11 · Prostate Cancer

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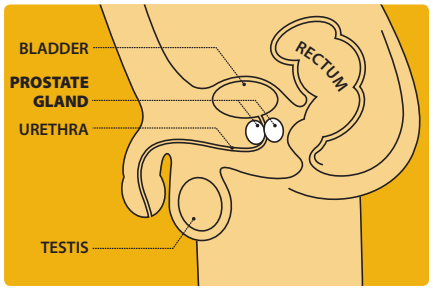
PROSTATE CANCER

The prostate is a small gland located beneath the bladder and in front of the rectum. It surrounds the uretha, which is the tube that empties urine from the bladder (Figure 11.1). Only men have a prostate. It is part of the reproductive system.

PROSTATE CANCER is the uncontrolled growth and invasion of malignant prostate cells. Not all prostate conditions are cancer. Common non-cancerous conditions of the prostate include benign prostatic hyperplasia and prostatitis.

FIGURE **11.1** Prostate Gland



Source: Adapted from diagram provided by US TOO International.

Burden of Prostate Cancer

Prostate cancer is the most commonly diagnosed non-skin cancer and it is the second cause of cancer death after lung cancer in US men. One in six men (17%) is diagnosed with prostate cancer during his lifetime, whereas the lifetime risk of dying from this cancer is only 3%.

DETAILS on the number of prostate cancer cases and rates in the US may be found on these Web sites:

- National Cancer Institute: Surveillance Epidemiology and End Results: http://seer.cancer.gov/.
- American Cancer Society: http://www.cancer.org/.

PROSTATE CANCER is also the most commonly diagnosed cancer in men living in other economically developed countries, although the incidence rate is lower because the PSA test (see Prostate Cancer Early Detection section) is

not routinely used for prostate cancer screening elsewhere. In developing countries, prostate cancer is not as common, but in some countries the rate is increasing. See the American Cancer Society Web site for more information: http://www.cancer.org/.

Similar to US men as a whole, prostate cancer is the most commonly diagnosed non-skin cancer among men in Maryland. In 2006, 3,897 Maryland men were diagnosed with prostate cancer. The age-adjusted prostate cancer incidence rate in Maryland in 2006 is 153.9 per 100,000 men; this rate is similar to the 2006 US SEER age-adjusted prostate cancer incidence rate of 154.0 per 100,000 men (Table 11.1).

Similar to US men as a whole, prostate cancer is the second most common cancer cause of death in Maryland men. In 2006, 531 Maryland men died of prostate cancer. The age-adjusted mortality rate in Maryland in 2006 is 26.3 per 100,000 men; this rate is slightly higher than the US SEER age-adjusted prostate cancer mortality rate of 23.5 per 100,000 men (Table 11.2). Prostate cancer mortality rates have been declining in the US, including in Maryland, since the mid-1990s (Figure 11.2).[1]

Additional details on prostate cancer in Maryland, including rates by county, stage at diagnosis, and survival may be found on this Maryland Department of Health and Mental Hygiene Web site (http://fha.maryland.gov/cancer/surv_data-reports.cfm). Additional details for the US may be found on these Web sites:

- National Cancer Institute: Surveillance Epidemiology and End Results: http://seer.cancer.gov/.
- American Cancer Society: http://www.cancer.org/.

TABLE 11.1 Prostate Cancer Incidence Data by Race, Maryland and the US, 2004-2006

	TOTAL	WHITES	BLACKS	OTHER
2004				
MD New Cases (count)	3,579	2,381	1,051	106
MD Incidence Rate	148.0	132.0	202.7	112.9
US SEER Rate	158.4	151.9	242.7	93.7
2005				
MD New Cases (count)	3,649	2,418	1,042	150
MD Incidence Rate	147.2	131.7	193.3	149.5
US SEER Rate	146.2	140.2	222.5	83.3
2006				
MD New Cases (count)	3,897	2,554	1,032	206
MD Incidence Rate	153.9	137.3	186.3	191.2
US SEER Rate	154.0	147.7	217.5	85.2

Rates are per 100,000 and are age-adjusted to 2000 US standard population.
Total includes cases reported as unknown race.
Sources: Maryland Cancer Registry, 2004m-2006.
NCI SEER*Stat (US SEER 17 rates).

