Meta-Analysis of Prostate-Specific Antigen and Digital Rectal Examination as Screening Tests for Prostate Carcinoma

Kishor Mistry, MD, PhD, and Greg Cable, PhD

Background: **Physicians commonly screen for prostate cancer by using prostate-specific antigen (PSA) and digital rectal examination (DRE). The usefulness of these screening mechanisms is not well established, however. A meta-analysis of PSA and DRE to detect prostate carcinoma was conducted with a focus on sensitivity, specificity, and positive predictive value.**

Methods: **A literature search of OVID database (1966 to November 1999) using the medical subject headings "prostate-specific antigen" and "mass screening," as well as "prostate carcinoma," was performed. Thirteen articles were selected for the meta-analysis in this study. Most studies included asymptomatic men older than 50 years from various countries. Pooled results were calculated from the individual reports for sensitivity, specificity, and positive predictive value for PSA and DRE based on biopsy result as the reference standard.**

Results: **The overall detection rate of prostate carcinoma was 1.8% based on a positive biopsy. Of the prostate carcinoma detected, 83.4% was localized. The pooled sensitivity, specificity, and positive predictive value for PSA were 72.1%, 93.2% and 25.1%, respectively; and for DRE were 53.2%, 83.6% and 17.8%, respectively.**

Conclusions: **There were two major outcomes of this meta-analysis. One was the potential for detecting early-stage prostate cancer with these screening tests, because 83.4% of total cancers detected were localized. The second important outcome was that the overall sensitivity, specificity, and positive predictive value for PSA were higher than those for DRE when used as a screening tool to detect prostate cancer. When a patient has abnormal findings using PSA and DRE, the chance of cancer is 1 in 4 or 5. Conversely, when findings from PSA and DRE are normal, the chance of missing a cancer is about 10%.**
(J Am Board Fam Pract 2003;16:95–101.)

In most industrialized countries, prostate cancer is the most common cancer among men after skin cancer. A recent survey in United States showed that about 198,100 new cases of prostate cancer are detected every year, or 29% of all the diagnosed cancers in men, with about 39,200 deaths in 1998.[1] One in 10 men in United States will have prostate cancer diagnosed in his lifetime.[2] At the time prostate cancer is first diagnosed, in two thirds of the men the cancer has spread beyond the prostate.[3] Reviews of prostate cancer risk factors have not found major environmental risk factors amenable to primary prevention measures.[2] A slight increase in prostate cancer has been reported with high consumption of meat, dairy products, and fats.[4] Hence, prevention is not currently feasible. In turn, considerable interest exists in screening as a potential approach to control prostate cancer.[5]

Since Kuriyama et al in 1980[6] developed an assay measuring prostate-specific antigen (PSA) in human serum, this antigen has become the most commonly used tumor marker for prostate cancer. PSA is a 33-kd glycoprotein consisting of 240 amino acids. It is a serine protease secreted by prostate into semen, where it causes lysis of seminal coagulum. PSA in blood occurs in three forms: free PSA, PSA complexed with α1-antichymotrypsin, and PSA complexed with β2-macroglobulin.[7]

Digital rectal examination (DRE) is another test commonly used to screen for prostate carcinoma. Although DRE has not been found to be effective in preventing metastatic prostate cancer or death

Submitted, revised, 22 May 2002.
From Family Practice (KM), Overlook Hospital, Summit, NJ, and the Atlantic Health System Quality Institute (GC), Florham Park, NJ. Address reprint requests to Kishor Mistry, MD, PhD, 36 Patton Dr, Bloomfield, NJ 07003.

