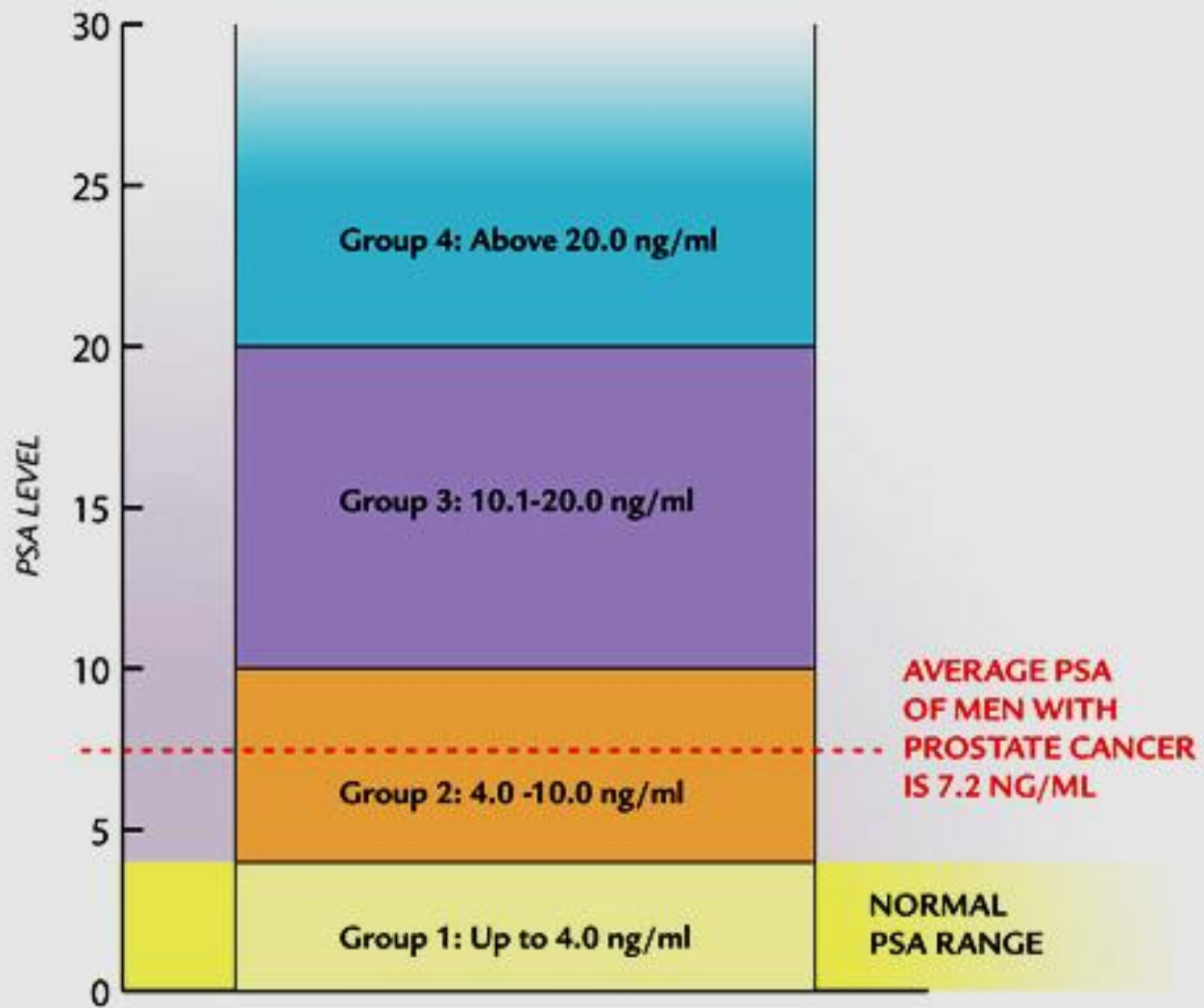
Olsson J<sup>1</sup>, Drott JB, Laurantzon L, Laurantzon O, Bergh A, Elgh F.

### **Author information**

#### **Abstract**

Chronic inflammation in the prostate, seen as infiltration of inflammatory cells into the prostate gland in histological samples, affects approximately half the male population without indication of prostate disease, and is almost ubiquitous in patients diagnosed with benign prostate hyperplasia and cancer. Several studies have demonstrated the gram-positive bacterium *Propionibacterium acnes* to be frequently present in prostate tissue from men suffering from prostate disease. *P. acnes* has been shown to be associated with histological inflammation in human prostatectomy specimens, and also to induce strong inflammatory response in prostate-derived tissue culture models. The present

