REVIEW ARTICLE

PROSTATE CANCER IN MISSISSIPPI: EPIDEMIOLOGY, RISK FACTORS, AND PREVENTION

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| ARTICLE INFO	ABSTRACT
	Background: Prostate cancer is the second most common type of cancer and the fifth leading cause of death in men worldwide. In 2018 it was estimated that there were 1.3 million new cases of prostate cancer worldwide, with developing countries having higher prevalence rates. It is the second leading cause of cancer deaths in the United States. About 248,000 new cases and 34,000 deaths were reported by the American Cancer Society in 2021, with a projection that 1 in 8 males will be diagnosed with prostate cancer in their lifetime. In the state of Mississippi, prostate cancer is the most common type of cancer for men (29%) followed by lung and bronchus (18 %), colon, and rectum (10 %). African American men are at a higher risk of developing this type of cancer. Prostate cancer is mostly asymptomatic in the early stages. Active surveillance is therefore necessary for early detection. There is currently no evidence of effective prevention of prostate cancer, but dietary modification and increased physical activity can reduce the risk of developing it. The United States Preventive Task Force recommends a voluntary screening for men aged 55 to 69 years. However, for the higher-risk population such as men with a family history of prostate cancer and African American males, screening is recommended from age 40. ***Method:*** This paper reviews the risk factors, trends, etiology, and prognosis of prostate cancer in Mississippi, with a view to disease prevention. ***Findings:*** Southern diet common in southern states such as Mississippi is typically low in healthy food and high in processed foods. These unhealthy food choices combined with poor lifestyles and low socioeconomic status further exacerbate the mortality and prevalence of prostate cancer among men in Mississippi. ***Conclusion:*** Understanding the epidemiology and risk factors of prostate cancer in Mississippi will help to formulate policies and programs for the prevention of the disease

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INTRODUCTION

Cancer consists of over 100 different groups of diseases that manifest as an uncontrolled growth of cells in tissues or organs of the body. The abnormal cells can grow and spread rapidly and if uncontrolled, may lead to death. The probable causes of cancer include 1. Internal factors, such as the body's immune system, genetic composition, and hormones. 2. External factors, e.g., exposure to radiation, carcinogenic chemicals, and viruses. 3. Lifestyle factors, including alcohol and tobacco use, poor nutrition, physical inactivity, and over-exposure to sunlight. Most cancers can be prevented by lifestyle modification and, when detected early, can be cured with prompt treatment. According to Global Cancer Statistics (GLOBACAN 2020), the worldwide incidence of all cancers is about 19.3 million, with a mortality rate of about 10 million in 2020 (1). In the United States, prostate cancer is the main type of cancer among men, with an incidence rate of 106.4 per 100,000 males (2). Cancer is the second leading cause of death with about 1600 new cases reported annually.

Between 2006 and 2010, there were over 30,000 cancer deaths in Mississippi, 32% of which could have been prevented by tobacco use cessation (4) and 25% averted by maintaining normal body weight and eating a healthy diet (5). In the same period, 54% of all cancer cases in Mississippi were in four major sites: prostate, lung/bronchus, breast, and colon/rectum. Prostate cancer is the second leading cause of death among men of all races. Incidence and mortality rates for all cancers among males are highest in African Americans (6). The most common types of cancer for men in Mississippi are prostate (29%), lung and bronchus (18 %), and colon and rectum (10 %) (7). Age is a major risk factor for several types of cancer. Cancer incidence and mortality rates increase significantly with age and the probability of any male between 50 and 59 years of age developing prostate cancer is 1.8% (2). About 90% of Mississippi males are 55 years and older at the time of diagnosis, and more than 58% are aged 65 or older at the time of diagnosis. Prostate cancer is usually asymptomatic in the early stages and has a slow progression that rarely requires treatment.

The common symptoms are increased frequency and urgency of urination, nocturia, dysuria, and erectile dysfunction. These symptoms are also common with prostatic hypertrophy or benign prostate hyperplasia (BPH) and this affects the validity of early screening. Urinary retention with back pain may occur at a more advanced stage of cancer. Screening for prostate cancer is based on the detection of high levels of a glycoprotein usually expressed by the prostate tissues called prostate-specific antigen (PSA). Men without prostate cancer may also present with elevated levels of PSA hence a confirmatory test, usually, a tissue biopsy is recommended. Diet and physical inactivity influence the development and progression of prostate cancer. The impact of dietary factors on incidence rates of prostate cancer has been associated with ethnic differences (8)(9). Several studies have identified the involvement of acquired gene mutations in the development of cancer (10)(11). There is therefore a need for a detailed analysis of the epidemiology of prostate cancer as well as an evaluation of risk factors to better understand the role of epigenetics in cancer formation and progression.