J Am Board Fam Pract: first published as 10.3122/jabfm.16.2.95 on 1 March 2003. Downloaded from http://www.jabfm.org/ on 19 May 2025 by guest. Protected by copyright.

from prostate cancer in a case-control study and a quasi-cohort study, DRE does detect some prostate cancers that are missed by PSA screening.[2]

Prostate cancer mortality has recently decreased by 6% after peaking in 1990s. It is hard to attribute this decrease to PSA screening implementation, because the effect is too proximate to the use of screening method. Also, there is no correlation between this drop in mortality and the intensity of the PSA screening conducted in various regions. Studies have shown that men with organ-confined prostate cancer managed with radical prostatectomy survive as long as men of similar age who never had prostate cancer.[8] Many studies have failed to show, however, any improvement in mortality or morbidity from screening for prostate cancer by whatever diagnostic test.[9–12]

Screening for prostate cancer remains a controversial issue. Even the American Cancer Society has modified its position on men eligible for prostate cancer screening from "should undergo digital rectal examination and PSA testing annually" to "recommends that both the PSA testing and digital examination be offered annually." American Academy of Family Physician and US Preventive Services task Force do not recommend routine screening in low-risk patients.[13]

This study is a meta-analysis of existing research of PSA and DRE as screening tests for detecting prostate carcinoma. The data from this study should help primary care physicians decide whether to use PSA and DRE to screen for prostate carcinoma.

Methods

Study Selection

A literature search of OVID database (1966 to November 1999) using the medical subject headings "prostate-specific antigen" and "mass screening," as well as "prostate carcinoma," was performed. The search was restricted to English-language studies and conducted in human subjects. The inclusion criteria for the meta-analysis were (1) studies in which data were available or could be calculated for percentage of population with abnormal PSA, DRE, and biopsy findings, or sensitivity and specificity for PSA and DRE testing; (2) studies that included biopsy as a reference standard to prove prostate carcinoma; and (3) subjects who were asymptomatic for prostate carcinoma. Letters without data were not included. In these studies biopsies were performed if PSA levels or DRE findings were abnormal. A total of 83 articles were found and reviewed to select 13 articles.[3,5,7,14–23]

Data Abstraction

Data were collected from the published studies only, without contacting the authors for additional information. The following parameters were collected or calculated from these studies:

1. Detection rate = population with prostate carcinoma/total population screened × 100
2. Percentage of local prostate cancer = localized prostate carcinoma/total prostate carcinoma ×100
3. Biopsy/prostate cancer = ratio of total biopsies performed to actual number of positive biopsies detected
4. Percentage of abnormal PSA = population with greater than 4 ng/mL PSA as a percentage of total population screened
5. Percentage of abnormal DRE = population with abnormal prostate examination on palpation (nodule, asymmetry, hard) as a percentage of total population screened
6. Positive predictive value of PSA (or DRE) = percentage of positive biopsies/total positive PSA (or DRE)
7. PSA (or DRE) sensitivity = percentage of abnormal PSA (or DRE)/total positive biopsies
8. PSA (or DRE) specificity = percentage of normal PSA (or DRE)/total negative biopsies

Statistical Analysis

Parameter estimates from each study were used to calculate pooled estimates. Pooled estimates were weighted averages constructed using the study sample sizes as weights. In the same manner that disproportionate stratified sampling parameter estimates are adjusted for stratum size, this simple device ensures that the contribution of each study was proportionate to the size of the study and that extreme individual parameter estimates did not result in overestimation or underestimation of the pooled data.[24] The confidence interval for pooled data calculation was 95%.

Results

The data are shown in Tables 1, 2, and 3. In some studies the data on sensitivity, specificity, and pos-

J Am Board Fam Pract: first published as 10.3122/jabfm.16.2.95 on 1 March 2003. Downloaded from http://www.jabfm.org/ on 19 May 2025 by guest. Protected by copyright.

Table 1. Detection Rate and Biopsies Performed to Detect Prostate Carcinoma (PCA).