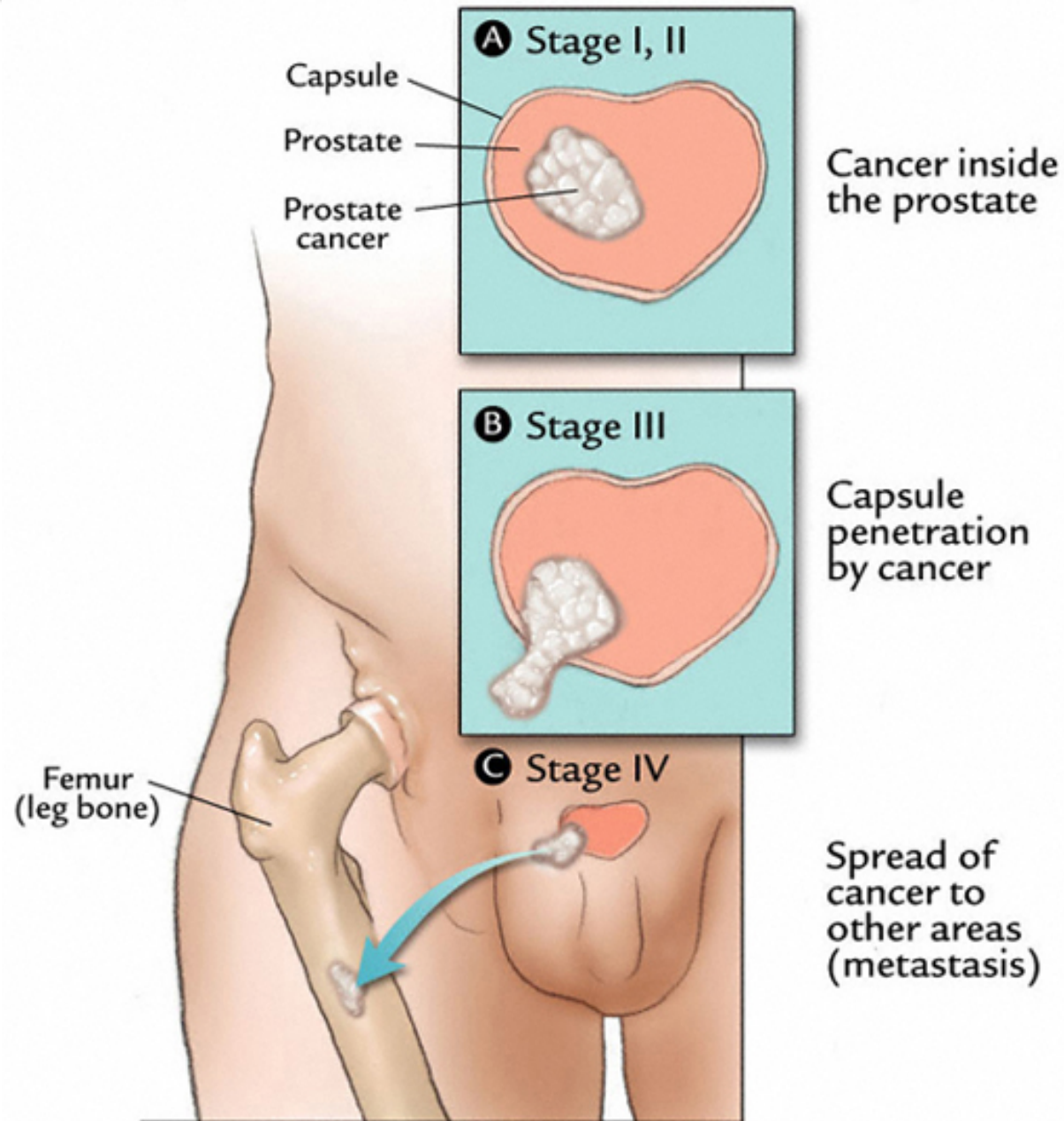
# Prostate Specific Antigen: PSA



## PSA Groups

Men with prostate cancer are classified into four groups based on PSA level.

# Metastasis of Prostate Cancer



# PSA And Chance of Microscopic Penetration

| <b>PSA</b>              | <b>Chance of Microscopic<br/>Capsule Penetration<br/>(Cancer Cell Leakage)</b> |
|-------------------------|--------------------------------------------------------------------------------|
| Up to 4.0 ng/ml.....    | 10 - 72%                                                                       |
| 4.1 – 10.0 ng/ml .....  | 20 - 87%                                                                       |
| 10.1 ng/ml or more..... | 38 - 94%                                                                       |

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## Final Recommendation Statement

### Prostate Cancer: Screening

*Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.*

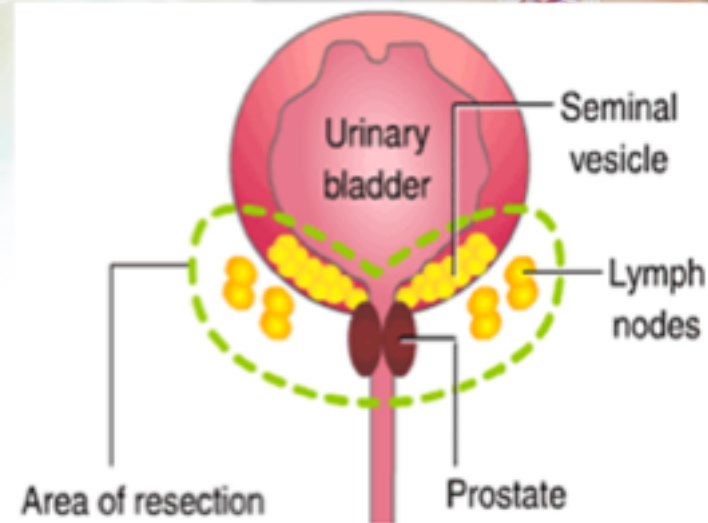
#### Recommendation Summary

| Population              | Recommendation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Grade<br>(What's This?) |
|-------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| Men aged 55 to 69 years | For men aged 55 to 69 years, the decision to undergo periodic prostate-specific antigen (PSA)-based screening for prostate cancer should be an individual one. Before deciding whether to be screened, men should have an opportunity to discuss the potential benefits and harms of screening with their clinician and to incorporate their values and preferences in the decision. Screening offers a small potential benefit of reducing the chance of death from prostate cancer in some men. However, many men will experience potential harms of screening, including false-positive results that require additional testing and possible prostate biopsy; overdiagnosis and overtreatment; and treatment complications, such as incontinence and erectile dysfunction. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of family history, race/ethnicity, comorbid medical conditions, patient values about the benefits and harms of screening and treatment-specific outcomes, and other health needs. Clinicians should not screen men who do not express a preference for screening. | C                       |
| Men 70 years and older  | The USPSTF recommends against PSA-based screening for prostate cancer in men 70 years and older.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | D                       |