TABLE 11.2 Prostate Cancer Mortality Data by Race, Maryland and the US, 2004-2006

	TOTAL	WHITES	BLACKS	OTHER
2004				
MD Deaths (count)	560	368	186	6
MD Mortality Rate	28.6	24.1	52.9	**
US Mortality Rate	25.4	23.4	55.5	12.1
2005				
MD Deaths (count)	519	328	178	13
MD Mortality Rate	25.7	20.9	47.7	**
US Mortality Rate	24.5	22.6	53.3	11.5
2006				
MD Deaths (count)	531	341	s	<6
MD Mortality Rate	26.3	21.7	51.2	**
US Mortality Rate	23.5	21.7	50.5	10.4

Rates are per 100,000 and are age-adjusted to 2000 US standard population.
**MD mortality rates based on death counts of 0-15 are suppressed per DHMH/CCSC Mortality Data Suppression Policy.
s = Counts are suppressed in CRF Cancer Report tables to prevent disclosure of data in other cell(s).
<6 = MD death counts of 0-5 are suppressed per DHMH/CCSC Mortality Data Suppression Policy.
Source: NCHS Compressed Mortality File in CDC WONDER.

Disparities

Similar to US men as a whole, black or African American men in Maryland are more likely to be diagnosed with prostate cancer (Table 11.1) and more likely to die of prostate cancer (Table 11.2) than white men in Maryland.

IN THE US, the lifetime risk of developing prostate cancer for black or African American men is one in five as opposed to one in six for white men (http://www.cancer.org/). However, when comparing black or African American men in Maryland to the US

as a whole, the prostate cancer incidence rate is lower in Maryland (Table 11.1).

Why black or African American men have a higher risk of prostate cancer is unknown. Fortunately, prostate cancer mortality rates in the US, including in Maryland, have been declining in both black or African American and white men (Figure 11.3 and http://www.cancer.org/).

Prostate Cancer Risk Factors and Primary Prevention

It has long been known that older men, men who have other relatives with prostate cancer, and black or African American men (including other men of African ancestry) have a higher risk of prostate cancer compared to white men.

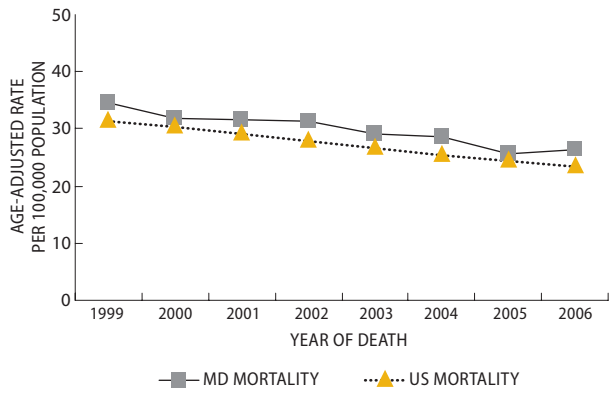
SINCE THE LAST CANCER PLAN prepared in 2004, results from studies investigating common variation in the sequence of DNA in men with and without prostate cancer have been published.[2,3,4] These findings may lead to understanding more about the genetic reasons why prostate cancer develops and who in the general population may be at greater risk.

However, unlike some other cancers, there are no well-established risk factors for prostate cancer that men can change to reduce their risk of developing it. Nevertheless, some research studies support that men who smoke and men who are obese are more likely to die of prostate cancer.[5,6,7]

Diet and nutrients may influence prostate cancer risk.[8,9] While not confirmed, men who eat a lot of meat, especially processed meat like bacon, and consume too many calories may have a higher risk of prostate cancer, whereas men who eat fish and foods containing tomato or cruciferous vegetables like broccoli may have a lower risk of prostate cancer. Taking vitamins or mineral supplements, such as vitamin E and selenium, does not appear to be beneficial for avoiding prostate cancer, except possibly in men who have deficiency. More research needs to be done in this area. Taking calcium at levels above the recommended amount for adult men in some studies appears to increase the risk of metastatic prostate cancer.