Reference	Population Size (all males)	Age (years)	Detection Rate (%)	Localized PCA (% of Total)*	Bx/PCA†
Bangma et al[14]	1,726 Netherlands	55–76	3.88	88.06	4.60
Brett[15]	211 Australian	50–79	1.42		3.67
Bretton[16]	1,027 American	40–89	3.80	64.40	5.77
Gustafsson et al[17]	1,782 Swedish	55–70	2.71		5.71
Higashihara et al[7]	701 Japanese	50–92	1.85		8.92
Horninger et al[18]	21,078 Austrian	45–79	0.94		3.95
Horninger et al[18]	21,078 Austrian	40–65	2.77	85.71	4.13
Imai et al[19]	1,680 Japanese	39–89	0.89		8.80
Imai et al[20]	3,276 Japanese	40–89	1.40	60.78	5.52
Jubelirer et al[3]	142 American	50–85		75.00	3.75
Maattanen et al[5]	5,053 Finish	55–75	2.34	90.00	3.80
Reissigl et al[21]	2,272 Austrian	40–65	2.85	86.00	3.97
Stenman et al[22]	7,204 Finish	45–84	0.61		
Tsukamoto et al[23]	1,639 Japanese		1.10		6.39
Pooled results	47,791		1.80	83.40	4.00

*% of local PCA = localized prostate carcinoma/total prostate carcinoma × 100.
†Bx/PCA = total biopsies performed/actual number of positive biopsies.

itive predictive value were published; however, in other studies these were calculated from the original published data. Pooled parameter estimates for measures at the interval or ratio level of measurement could not be calculated without the raw data.

As shown in Table 1, the overall detection rate for prostate carcinoma by biopsy was 1.8%, with a wide range of 0.6% to 3.9%. There was no specific correlation with the country in which the study was conducted. Of the total prostate carcinoma detected using PSA or DRE as screening tests, 83.4% were localized, with a range of 64.4% to 90.0%. The overall ratio of total biopsies performed to actual positive prostate carcinoma detected was 4.0, with a range of 3.7 to 8.9.

Table 2. Positive Predictive Value, Sensitivity, and Specificity of Prostate-Specific Antigen (PSA) as Screening Parameter.

Reference	Population with PSA > 4 ng/mL (%)	Positive Predictive Value (%)	Sensitivity (%)	Specificity (%)
Bangma et al[14]	10.31	30.90		
Brett[15]	9.50		66.67	18.00
Bretton[16]	13.00	27.91	92.31	
Gustafsson et al[17]	17.17	17.00	80.00	
Higashihara et al[7]	11.27	24.00	92.30	63.10
Horninger et al[18]	8.88	25.32		
Horninger et al[18]	12.50	22.18		
Imai et al[19]	4.46	27.50	73.33	99.75
Imai et al[20]	5.13	45.10	80.40	
Jubelirer et al[3]	12.60	30.00	100.00	100.00
Maattanen et al[5]	8.47	27.00		
Reissigl et al[21]	10.74	18.00		
Stenman et al[22]		57.00	97.00	
Tsukamoto et al[23]	4.30	23.20	88.90	
Pooled results	10.10	25.10	72.10	93.20

Positive predictive value of PSA = percent of positive biopsies/total positive PSA.

J Am Board Fam Pract: first published as 10.3122/jabfm.16.2.95 on 1 March 2003. Downloaded from http://www.jabfm.org/ on 19 May 2025 by guest. Protected by copyright.

Table 3. Positive Predictive Value, Sensitivity and Specificity of Digital Rectal Examination (DRE) as a Screening Parameter.

Reference	Population Abnormal (%)	Positive Predictive Value (%)	Sensitivity (%)	Specificity (%)
Bangma et al[14]	6.84	33.06		
Brett[15]	19.00		66.67	18.00
Bretton[16]	7.60			
Gustafsson et al[17]		27.39		
Higashihara et al[7]	19.30	10.60	69.20	26.20
Imai et al[19]	9.41	13.33	53.33	99.54
Imai et al[20]	10.78	17.20	49.00	93.33
Jubelirer et al[3]	14.08	22.22	50.00	50.00
Reissigl et al[21]		5.00		
Tsukamoto et al[23]	4.21			
Pooled results	5.00	17.80	53.20	83.60

Positive predictive value of DRE = percent of positive biopsies/total positive DRE.