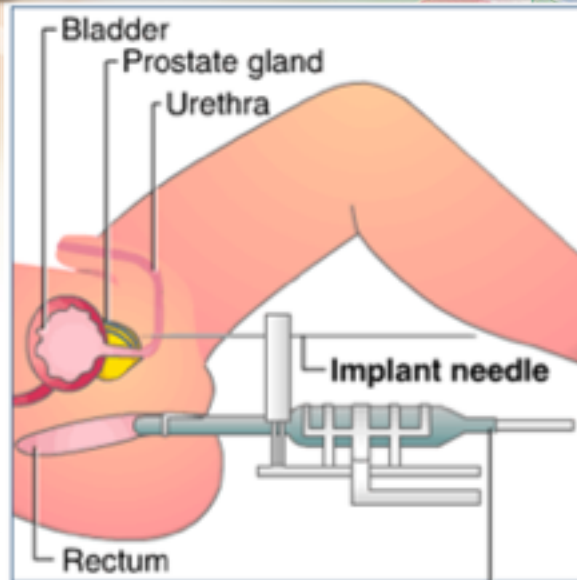
# Treatment

- ❑ **Watchful waiting** —not treated immediately; monitor status through regular examinations and PSA tests — typically reserved for non-aggressive tumor in elderly men too ill to tolerate radiation or surgery, limited life expectancies.
- ❑ **Radiation therapy** — In external-beam, 5-7 weeks. **Brachytherapy**, radioactive seeds or pellets are implanted directly inside the prostate. Side effects can include impotence, diarrhea, rectal bleeding and incontinence.
- ❑ **Surgery** — Radical prostatectomy removes the entire prostate gland, seminal vesicles and sometimes the nearby pelvic lymph nodes. Side effects include incontinence and impotence.

# Treating Prostate Cancer

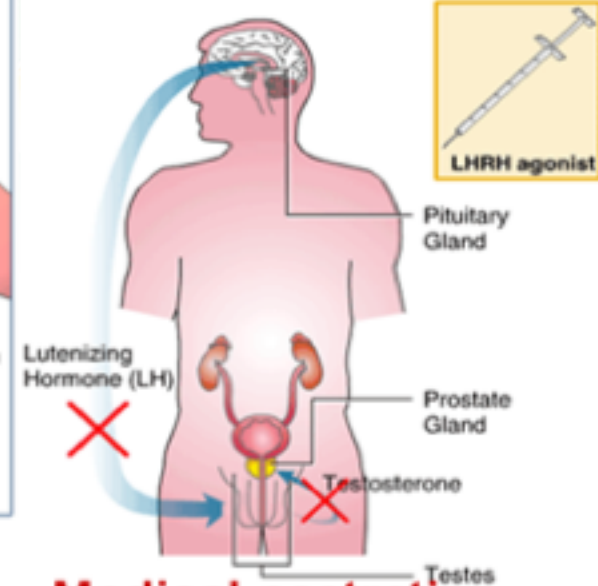


**Surgery**

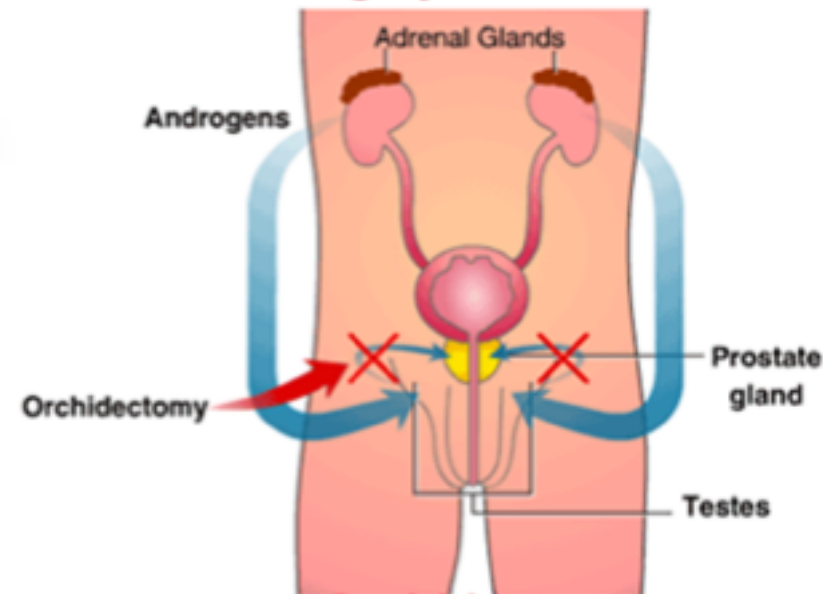


**Endorectal ultrasound probe**  
**Brachytherapy**

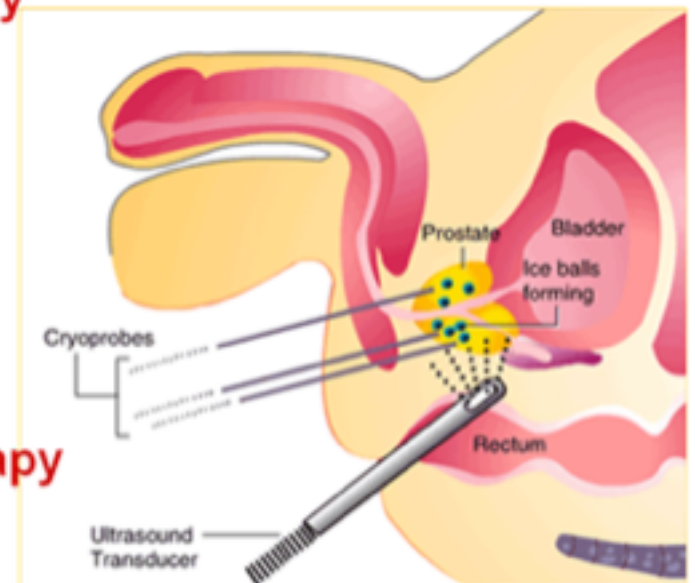
**LHRH Agonists**



**Medical-castration**



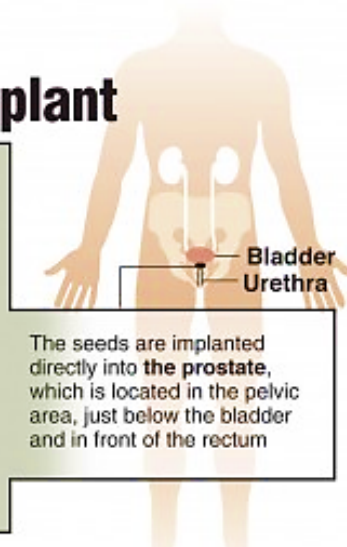
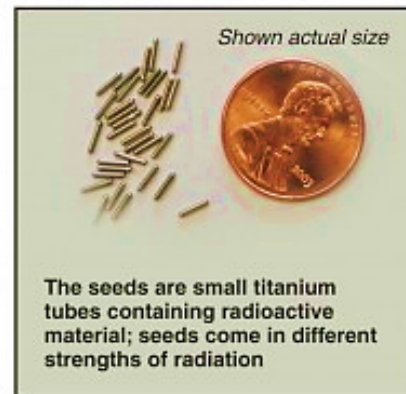
**Orchidectomy**