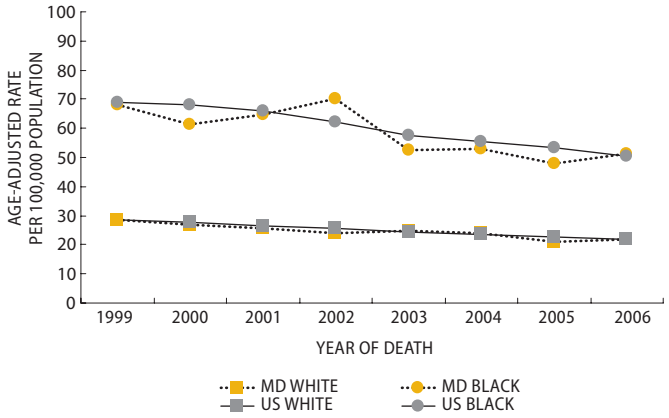
More research needs to be done on whether common medications influence prostate cancer risk, but there are some interesting leads. Men who regularly take aspirin or other non-steroidal anti-inflammatory drugs, such as ibuprofen, may have a lower risk of prostate cancer.[10] Men who take a statin, a type of medication that is

FIGURE 11.2 Prostate Cancer Mortality Rates, Maryland and US, 1999-2006



Rates are age-adjusted to the 2000 US standard population.
Source: NCHS Compressed Mortality File in CDC WONDER.

FIGURE 11.3 Prostate Cancer Mortality Rates by Race Maryland and US, 1999-2006



Rates are age-adjusted to 2000 US standard population.
Source: NCHS Compressed Mortality File in CDC WONDER.

commonly prescribed to lower serum cholesterol, may have a lower risk of metastatic prostate cancer.[11]

Smoking, obesity, and poor diet are leading causes of cardiovascular disease and other cancers in men and women. Therefore, preventing people from starting smoking and from gaining weight, intervening so that people can stop smoking and lose weight, and advocating a balanced diet are not only important strategies for good health in general, but also may be beneficial for avoiding prostate cancer.

Two drugs, finasteride and dutasteride, have been shown to reduce the risk of prostate cancer by about 25% in randomized controlled clinical trials.[12,13] Finasteride and dutasteride are sometimes prescribed to treat benign prostatic hyperplasia. These drugs are called "5α-reductase inhibitors" because they block 5α-reductase, an enzyme that helps convert testosterone to dihydrotestosterone, a more potent androgen. Based on the findings of these studies, the American Society of Clinical Oncology/American Urological Association issued a Clinical Practice Guideline recommending that healthy men who are screened regularly for prostate cancer and show no symptoms of the disease should talk to their doctors about using 5α-reductase inhibitors to prevent the disease. However, these men should also understand the potential risks of using 5α-reductase inhibitors including sexual side effects and the possibility of high-grade prostate cancer.[14]

For more information on prostate cancer risk factors and primary prevention, see the NCI Prostate Cancer Prevention Physician Data Query (PDQ) at www.cancer.gov.

FAST FACT Many organizations (including the American Cancer Society, the US Preventive Services Task Force, and the National Comprehensive Cancer Network) recommend that men discuss the benefits and risks of prostate cancer screening with a physician before deciding whether or not to be screened.

Prostate Cancer Early Detection

Two tests are used to screen for prostate cancer: a blood test called the prostate-specific antigen or PSA test, and a physical examination call the digital-rectal examination or DRE.

THE PSA TEST is done by drawing a man's blood and measuring the level of PSA, which is a protein made by the prostate. The risk of prostate cancer rises gradually with an elevated PSA level.[15] However, an elevated PSA level does not necessarily mean that a man has prostate cancer. PSA levels are sometimes elevated when a man has benign prostatic hyperplasia or prostatitis. Because the PSA test is not specific for prostate cancer, some doctors calculate the change in PSA levels across at least three tests done over at least 18 months. This calculation is called the PSA velocity. Men who have a high PSA velocity are more likely to have prostate cancer. Measurement of PSA components such as free PSA improves the discrimination between cancer and benign prostatic disease. In men with prostate cancer, the percentage of free PSA (percent-free PSA) is lower in blood.

The DRE involves a physician inserting a gloved and lubricated finger into the rectum to feel the back portion of the prostate gland. Most often men are screened with both the PSA test and the DRE.