The positive predictive value, sensitivity, and specificity values for PSA are shown in Table 2. A total of 10.1% of the population was positive for PSA > 4 ng/mL, with a range of 4.3 to 17.2 ng/mL. The positive predictive value was 25.1%, with a range of 17.0% to 57.0%. The sensitivity of PSA in detecting prostate carcinoma was 72.1%, with a range of 66.7% to 100.0%. The specificity of PSA in the detection of prostate carcinoma was 93.2%, with a range of 63.1% to 100.0%.

The data on positive predictive value, sensitivity, and specificity of DRE are shown in Table 3. Overall, 5.0% of the population had abnormal findings on DRE, ranging between 4.2% to 19.3%. The positive predictive value for DRE in detecting prostate carcinoma was only 17.8%, with a range of 5.0% to 33.1%. The sensitivity of DRE in detecting prostate carcinoma was 53.2%, with a range of 49.0% to 69.2%. The overall specificity of DRE was 83.6%, with a wide range of 18% to 99.5%.

Discussion

There were two major outcomes of this meta-analysis. One was the potential for detecting early-stage prostate cancer with these screening tests, because 83.4% of total cancers detected was localized. The second important outcome was with the comparison of PSA and DRE as screening tools to detect prostate cancer. The overall sensitivity, specificity, and positive predictive value for PSA were 72.1%, 93.2% and 25.1%, respectively; and those for DRE were 53.2%, 83.6% and 17.8%, respectively. When a patient has abnormal PSA levels or DRE findings, the chance of having cancer is 1 in 4 or 5; conversely, when PSA levels or findings on DRE are normal, the chance of missing the cancer is about 10%.

There are two major limitations of the studies available for current meta-analysis. The most serious flaw is that these studies lack a control group that had no screening or treatment.[25] This limitation is not unique to prostate carcinoma studies. For many clinical studies it would be unethical to observe patients without providing the current standards of screening and treatment. The other limitation was a lack of biopsy results (the extant reference standard) for all the participating patients, specially those with normal PSA levels and DRE findings, because of the invasiveness of this test. As a result, all specificity, sensitivity, and positive predictive values reported in the published studies are potentially biased by the effect of aggressiveness in performing the biopsies and the variations in the determination of PSA levels and DRE findings. This point is well illustrated by the reported studies using a lower cutoff value of abnormal PSA levels. Two studies[26,27] show that of a total population with prostate carcinoma, 14% have a PSA level of less than 3 ng/mL, 23% to 24% have a PSA level of 3 to 4 ng/mL, and 62% have a PSA level of more than 4 ng/mL. By using a currently accepted cutoff level of more than 4 ng/mL, we are able to detect 62% of prostate cancers,

J Am Board Fam Pract: first published as 10.3122/jabfm.16.2.95 on 1 March 2003. Downloaded from http://www.jabfm.org/ on 19 May 2025 by guest. Protected by copyright.

because 38% cancer patients have PSA levels of less than 4 ng/mL.

Criteria for a clinically useful screening test are as follows[28]: (1) the disease must constitute a serious public health problem; (2) the disease must be able to be diagnosed during an asymptomatic, localized phase; (3) the screening test must have appropriate sensitivity, specificity, and predictive value; (4) the potential for cure must be greater among patients with prostate cancer detected by screening; and (5) improved outcomes related to screening must be shown. After these criteria are satisfied, the cost-effectiveness of the screening program must also be justified.

The importance of prostate cancer as a public health problem and that it can be diagnosed during an asymptomatic, localized stage easily satisfy using PSA and DRE as screening tools for the first two of the above-listed criteria; however, there are no clear answers for the remaining criteria.