**Cryotherapy**

# Prostate brachytherapy: Permanent radioactive seed implant

*During this treatment for prostate cancer, a doctor inserts hollow needles into the prostate, while watching ultrasound images. A template grid is used for accurate needle placement. Fifty to 100 permanent radioactive seeds are implanted; they emit low-level radiation for several months, destroying the cancer.*



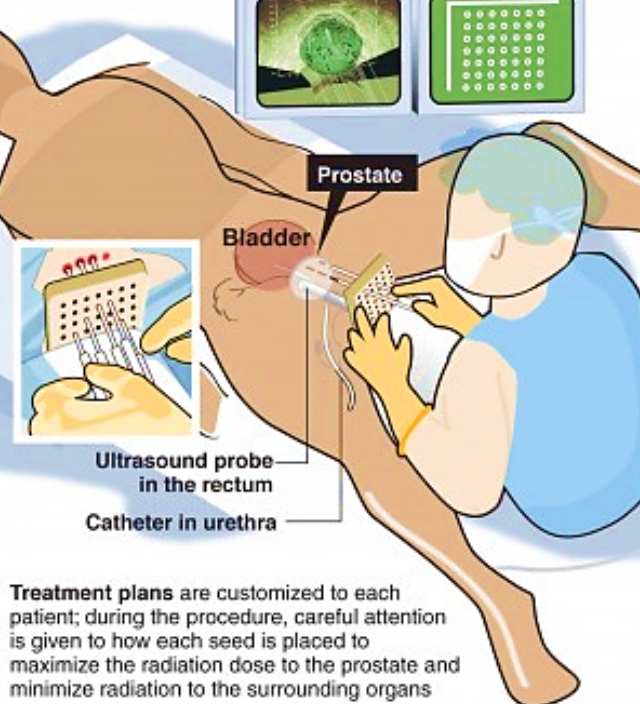
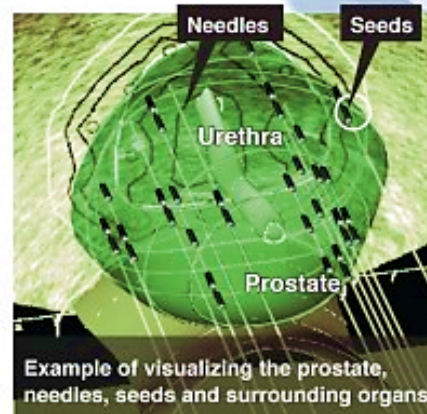
## The procedure

A team, including a radiation oncologist, urologist and a medical physicist, performs the procedure

**Under anesthesia**, the patient is put in a position so the doctor has access to the prostate, which is located directly behind the perineum, the patch of skin between the legs

**The prostate is visualized** using ultrasound; treatment planning software determines placement and location of seeds; the needles are pushed through a grid to align them properly

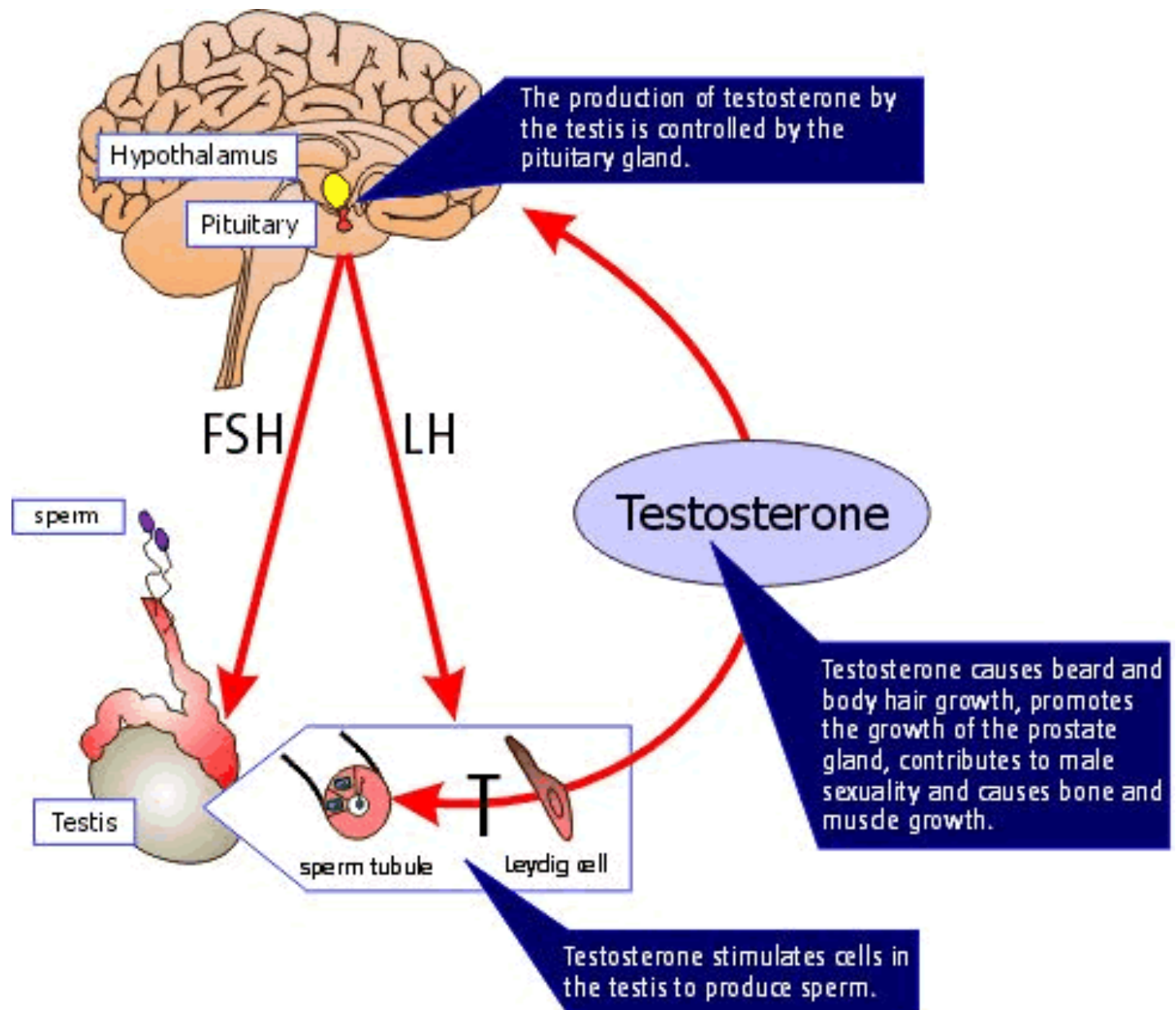
A grid on the screen corresponds to the template grid for implant needles