Epidemiology of Prostate Cancer: Prostate cancer is the second leading cause of cancer death in American men. About 1 in 8 American males are projected to be diagnosed with prostate cancer during their lifetime and about 1 man in 41 will die of prostate cancer. Though prostate cancer is a serious disease, the mortality rate is low compared to other cancer diseases. The American Cancer Society estimates that in 2022, there will be about 2,970 new cases and about 520 deaths from prostate cancer in Mississippi (12). Non-Hispanic blacks and elderly men have the highest incidence of prostate cancer, and 60% of new cases occur in men ages 65 years and older. The incidence is low below age 40. Nationally, the average age of diagnosis is 66 years, with African American men having the highest incidence and mortality rates (13). The pattern is the same in Mississippi, with incidence rates of 158.3 new cases diagnosed per 100,000 men. African American men in Mississippi have a mortality rate three times that of their White counterparts (7). Explanations for this disparity in survival rates include differences in socioeconomic status, access to care, genetic, and environmental factors. The incidence rate and mortality rate of prostate cancer in Mississippi are shown in figures A and figure B below.
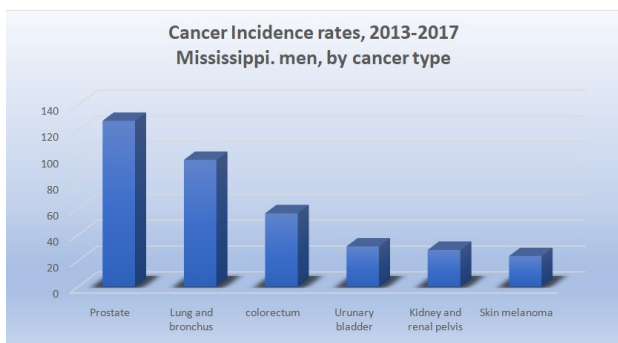

Data sources: North American Association of Central Cancer Registries (NAACCR), 2020

Fig. A. Incidence rates of cancer among men in Mississippi

ETIOLOGY

The main triggers that cause prostate cells to become cancerous are not known. However, the underlying factor is a mutation in the DNA of a normal prostate cell which leads to modification of the functions of oncogenes and tumor suppressor genes. Uncontrolled growth and metastasis of cancer cells occur when DNA mutation turns off tumor suppressor genes or keeps the oncogenes turned on. DNA mutation can be inherited from a parent or acquired during a person's lifetime (14). Studies show that inflammation of the prostate (prostatitis) may cause cell damage which could lead to the development of benign prostate hyperplasia (BPH), or prostate cancer (15). Environmental factors such as exposure to radiation or carcinogenic chemicals may trigger DNA mutations and lead to the development of cancer cells.

Other risk factors for prostate cancer include diet (eating red meat and saturated animal fat, and reduced intake of fruits and vegetables), obesity, physical inactivity, hyperglycemia, inflammation, infections, and exposure to chemicals or ionizing radiation (16)(17)(18). Notably, the consumption of whole milk has been implicated as a major risk factor in adults. Adult males who consumed whole milk were found to be 1.5 times more likely to develop prostate cancer than those who consumed skim milk or 2% milk and were also at higher risk of disease recurrence (19)(20). There are mixed reports on the effect of dietary and supplemental vitamins on prostate cancer. Retinol, a form of vitamin A is a primary product of beta-carotene, commonly found in yellow and leafy green vegetables and tomatoes, milk, and other dairy products, as well as fish oil, and is linked to an increased risk of prostate cancer (21)(22). However, some studies have found no such association (23)(24)(25) or an inverse association (26)(27). One of the largest studies on the relationship between circulating retinol concentration and prostate cancer risk, based on a randomized, double-blind, placebo-controlled trial, reported a positive association between blood retinol level and the risk of prostate cancer. According to this study, the risk of both total and aggressive prostate cancer was increased by 20% in men with high circulating retinol levels (28).
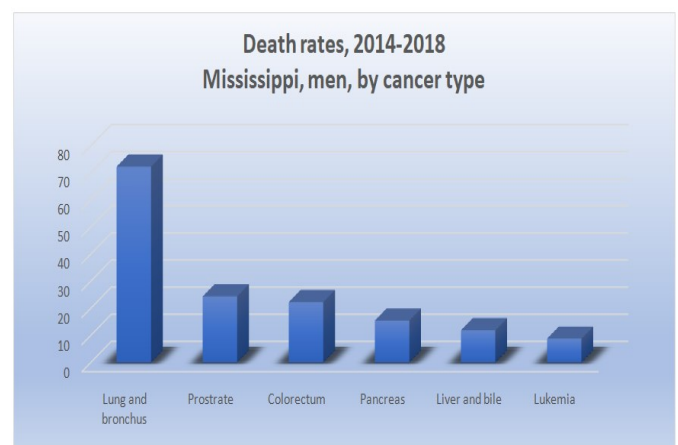
Data sources: National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention, 2020