An autopsy study of Detroit men found unsuspected prostate cancers in 30% of men in their 20s through 40s, and in more than one half of men older than 50 years. The prevalence of these unsuspected prostate cancers is frequently estimated to be about 33%.[2] These high rates of unsuspected prostate cancers are in sharp contrast to the 3.64% estimated lifetime risk of dying from prostate cancer, as well as lower pooled data of 1.8% detection rate of prostate carcinoma in the current meta-analysis. Once regional lymph node involvement occurs, the probability of death from prostate cancer is 70%, and 50% of those will die in 2 years. Prostate cancer is a real risk for the aging man, because almost 10% of men older than 50 years are likely to develop clinically serious disease; therefore, it must be detected at an early stage.[29]

It is necessary to increase the sensitivity to detect more cancers at an early stage. In the current study, the sensitivities of PSA and DRE screening tests were 72.1% and 53.2%, respectively. Reducing the PSA cutoff point from 4 ng/mL to 3 ng/mL can increase the sensitivity, but doing so will reduce further the positive predictive value.[30] It is also well known that PSA values for prostate cancer and benign prostate hyperplasia overlap considerably. Between 21% and 47% of men with histologically proven benign prostate hyperplasia have PSA levels of more than 4 ng/mL, and up to 43% of men with prostate cancer will have a PSA level of less than 4 ng/mL. This overlap makes it harder to differentiate benign prostate hyperplasia from prostate carcinoma in the absence of a biopsy. PSA values also increase with age.[17]

With prostate cancer, the risk of overdiagnosis is likely to be much more relevant than with other cancer screening, because in men aged 55 to 60 years, the risk of death from other causes is considerably higher than from prostate cancer. It is estimated that for every patient who dies of prostate cancer, at least 380 others have prostate cancer that cannot be detected clinically.[31,32] The treatment of prostate cancer consists of radical surgery or radiotherapy, and both can cause complications, including a high frequency of sexual impotence, with a relevant frequency of major rectal and urinary dysfunction, as well as 1% to 2% mortality.

In the current study the positive predictive values for PSA and DRE are about 25% and 18%, respectively, which means 1 of 4 or 5 biopsies is unnecessary. Unnecessary biopsies can lead to multiple invasive procedures, anxiety to the patient, related complications, and high cost of health delivery. To reduce further unnecessary procedures, Oesterling[33] has proposed transrectal ultrasonography (TRUS) in the patient with elevated PSA levels but benign DRE findings, then biopsy of visible abnormal lesions only. If findings on the DRE are abnormal, the patient should undergo TRUS and then a biopsy, regardless of the value of PSA. From the rate of growth, a small, organ-confined prostate tumor has been estimated to double in about 4 years. Thus, it will take about 15 years for a 1-mL tumor to become life threatening. It would be more straightforward to say that, until there is evidence about effectiveness of screening in decreasing mortality, based on these growth rates, a man would have at least 15 years of life expectancy to benefit from PSA screening.

The cost burden for prostate cancer screening was calculated by the authors from the current data based on fees charged at a urologist's office in New Jersey. In the United States, there are 30.8 million men older than 50 years who qualify for PSA screening.[34] The cost of screening all these men for PSA would be $3.1 billion. Of this population, 10.1% (approximately 3.1 million) will have PSA levels of more than 4 ng/mL. Assuming all patients with abnormal PSA levels are referred to a urologist for further evaluation, the first visit will cost $275 (for office visit, urine analysis, and culture). The second visit will involve sonography of the

J Am Board Fam Pract: first published as 10.3122/jabfm.16.2.95 on 1 March 2003. Downloaded from http://www.jabfm.org/ on 19 May 2025 by guest. Protected by copyright.

prostate, bladder, pelvis, and renal organs, as well as guided needle biopsy, which can cost $ 2,170 per patient. The total cost of these two visits will exceed $7.6 billion for 3.1 million men. Of 3.1 million biopsies performed, 75%, ie, 2.3 million, will be negative for prostate carcinoma.