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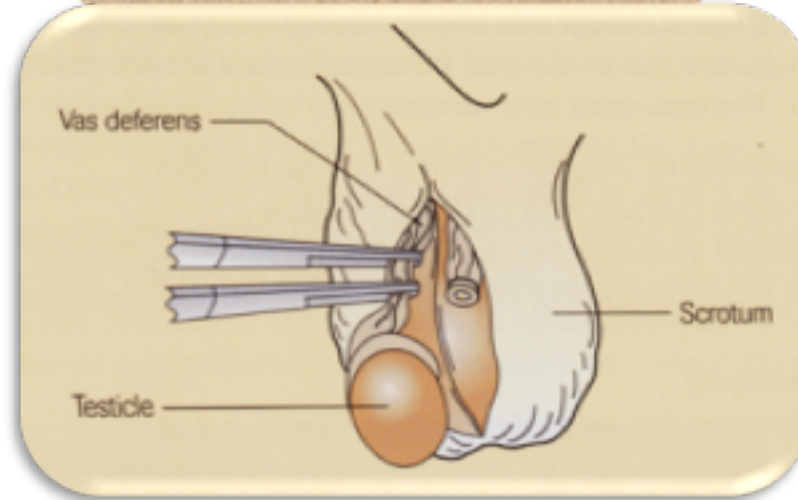
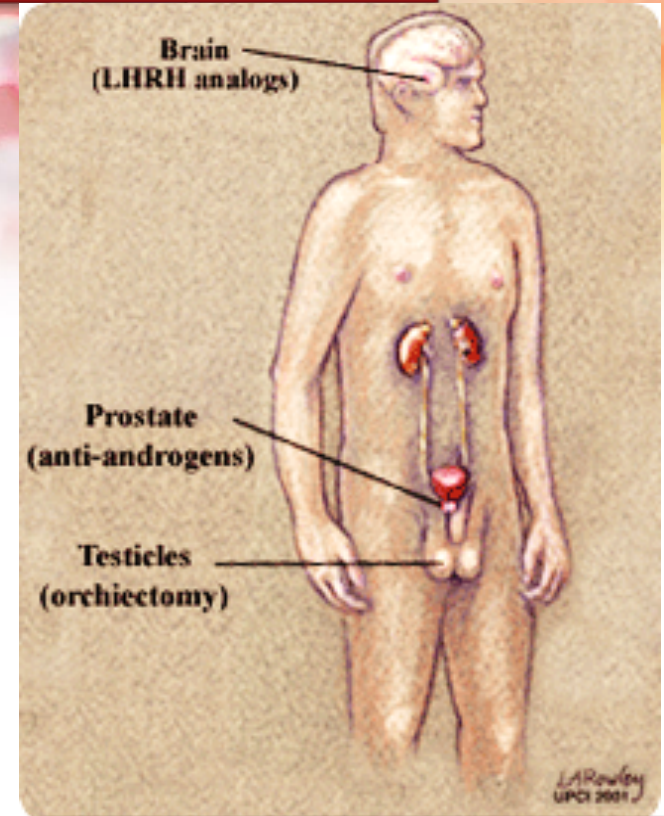
Source: Dr. Adam Dicker, Thomas Jefferson University;  
Dr. Gregory S. Merrick, Wheeling Hospital, Wheeling, W. Va.  
Graphic: Cynthia Greer and Stephanie Cope, The Philadelphia Inquirer