The benefits versus the problems of PSA screening are controversial. Two randomized controlled trials investigated whether PSA screening coupled with earlier treatment reduces the risk of prostate cancer death. The trial, conducted in Europe in populations without prior routine PSA screening, showed that the men who were randomized to receive PSA screening had a lower risk of dying from prostate cancer.[16] The trial conducted in US populations with prior routine PSA screening did not find that screening had any benefit in lowering deaths from prostate cancer.[17] Both trials found that in the group of men who were screened, many men were diagnosed and treated even though their prostate cancer was unlikely to have ever caused them ill health or death.[18,19]

At the time of the publication of the Prostate Cancer chapter, recommendations for prostate cancer screening vary by organization. However, many groups recommend against screening men who are older than 75 years or whose expected remaining lifespan is less than ten years, or recommend individualized decision-making for men over 75 years. Visit the Prostate Cancer page of www.marylandcancerplan.org to learn more about prostate cancer screening recommendations.

The uncertainties of the benefits of screening versus the potential complications of treatment for prostate cancer have led many organizations—including the ACS, the US Preventive Services Task Force, and the National Comprehensive Cancer Network (NCCN)—to recommend that men discuss the benefits and risks of prostate cancer screening with a physician before deciding whether or not to be screened.

The American Cancer Society Web site has materials that may be helpful to men in deciding whether to be screened for prostate cancer: http://www.cancer.org/.

Prostate cancer screening is commonly offered to patients in physicians' offices. Sometimes screening is offered at community hospitals and in the community at health fairs and other special occasions focused on health. The Prostate Cancer Medical Advisory Committee of the Maryland State Department of Health and Mental Hygiene has developed guidelines (entitled Prostate Cancer Minimal Elements for Information, Screening, Diagnosis, Treatment and Follow-up) to provide guidance for public health programs that decide to screen for prostate cancer: http://fha.maryland.gov/cancer/resources.cfm/.

If a man has an abnormal screening PSA test and/or an abnormal screening DRE, he and his doctor may decide that the man should have a prostate biopsy. The biopsy involves removing samples of prostate tissue using needles inserted into the prostate through the rectum. A pathologist then reviews the prostate biopsy tissue to determine whether prostate cancer is present. If cancer is present, the pathologist will assign a Gleason score, a measure of how disorganized the cancer tissue appears relative to normal prostate tissue. Prostate cancers with a higher Gleason score are more likely to progress. For more detail on the Gleason score, visit the Prostate Cancer page of the Cancer Plan Web site: www.maryland-cancerplan.org.

TERMS TO KNOW *Watchful waiting, active surveillance*, and *expectant management* are all terms that describe an approach of prostate cancer management where a man diagnosed with prostate cancer that has not grown outside of the prostate and appears to be slow growing chooses to be monitored by his doctor, being treated only if additional biopsies indicate that the disease has worsened.

After a man is diagnosed with prostate cancer, his cancer stage is determined. Local stage means that the prostate cancer is confined to the prostate gland. Regional stage means that the prostate cancer has grown beyond the prostate gland to surrounding organs or tissues and/or regional lymph nodes. Distant stage means that the prostate cancer has spread to other parts of the body remote from the prostate gland, such as bone.

Prostate Cancer Treatment

Treatment for prostate cancer may involve surgery, radiation therapy, or hormonal therapy. Treatment options for prostate cancer depend, in part, on a man's age, overall health, and whether the cancer has grown outside of the prostate and spread elsewhere.

FOR CANCERS THAT HAVE NOT GROWN OUTSIDE OF THE PROSTATE, surgery and radiation therapy are common treatment options. Surgery involves the removal of the entire prostate (radical prostatectomy). This surgery can be done either in an open fashion or laparoscopically. In the traditional open surgery for prostate cancer, the operation is performed after making an incision in the lower abdomen or perineum. In laparoscopic surgery, the operation is performed through small incisions with the aid of a camera. In most laparoscopic surgeries for prostate cancer, a surgical robot is used. Radiation therapy uses x-rays to

kill cancer cells. The radiation is delivered by an external beam or by radioactive seeds that are implanted in the prostate in or near the tumor (brachytherapy).