We need more data showing improved mortality or morbidity before investing in these expensive procedures. In fact, such an answer might come after the PLCO (prostate, colorectal, and ovarian) screening study. This NIH/European randomized study of 148,000 patients to determine whether screening reduces mortality is expected to provide definitive results in 2005 to 2008.[35]

Conclusions

Our study showed that screening using PSA and DRE can detect 83.4% of prostate cancers in an early, localized stage. In contrast, two thirds of patients with prostate cancer have metastatic disease by the time they become clinically symptomatic. We must improve the sensitivity and specificity of the screening methods by using such tools as age-specific cutoff values, determining free and bound forms of PSA, correcting PSA for benign prostate hyperplasia, and standardizing DRE. More precise screening will permit detection of prostate cancer in a younger population and thus achieve compelling improvements in mortality and morbidity.

Stuart Green, Dr. Thomas Holland, Dr. Susan Kaye and Dr. John Siegal provided the support, help, and advice to carry out this research project.

References

1. Greenelee RT, Hill-Harmon MB, Murry T, Thun M. Cancer statistics, 2001. CA Cancer J Clin 2001; 51:15–36.
2. Godley PA. Prostate cancer screening: promise and peril—a review. Cancer Detect Prev 1999;23:316–24.
3. Jubelirer SJ, Tierney JP, Oliver S, et al. The value of prostatic specific antigen in prostate cancer screening in the community. W Va Med J 1994;90:140–2.
4. Marwick C. Global review of diet and cancer links available. JAMA 1997;278:1650–1.
5. Maattanen L, Auvinen A, Stenman UH, et al. European randomized study of prostate cancer screening: first-year results of the Finnish trial. Br J Cancer 1999;79:1210–4.
6. Kuriyama M, Wang MC, Papsidero LD, et al. Quantitation of prostate-specific antigen in serum by a sensitive enzyme immunoassay. Cancer Res 1980; 40:4658–62.
7. Higashihara E, Nutahara K, Kojima M, et al. Significance of free prostate-specific antigen and gamma-seminoprotein in the screening of prostate cancer. Prostate Suppl 1996;7:40–7.
8. Jewett HJ, Bridge RW, Gray GF Jr, Shelley WM. The palpable nodule of prostatic cancer. Results of 15 years after radical excision. JAMA 1968;203: 403–6.
9. Osterling JE. Early detection of prostate cancer. Decreasing the mortality rate. Minn Med 1996;79: 46–9.
10. Guide to clinical preventive services. 2nd ed. Report of the US Preventive Services Task Force. Baltimore, Md: Williams & Wilkins 1996:119–34.
11. Kramer BS, Brown ML, Prorok PC, Potosky AL, Gohagan JK. Prostate cancer screening: what we know and what we need to know. Ann Intern Med 1993;119:914–23.
12. Woolf HS. Screening for prostate cancer with prostate-specific antigen: an examination of evidence. N Engl J Med 1995;333:1401–5.
13. Zoorob R, Anderson R, Cefalu C, Sidani M. Cancer screening guidelines. Am J Fam Physician 2001;63: 1101–12.
14. Bangma CH, Kranse R, Blijenberg BG, Schroder F. The value of screening tests in the detection of prostate cancer. Part II: retrospective analysis of free/total prostate-specific analysis ratio, age-specific reference ranges, and PSA density. Urology 1995;46: 779–84.
15. Brett TD. An analysis of digital rectal examination and serum-prostate-specific antigen in the early detection of prostate cancer in general practice. Fam Pract 1998;15:529–33.
16. Bretton PR. Prostate-specific antigen and digital rectal examination in screening for prostate cancer: a community-based study. South Med J 1994;87: 720–3.
17. Gustafsson O, Mansour E, Norming U, Carlsson A, Tomblom M, Nyman CR. Prostate-specific antigen (PSA), PSA density and age-adjusted PSA reference values in screening for prostate cancer—a study of a randomly selected population of 2,400 men. Scand J Urol Nephrol 1998;32:373–7.
18. Horninger W, Reissigl A, Rogatsch H, et al. Prostate cancer screening in Tyrol, Australia: experience and results. Eur Urol 1999;35:523–38.
19. Imai K, Ichinose Y, Kubota Y, et al. Clinical significance of prostate specific antigen for early stage prostate cancer detection. Jpn J Clin Oncol 1994;24: 160–5.
20. Imai K, Ichinose Y, Kubota Y, Yamanaka H, Sato J. Diagnostic significance of prostate specific antigen and the development of a mass screening system for prostate cancer. J Urol 1995;154:1085–9.