# Hormones and Prostate Cancer

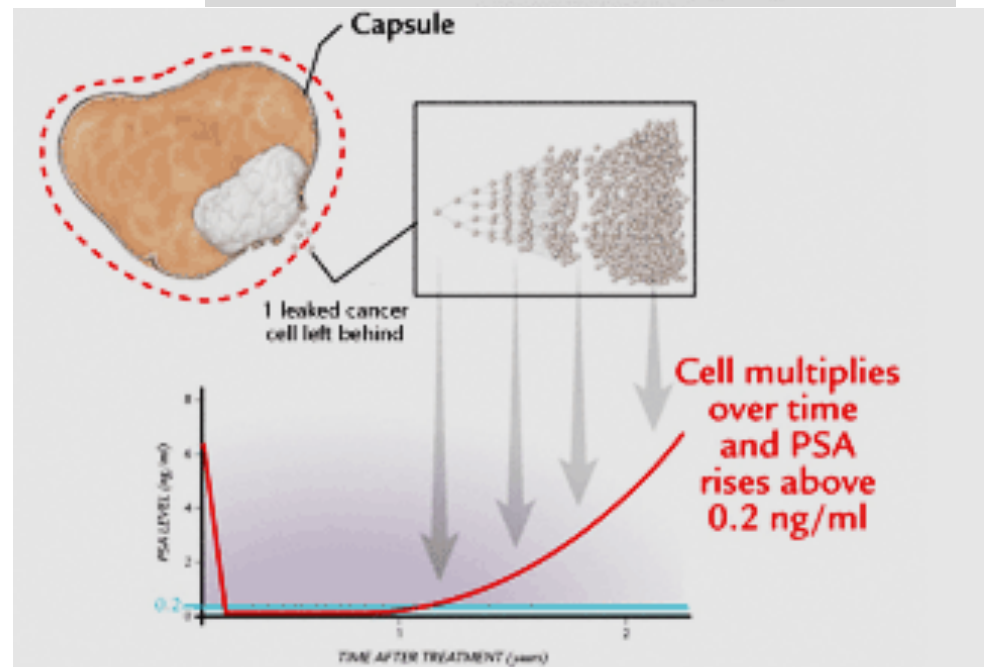
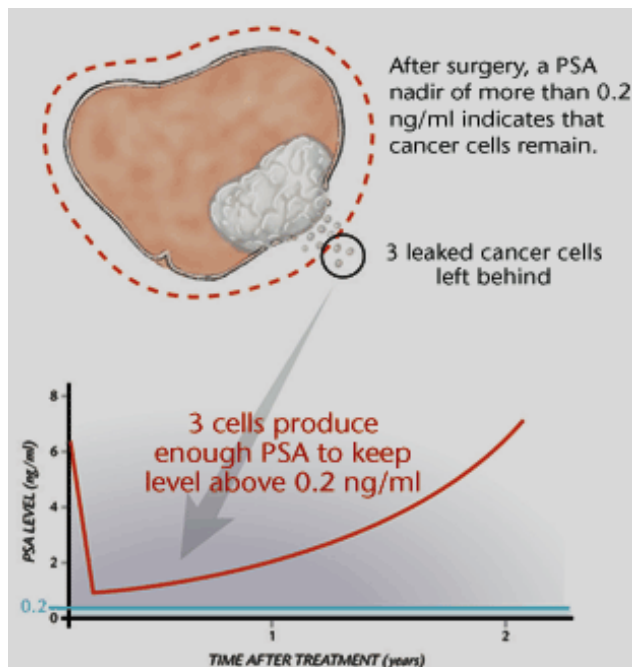
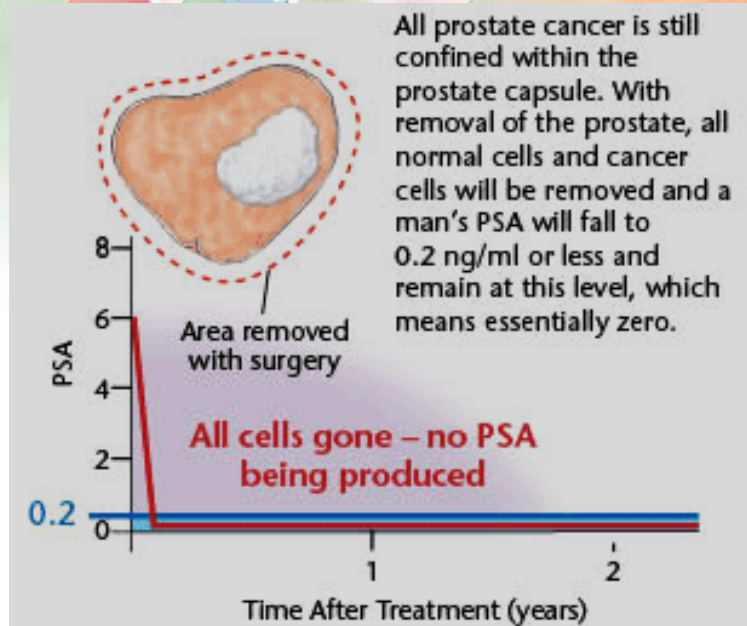
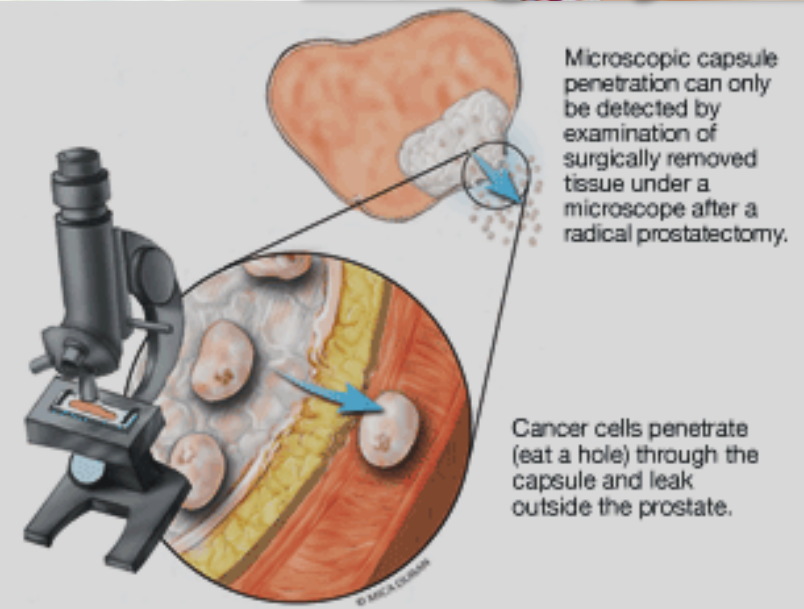