For some men whose prostate cancer has not grown outside of the prostate and appears to be slow growing, especially if they are older or have other serious medical problems, the risks and possible side effects of surgery and radiation therapy may outweigh the possible benefits. These men often choose to be monitored by their doctor and are treated only if additional biopsies indicate that the disease has worsened.[20] This approach to managing prostate cancer goes by several names including watchful waiting, active surveillance, and expectant management.

For cancers that have grown outside of the prostate, hormonal therapy is commonly used. Hormonal therapy combats prostate cancer by cutting off the supply of male hormones that encourage prostate cancer growth. Hormonal control can be achieved by drugs or by surgery to remove the testicles.

Clinical trials are being conducted to determine new ways of treating prostate cancer. The National Cancer Institute has a Web site for learning about clinical trials for prostate cancer treatment: http://www.cancer.gov/.

Each treatment for prostate cancer has risks, including impotence (erectile dysfunction), urinary incontinence, and bowel problems, such as diarrhea or rectal bleeding.

For more information on prostate cancer treatment options:

- National Cancer Institute: http://www.cancer.gov/.
- For physicians (requires registration): The National Comprehensive Cancer Network (NCCN): http://www.nccn.org/index.asp.

GOALS ▪ OBJECTIVES ▪ STRATEGIES

GOAL 1

Reduce morbidity related to the detection and management of prostate cancer in Maryland men.

OBJECTIVE 1

By 2015, increase the proportion of men 40 years and older who report having had a discussion with their healthcare provider about prostate cancer screening to 74% (2008 Baseline: 64%).

Source: Maryland Cancer Survey.

STRATEGIES

1. **EDUCATE MEN AND THEIR FAMILIES AND FRIENDS** through public service announcements, Web sites, printed materials, etc. about the risks and benefits of prostate cancer screening and encourage them to discuss whether prostate cancer screening is right for them with their primary care provider or urologist.
2. **EDUCATE PROVIDERS** with updated information about the potential benefits and problems of prostate cancer screening.
3. **DEVELOP STRATEGIES FOR MONITORING** Objective 1, including:
   - Promote inclusion of questions about prostate cancer screening on the Maryland BRFSS.
   - Identify sources of funding for future Maryland Cancer Surveys and include questions about prostate cancer screening.
   - Encourage state-funded or other healthcare systems to monitor adherence to prostate cancer screening guidelines via electronic medical records systems.
4. **REDUCE** the number of men being screened for prostate cancer past age 75.

OBJECTIVE 2

By 2015, use Web sites, printed materials, and other media to educate Maryland men who have been diagnosed with prostate cancer and their families and friends about prostate cancer treatment options.

STRATEGIES

1. **EDUCATE MEN RECENTLY DIAGNOSED** with prostate cancer and their families and friends through Web sites, printed materials, and other media about evidence-based treatment options, including active surveillance. Include information about how and why treatment options vary by the stage and grade of the man's disease and age. Encourage them to discuss treatment options and accompanying risks and benefits with their doctor (or doctors if the men choose to have a second opinion or attend a multidisciplinary clinic).
2. **EDUCATE MEN RECENTLY DIAGNOSED** with prostate cancer and their families and friends through Web sites, printed material, and other media about prostate cancer staging and grading (Gleason score) and how this information is used by doctors, in part, to determine treatment options for a given patient.
3. **EXPLORE THE POSSIBILITY** of insurance companies in Maryland sending an educational pamphlet about prostate cancer treatment options to men with a pathologically confirmed diagnosis of prostate cancer.
4. **DEVELOP A CLEARINGHOUSE** Web site to point men to information on treatment options.
5. **SET UP AND ENCOURAGE MEN TO REGISTER** on a Web site that will provide them updated information on screening and treatment options.

GOALS ▪ OBJECTIVES ▪ STRATEGIES

OBJECTIVE 3

By 2015, increase the information available on overall well being for men recently diagnosed with prostate cancer and men who have survived prostate cancer.

STRATEGIES

1. **INFORM MEN AND THEIR FAMILIES AND FRIENDS** at the time of diagnosis about the availability of support and survivorship groups.
2. **EDUCATE MEN, INCLUDING MEN DIAGNOSED WITH PROSTATE CANCER,** about the major causes of death in the US and how to reduce their risks of premature death through dietary and lifestyle modification and medical care.