J Am Board Fam Pract: first published as 10.3122/jabfm.16.2.95 on 1 March 2003. Downloaded from http://www.jabfm.org/ on 19 May 2025 by guest. Protected by copyright.

21. Reissigl A, Pointner J, Horninger W, et al. PSA-based screening for prostate cancer in asymptomatic younger males: pilot study in blood donors. Prostate 1997;30:20–5.
22. Stenman UH, Hakama M, Knekt P, Aromaa A, Teppo L, Leinonen J. Serum concentrations of prostatic specific antigen and its complex with alpha1-antichymotrypsin before diagnosis of prostate cancer. Lancet 1994;344:1594–8.
23. Tsukamoto T, Kumamoto Y, Masumori N, et al. Mass screening for prostate carcinoma: a study in Hokkaido, Japan. Eur Urol 1995;27:177–81.
24. Cochran WG. Sampling techniques. 3rd ed. New York: John Wiley & Sons, 1977:89–96.
25. Woolf HS. Prostate cancer: to screen or not to screen? Commentary. Oncology 1997; 11:451–2.
26. Tornblom M, Norming U, Adolfsson J, et al. Diagnostic value of percent free prostate-specific antigen: retrospective analysis of a population-based screening study with emphasis on men with PSA levels less than 3 ng/mL. Urology 1999;53:945–50.
27. Lodding P, Aus G, Bergdahl S, et al. Characteristics of screening detected prostate cancer in men 50 to 66 years old with 3 to 4 ng/mL prostate-specific antigen. J Urol 1998;159:899–903.
28. Svetec D, Thompson IM. PSA screening—current controversy. Ann Oncol 1998;9:1283–8.
29. Scardino PT. Early detection of prostate cancer. Urol Clin North Am 1989;16:635–55.
30. Rationale for randomised trials of prostate cancer screening. The International Prostate Screening Trial Evaluation Group. Eur J Cancer 1999;35: 262–71.
31. Zappa M, Ciatto S, Bonardi R, Mazzotta A. Overdiagnosis of prostate carcinoma by screening: An estimate based on the results of the Florence screening pilot study. Ann Oncol 1998;9:1297–1300.
32. Brawer MK. prostate-specific antigen. Diagn Clin Testing 1990;28:16–21.
33. Oesterling JE. Prostate-specific antigen. Cancer 1995;75:1795–1804.
34. Statistical abstract of the United States. 17th ed. US Department of Commerce, Economics and Statistics Administration, Bureau of the Census. Lantham, Md: Bernan Press, 1997:15.
35. de Koning HJ, Auvinen A, Berenguer Sanchez AB, et al. Large-scale randomized prostate cancer screening trials: program performances in the European Randomized Screening for Prostate Cancer trial and the Prostate, Lung, Colorectal and Ovary cancer trial. Int J Cancer 2002;97:237–44.

J Am Board Fam Pract: first published as 10.3122/jabfm.16.2.95 on 1 March 2003. Downloaded from http://www.jabfm.org/ on 19 May 2025 by guest. Protected by copyright.