# Hormone Treatment

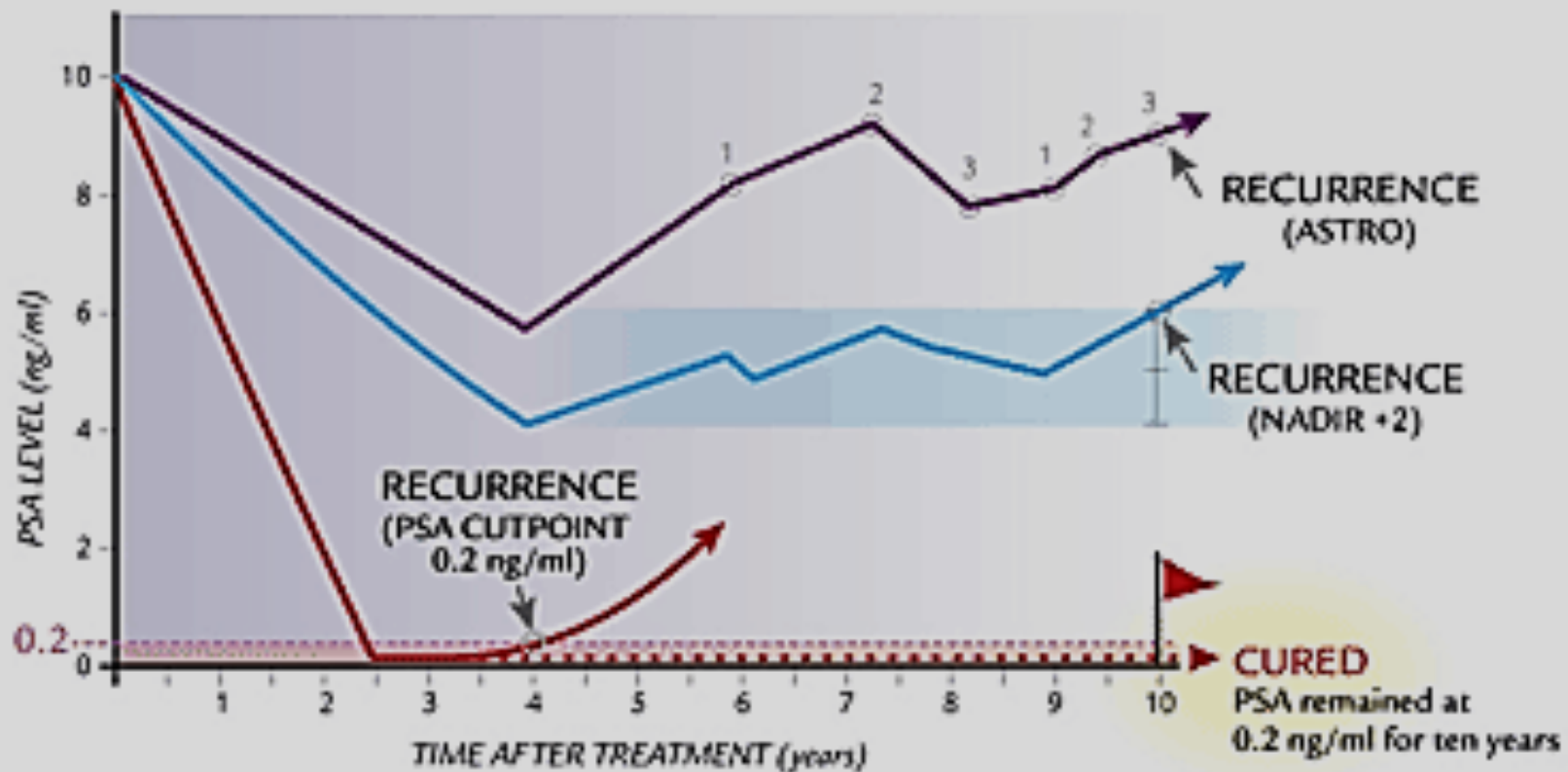
- ❑ Prostate cancer is *hormone-sensitive* or *hormone-dependent*; growth depends on androgens
- ❑ The goal of hormone therapy is to dramatically reduce testosterone levels in the blood, slowing the growth rate of prostate cancer
- ❑ Hormone therapy is the primary treatment for metastatic prostate cancer
- ❑ hormone therapy can shrink tumors and may stop or limit spread of prostate cancer for many years
- ❑ Orchiectomy and luteinizing hormone-releasing hormone (LHRH) analogs & anti-androgens



# Surgery and PSA Monitoring



# How do you determine if a man is cured of prostate cancer?



## DEFINITIONS OF RECURRENCE

- PSA Cutpoint: PSA rises above 0.2
- Nadir +2: PSA rises 2.0 above the lowest level achieved
- ASTRO: PSA rises three consecutive times above the lowest level achieved

# Treat or wait and watch?

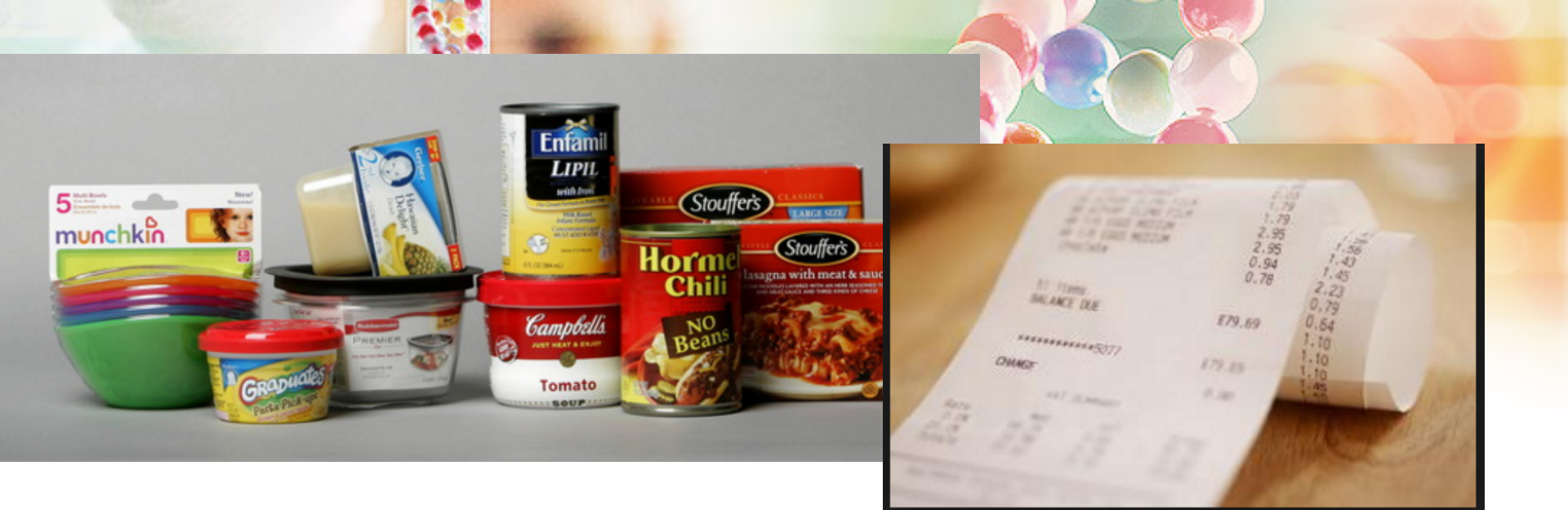


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## Radical Prostatectomy or Watchful Waiting in Early Prostate Cancer