GOAL 2

Continue to reduce the prostate cancer mortality rate in Maryland men.

TARGET (2015)

MORTALITY	14.9 per 100,000 (2006 Baseline: 26.3 per 100,000) Source: CDC WONDER.

OBJECTIVE 1

By 2015, increase the percentage of Maryland men receiving appropriate treatment for prostate cancer.

STRATEGIES

1. **DEVELOP METHODS TO MEASURE APPROPRIATE TREATMENT,** including by modifying cancer registry reporting criteria.
2. **INCREASE ACCESS TO APPROPRIATE TREATMENT** based on stage, grade, and other patient-specific characteristics, such as co-morbidities.
3. **IMPROVE TREATMENT ADHERENCE** for men diagnosed with prostate cancer through enhanced efforts to care for uninsured and underinsured men and increased availability of patient navigation.
4. **REDUCE THE PREVALENCE** of unstaged prostate cancer cases by continuing to modify cancer registry criteria for staging of early disease, by encouraging complete reporting from hospitals, doctors, and independent pathology groups, and by ensuring adequate patient staging, which is needed to make treatment decisions.

OBJECTIVE 2

By 2015, reduce the disparity in prostate cancer mortality rates between black or African American and white men to reach the following targets:

WHITE	12.4 per 100,000 (2006 Baseline: 21.7 per 100,000)
BLACK OR AFRICAN AMERICAN	23.0 per 100,000 (2006 Baseline: 51.2 per 100,000)

Source: Maryland Vital Statistics.

STRATEGIES

1. **UTILIZE PATIENT NAVIGATORS,** community health workers and case managers to increase access to appropriate treatment (based on stage, grade, and other patient-specific characteristics).
2. **IMPROVE THE QUALITY** of and adherence to treatment for black or African American men diagnosed with prostate cancer through enhanced efforts to reach underserved populations and increased availability of patient navigators.

OBJECTIVE 3

By 2015, create and maintain a Web site to educate Marylanders, including men diagnosed with and surviving prostate cancer, about ongoing research on risk factors for prostate cancer incidence and mortality, explanations for the racial disparity in these rates, screening, prognosis, treatment, and survivorship.

1. **DETERMINE WHICH GROUPS** are best able to develop and maintain the Web site and identify funding to do so.

REFERENCES

1 Jemal A, Ward E, Thun M. Declining death rates reflect progress against cancer. PLoS One. 2010 Mar 9;5(3):e9584. PubMed PMID: 20231893; PubMed Central PMCID: PMC2834749.

2 Eeles RA, Kote-Jarai Z, Al Olama AA, Giles GG, Guy M, Severi G, Muir K, Hopper JL, Henderson BE, Haiman CA, et al.; UK Genetic Prostate Cancer Study Collaborators/British Association of Urological Surgeons' Section of Oncology; UK ProtecT Study Collaborators; PRACTICAL Consortium, Easton DF. Identification of seven new prostate cancer susceptibility loci through a genome-wide association study. Nat Genet. 2009 Oct;41(10):1116-21. Epub 009 Sep 20. PubMed PMID: 19767753; PubMed Central PMCID: PMC2846760.

3 Thomas G, Jacobs KB, Yeager M, Kraft P, Wacholder S, Orr N, Yu K, Chatterjee N, Welch R, Hutchinson A, et al. Multiple loci identified in a genome-wide association study of prostate cancer. Nat Genet. 2008 Mar;40(3):310-5. Epub 2008 Feb 10. PubMed PMID: 18264096.

4 Schumacher FR, Feigelson HS, Cox DG, Haiman CA, Albanes D, Buring J, Calle EE, Chanock SJ, Colditz GA, Diver WR, et al. A common 8q24 variant in prostate and breast cancer from a large nested case-control study. Cancer Res. 2007 Apr 1;67(7):2951-6. PubMed PMID:17409400.

