

PSA Test – Prostate Specific Antigen Testing

Definition : The **PSA test** is a blood **test** used primarily to screen for prostate cancer.

The **test** measures the amount of **prostate-specific antigen (PSA)** in your blood. **PSA** is a protein produced by both cancerous and noncancerous tissue in the prostate, a small gland that sits below the bladder in men.

What is normal PSA by age?

The use of **age-specific PSA ranges** for the detection of prostate cancer is helpful to avoid unnecessary investigations in older men with larger prostate glands (typically walnut-sized). Median **PSA** value for men **aged** 40 to 49 years is 0.7 ng/mL and for men 50 to 59 years is 0.9 ng/mL.

What is a dangerous PSA level?

The following are some general PSA level guidelines: 0 to 2.5 ng/mL is considered safe. 2.6 to 4 ng/mL is safe in most men but talk with your doctor about other risk factors. 4.0 to 10.0 ng/mL is suspicious and might suggest the possibility of **prostate cancer**. It is associated with a 25% chance of having **prostate** carcinoma. The lowered indicated level is much safe.

PSA Test – Prostate Specific Antigen Testing

Introduction

- The prostate specific antigen (PSA) test is a blood test for prostate cancer screening;
- According to the American Medical Association, 3/4th of US men older than 50 years old have been screened with this PSA test;
- A PSA value >4.0ng/mL is a standard threshold for prostate cancer suggesting further diagnostic investigation (biopsies).

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- ▶ The PSA test is used primarily to screen for prostate cancer. A PSA test measures the amount of prostate-specific antigen (PSA) in your blood. PSA is a protein produced in the prostate, a small gland that sits below a man's bladder.



- ▶ Prostate cancer is the most common nonskin cancer in men, and it's the second leading cause of cancer-related death in men after lung cancer. Early detection may be an important tool in getting appropriate and timely treatment.



- ▶ The PSA test can detect high levels of PSA that may indicate the presence of prostate cancer. However, many other conditions, such as an enlarged or inflamed prostate, can also increase PSA levels.



- ▶ There is a lot of conflicting advice about PSA testing. Ultimately, whether you have a PSA test is something you should decide after discussing it with your doctor, considering your risk factors and weighing your personal preferences.



- ▶ The PSA test is only one tool used to screen for early signs of prostate cancer. Another common screening test, usually done in addition to a PSA test, is a digital rectal exam. In this test, your doctor inserts a lubricated, gloved finger into your rectum to reach the prostate. By feeling or pressing on the prostate, the doctor may be able to judge whether it has abnormal lumps or hard areas.



The US Preventive Service Task Force Statement

- ▶ In October 2011, the USPSTF posted for public comment the draft of its recommendation regarding prostate cancer screening. Since then, Task Force members have read the many comments received and reviewed the most up-to-date evidence.
- ▶ Based on this work, the Task Force concludes that many men are harmed as a result of prostate cancer screening and few, if any, benefit.
- ▶ A better test and better treatment options are needed. Until these are available, the USPSTF has recommended against screening for prostate cancer.



So, Now What?

- ▶ Beginning at the age of 50, all men should discuss their need for prostate screening with their personal physician.
- ▶ Men should not hesitate to ask their physician about the task force statement, and realize that in the absence of a optimal prostate test, your physician and you need to decide what is the best prostate screening for you.

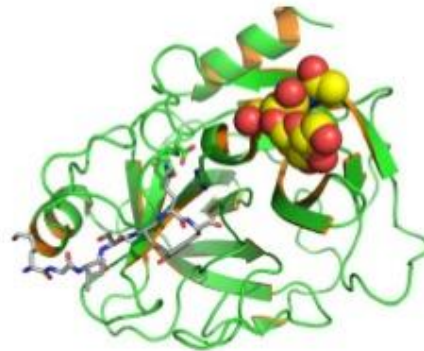


How accurate is this test?

- It depends on the age of the patient;
- The older the patient, the more prevalent prostate cancer is and the more accurate the test is;
- Age-specific prostate cancer prevalence statistics are not readily available. You have to construct them from age-specific incidence rate.

Prostate specific antigen

- kallikrein-3 (hK3) or γ -seminoprotein
- Secreted by epithelial cells of the acini and ducts of prostate gland
- Glycoprotein enzyme that liquefies semen
- Normally present in the blood at low levels.



MEASUREMENT OF PROSTATE-SPECIFIC ANTIGEN IN SERUM AS A SCREENING TEST FOR PROSTATE CANCER

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- **Aim:** evaluate usefulness of PSA in the detection and staging of CaP
- **Methods:** Measured serum PSA concentrations in 1653 men ≥ 50 years old. Those with PSA ≥ 4.0 underwent DRE and US. TRUS bx was performed in men with abnormal DRE, US or both. Results were compared with 300 men who underwent bx because of symptoms or abnormal DRE.