### RESULTS

During 23.2 years of follow-up, 200 of 347 men in the surgery group and 247 of the 348 men in the watchful-waiting group died. Of the deaths, 63 in the surgery group and 99 in the watchful-waiting group were due to prostate cancer; the relative risk was 0.56 (95% confidence interval [CI], 0.41 to 0.77;  $P=0.001$ ), and the absolute difference was 11.0 percentage points (95% CI, 4.5 to 17.5). The



PLoS One. 2014 Mar 3;9(3):e90332. doi: 10.1371/journal.pone.0090332. eCollection 2014.

## Exposure to bisphenol a correlates with early-onset prostate cancer and promotes centrosome amplification and anchorage-independent growth in vitro.

Tarapore P<sup>1</sup>, Ying J<sup>2</sup>, Ouyang B<sup>1</sup>, Burke B<sup>3</sup>, Bracken B<sup>3</sup>, Ho SM<sup>4</sup>.

### Author information

### Abstract

Human exposure to bisphenol A (BPA) is ubiquitous. Animal studies found that BPA contributes to development of prostate cancer, but human data are scarce. Our study examined the association between urinary BPA levels and Prostate cancer and assessed the effects of BPA on induction of centrosome abnormalities as an underlying mechanism promoting prostate carcinogenesis. The study, involving 60 urology patients, found higher levels of urinary BPA (creatinine-adjusted) in Prostate cancer patients (5.74  $\mu\text{g/g}$  [95% CI; 2.63, 12.51]) than in non-Prostate cancer patients (1.43  $\mu\text{g/g}$  [95% CI; 0.70, 2.88]) ( $p=0.012$ ). The difference was even more significant in patients <65 years old.



*Cancer Epidemiol.* 2014 Aug;38(4):329-38. doi: 10.1016/j.canep.2014.06.002. Epub 2014 Jun 28.

## **Sexually transmitted infections and prostate cancer risk: a systematic review and meta-analysis.**

Caini S<sup>1</sup>, Gandini S<sup>2</sup>, Dudas M<sup>3</sup>, Bremer V<sup>4</sup>, Severi E<sup>5</sup>, Gherasim A<sup>6</sup>.

### **Author information**

### **Abstract**

Prostate cancer (PC) is the second most incident cancer and the sixth cause of death by cancer in men worldwide. Despite extensive research efforts, no modifiable risk factors have been consistently identified for PC risk. A number of studies have focused on possible relationships between sexually transmitted infections (STIs) and PC. We performed a meta-analysis to explore the association between infection caused by *Neisseria gonorrhoeae*, *Treponema pallidum*, *Chlamydia trachomatis*, *Trichomonas vaginalis*, *Ureaplasma urealyticum*, *Mycoplasma hominis*, Herpes Simplex Virus types 1 and 2, Human Herpes Virus 8 and Cytomegalovirus, and PC. We conducted a comprehensive, systematic bibliographic search of medical literature to identify relevant studies. We calculated summary relative risk (SRR) and 95% confidence intervals (CI) for the association between each STI and PC through random effect models. Subgroup, meta-regression and sensitivity analyses were carried out to detect between-study heterogeneity and bias. We included 47 studies published between 1971 and 2011. Men who reported having ever had any STI in lifetime had an increased PC (SRR 1.49, 95% CI 1.19-1.92). We found a significantly increased PC risk in men having had gonorrhoea (SRR 1.20, 95% CI 1.05-1.37). No other single STI was significantly associated with PC. Due to high incidence of both STIs and PC worldwide, prevention of STIs may help preventing a considerable number of PC cases.



J Natl Cancer Inst. 2009 Oct 21;101(20):1406-11. doi: 10.1093/jnci/djp306. Epub 2009 Sep 9.

## Prospective study of *Trichomonas vaginalis* infection and prostate cancer incidence and mortality: Physicians' Health Study.

Stark JR<sup>1</sup>, Judson G, Alderete JF, Mundodi V, Kucknoor AS, Giovannucci EL, Platz EA, Sutcliffe S, Fall K, Kurth T, Ma J, Stampfer MJ, Mucci LA.

### Author information

#### Abstract

**BACKGROUND:** A recent nested case-control study found that the presence of antibodies against *Trichomonas vaginalis*, a common nonviral sexually transmitted infection, was positively associated with subsequent incidence of prostate cancer. We confirmed these findings in an independent population and related serostatus for antibodies against *T vaginalis* to prostate cancer incidence and mortality.

**METHODS:** We conducted a case-control study nested within the Physicians' Health Study that included 673 case subjects with prostate cancer and 673 individually matched control subjects who had available plasma samples. Plasma from blood samples collected at baseline was assayed for antibodies against *T vaginalis* with an enzyme-linked immunosorbent assay. We used conditional logistic regression to estimate the odds ratios (ORs) of incident prostate cancer, extraprostatic prostate cancer, and cancer that would ultimately progress to bony metastases or prostate cancer-specific death.

**RESULTS:** Although not statistically significant, the magnitude of the association between *T vaginalis*-seropositive status and overall prostate cancer risk (OR = 1.23, 95% confidence interval [CI] = 0.94 to 1.61) was similar to that reported previously. Furthermore, a seropositive status was associated with statistically significantly increased risks of extraprostatic prostate cancer (OR = 2.17, 95% CI = 1.08 to 4.37) and of cancer that would ultimately progress to bony metastases or prostate cancer-specific death (OR = 2.69, 95% CI = 1.37 to 5.28).

**CONCLUSIONS:** This large prospective case-control study obtained further support for an association between a seropositive status for antibodies against *T vaginalis* and the risk of prostate cancer, with statistically significant associations identified for the risk of extraprostatic prostate cancer and for clinically relevant, potentially lethal prostate cancer.