5 US Department of Health and Human Services. The health consequences of smoking: a report of the Surgeon General, 2004 [Internet]. Bethesda (MD): US Department of Health and Human Services; 2004 [cited 2010 July 19]. Available from: http://www.surgeongeneral.gov/library/smokingconsequences

6 Giovannucci E, Liu Y, Platz EA, Stampfer MJ, Willett WC. Risk factors for prostate cancer incidence and progression in the health professionals follow-up study. Int J Cancer. 2007 Oct 1;121(7):1571-8. PubMed PMID: 17450530; PubMed Central PMCID: PMC2430098.

7 Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of US adults. N Engl J Med. 2003 Apr 24;348(17):1625-38. PubMed PMID: 1271173.

8 World Cancer Research Fund/American Institute for Cancer Research (US). Food, nutrition, physical activity, and the prevention of cancer: a global perspective. Washington DC: American Institute for Cancer Research (US); 2007.

9 See note 6

10 Mahmud SM, Franco EL, Aprikian AG. Use of nonsteroidal anti-inflammatory drugs and prostate cancer risk: A meta-analysis. Int J Cancer. 2010 Jan 20. [Epub ahead of print] PubMed PMID: 20091856.

11 Boudreau DM, Yu O, Johnson J. Statin use and cancer risk: a comprehensive review. Expert Opin Drug Saf. 2010 Jul;9(4):603-21. PubMed PMID: 20377474.

12 Thompson IM, Goodman PJ, Tangen CM, Lucia MS, Miller GJ, Ford LG, Lieber MM, Cespedes RD, Atkins JN, Lippman SM, et al. The influence of finasteride on the development of prostate cancer. N Engl J Med. 2003 Jul 17;349(3):215-24. Epub 2003 Jun 24. PubMed PMID:12824459.

13 Andriole GL, Bostwick DG, Brawley OW, Gomella LG, Marberger M, Montorsi F, Pettaway CA, Tammela TL, Teloken C, Tindall DJ, et al.; REDUCE Study Group. Effect of dutasteride on the risk of prostate cancer. N Engl J Med. 2010 Apr 1;362(13):1192-202. PubMed PMID: 20357281.

14 Kramer BS, Hagerty KL, Justman S, Somerfield MR, Albertsen PC, Blot WJ, Ballentine Carter H, Costantino JP, Epstein JI, Godley PA, et al.; American Society of Clinical Oncology Health Services Committee; American Urological Association Practice Guidelines Committee. Use of 5-alpha-reductase inhibitors for prostate cancer chemoprevention: American Society of Clinical Oncology/American Urological Association 2008 Clinical Practice Guideline. J Clin Oncol. 2009 Mar 20;27(9):1502-16. Epub 2009 Feb 24. Review. Erratum in: J Clin Oncol. 2009 Jun 1;27(16):2742. PubMed PMID: 19252137; PubMed Central PMCID: PMC2668556.

15 Thompson IM, Ankerst DP, Chi C, Lucia MS, Goodman PJ, Crowley JJ, Parnes HL, Coltman CA Jr. Operating characteristics of prostate-specific antigen in men with an initial PSA level of 3.0 ng/ml or lower. JAMA. 2005 Jul 6;294(1):66-70. PubMed PMID: 15998892.

16 Schröder FH, Hugosson J, Roobol MJ, Tammela TL, Ciatto S, Nelen V, Kwiatkowski M, Lujan M, Lilja H, Zappa M, et al.; ERSPC Investigators. Screening and prostate-cancer mortality in a randomized European study. N Engl J Med. 2009 Mar 26;360(13):1320-8. Epub 2009 Mar 18. PubMed PMID: 19297566.

17 Andriole GL, Crawford ED, Grubb RL 3rd, Buys SS, Chia D, Church TR, Fouad MN, Gelmann EP, Kvale PA, Reding DJ, et al.; PLCO Project Team. Mortality results from a randomized prostate-cancer screening trial. N Engl J Med. 2009 Mar 26;360(13):1310-9. Epub 2009 Mar 18. Erratum in: N Engl J Med. 2009 Apr 23;360(17):1797. PubMed PMID: 19297565.

18 See note 16

19 See note 17

20 Ross AE, Loeb S, Landis P, et al. Prostate-specific antigen kinetics during follow-up are an unreliable trigger for intervention in a prostate cancer surveillance program. J Clin Oncol. 2010 June 10;28(17):2810-2816.