Table 1. Serum PSA Concentrations and the Incidence of Cancer as a Function of Age in 1653 Men in the Study Group and 235 Men in the Comparison Group.*

Group/Age (yr)	No. of Men (% of Total)	Serum PSA Level (ug per Liter)					
		<4.0		4.0-9.9†		≥10.0	
		no. (%)	no. (%) with cancer‡	no. (%)	no. with cancer‡ no. with biopsy (%§)	no. (%)	no. with cancer‡ no. with biopsy (%§)
Study group							
50-59	629 (38)	613 (97)	—	12 (2)	2/11 (18)	4 (1)	1/3 (33)
60-69	737 (45)	669 (91)	—	53 (7)	8/40 (20)	15 (2)	12/15 (80)
70-79	264 (16)	215 (81)	—	39 (15)	9/32 (28)	10 (4)	4/8 (50)
80-89	23 (1)	19 (83)	—	3 (13)	0/2 (0)	1 (4)	1/1 (100)
All	1653	1516 (92)	—	107 (6)	19/85 (22)	30 (2)	18/27 (67)
Comparison group							
50-59	46 (20)	27 (59)	0 (0)	13 (28)	0 (0)	6 (13)	4 (67)
60-69	93 (40)	51 (55)	6 (12)	37 (40)	12 (32)	5 (5)	3 (60)
70-79	80 (34)	37 (46)	7 (19)	21 (26)	5 (24)	22 (28)	13 (59)
80-89	16 (7)	1 (6)	0 (0)	3 (19)	2 (67)	12 (75)	9 (75)
All	235	116 (49)	13 (11)	74 (32)	19 (26)	45 (19)	29 (64)

- PSA level 4.0-9.9 ug/L in 6.5% (n=107) with 22% of those found to have CaP
- PSA level ≥10 ug/L in 1.8% (n=33) with 67% of those found to have CaP

What is a “normal” PSA?

- <4.0 ng/mL →
 - Consensus based on early studies from 1980s suggesting high sensitivity
 - Actually sensitivity 21-50% and specificity 60-70%
 - 10-15% of men in their initial PSA screening will have PSA>4 and be recommended to undergo biopsy (Crawford, Prostate, 1999)
 - In 2950 men with PSA<4 in the PCPT control arm, 15% had prostate cancer diagnosed on biopsy (Thompson, NEJM, 2004)
 - Annual variations in PSA (Eastham, JAMA, 2003)

Causes of elevated PSA

- Prostate cancer
- Benign prostatic hyperplasia
 - Prostate size accounts for 23% of the variance in serum PSA (*Nadler, J Urol, 1995*)
 - PSA density may account for prostate size
 - Serum PSA divided by prostate volume to give a PSA density
 - Higher PSA density values (>0.15 ng/mL/cc) are more suggestive of CaP while lower values are more suggestive of BPH (*Benson, J Urol, 1992*)

Causes of elevated PSA

- Prostate cancer
- Benign prostatic hyperplasia
- Prostate inflammation / infection
- Prostate manipulation
 - After DRE, men with PSA <20 had insignificant changes in PSA (*Crawford, JAMA, 1992*)
 - After prostate massage, PSA changed by 3.68 ± 0.61 ng/mL (*Tarhan, Urology, 2005*)
 - Variable PSA changes after cysto (+0.1 ng/mL), prostate bx (+7.9 ng/mL), or TURP (+5.9 ng/mL) (*Oesterling, Urology, 1993*)

Causes of elevated PSA

- Prostate cancer
- Benign prostatic hyperplasia
- Prostate inflammation / infection
 - Prostatitis +/- active infection can elevate PSA (*Nadler, J Urol, 1995*)
 - Reduction in PSA levels can be expected if prostatitis with infection is responsible; PSA will not uniformly normalize without infection (*Greiman, J Urol, 2016*)
 - "Don't treat an elevated PSA with antibiotics for patients not experiencing other symptoms." –AUA Choosing Wisely campaign

Causes of elevated PSA

- Prostate cancer
- Benign prostatic hyperplasia
- Prostate inflammation / infection
- Prostate manipulation
- Sexual activity
 - Mild elevation in PSA (0.4-0.5 ng/mL) for 48-72 hours after ejaculation (*Tchetgen, Urology, 1996*)

PSA Test Accuracy across Prevalence Rates

PSA test

Sensitivity (true positive rate)	20.5%
Specificity (true negative rate)	93.8%

Source: Operating Characteristics of Prostate-Specific Antigen in Men

Age	Avg. prevalence out of 100,000	Avg. prevalence in %	A True positive	C False negative	D True negative	B False positive	A/(A + B) Accuracy positive	C/(C+D) Accuracy negative
45-49	176	0.2%	36	140	93,635	6,189	0.6%	99.9%
50-54	669	0.7%	137	532	93,172	6,159	2.2%	99.4%
55-59	1,911	1.9%	392	1,519	92,008	6,082	6.1%	98.4%
60-64	4,258	4.3%	873	3,385	89,806	5,936	12.8%	96.4%
65-69	7,951	8.0%	1,630	6,321	86,342	5,707	22.2%	93.2%
70-74	12,494	12.5%	2,561	9,932	82,081	5,425	32.1%	89.2%
75-79	17,129	17.1%	3,511	13,617	77,733	5,138	40.6%	85.1%
80-84	21,239	21.2%	4,354	16,885	73,878	4,883	47.1%	81.4%
85	23,361	23.4%	4,789	18,572	71,887	4,752	50.2%	79.5%

Using the same Bayesian logic as on the previous page, we can see how the test accuracy when positive decreases very quickly when the age-specific prevalence drops and vice versa.