Fig. B. Death rates among men in Mississippi

DIAGNOSIS: The prostate-specific antigen (PSA) test is the common diagnostic tool for prostate cancer. The use of PSA is controversial, as there is evidence of frequent false positives and false negatives in the diagnosis of prostate cancer (29). Most prostate cancer diagnoses are made in symptomatic men. Annual screening is generally recommended for men over age 50, especially those presenting with erectile dysfunction, lower urinary tract infection (LUTS), or haematuria. Since African American males are at a higher risk, screening is recommended to start at age 40.

Prostate cancer shares s,milar symptoms with benign prostate hyperplasia (BPH) and prostatitis, thus making the PSA test problematic for the diagnosis. Better diagnosis can be achieved by using digital rectal examination (DRE) along with PSA to aid diagnostic testing. According to a recent study, DRE shows high specificity and positive predictive value (PPV) for symptomatic prostate cancer cases (30). Other tests that may enhance the diagnosis of prostate cancer in symptomatic patients are kallikrein serine protease biomarkers, genome-wide association studies (GWAS), and multiparametric magnetic resonance imaging (mpMRI). mpMRI is also used for monitoring progression in men with localized prostate cancer (31).

RISK FACTORS: A risk factor is anything that increases the probability of a person developing a disease. However, the presence of one or more risk factors does not automatically guarantee that one will get the disease. While some men without a risk factor may

develop the disease, others with one or more risk factors may never develop it. Risk factors for prostate cancer that are classified as modifiable are mostly lifestyle dependent. Non-modifiable factors are those that are beyond an individual's capacity to change.

Non-Modifiable Risk Factors

- **Age:** Studies show that there is an increased risk of prostate cancer after 50 years in white men without a family history of cancer and after 40 years in black/African American males. For men with a family history of the disease, the risk increases significantly after age 40 (32).
- **Race/ Ethnicity:** There is significant variation in the incidence and prevalence of prostate cancer among racial groups. African American males have an incidence rate of prostate cancer that is twice that of Caucasian males. The role of vitamin D in blocking UV radiation in darkly pigmented skin may be a factor in the variation of cancer among ethnic groups (33). American Indians/Alaskans (46.9 per 100,000) have the lowest incidence rates while African American men (157.6 per 100,000) have the highest rate. The wide gap is believed to be due to socioeconomic factors and biological factors (34). Researchers suggest that African Americans receive lower-quality healthcare and are also less likely to undergo early screening for cancer disease (35).
- **Family History/Genetic Mutation:** Over 20% of prostate cancer cases are associated with a family history of the disease. This may be attributable to hereditary genes as well as similar lifestyle habits and a similar pattern of exposure to environmental carcinogens (36)(37). Several findings indicate that inherited genetic background contributes about 5% to the risk of prostate cancer (38)(39).

Modifiable Risk Factors

- **Diet:** Diet is a notable risk factor as some foods present a high risk while others are protective against prostate cancer. Examples of high-risk diets include red meat, saturated animal fat, and dairy products. These are positively correlated with prostate carcinogenesis and mortality. Fruits, vegetables, and diets rich in antioxidants, lycopene, and selenium are protective against prostate cancer disease.
- **Obesity:** Obesity and a high body mass index are associated with aggressive prostate cancer with a dire prognosis (40)(41). Studies link variations in levels of circulating metabolic and sex hormones in obese men to the development of prostate cancer (42).
- **Smoking:** Tobacco use has been linked to increased incidence and mortality of prostate cancer. Cigarette smoke is a known carcinogen and exposure, whether active or passive, is a risk factor. The association of smoking with the risk of prostate cancer may be due to hormonal or genetic influences. Men who smoke have higher levels of circulating sex hormones, which may increase their risk of prostate cancer development or progression (43)(44).

Other Risk Factors

- **Chemical exposure:** There is some evidence that firefighters are exposed to chemicals that may increase the risk of prostate cancer. Studies show a link between Agent Orange, a chemical used widely during the Vietnam War, and the risk of prostate cancer.
- **Inflammation of the prostate:** Inflammation of the prostate gland (prostatitis) is linked to an increased risk of prostate cancer as inflammation is very common in cancerous prostate tissues.
- **Sexually transmitted infections:** STDs, especially gonorrhea and chlamydia infection, increase the risk of prostate cancer because they can lead to inflammation of the prostate. A study among African American and white males revealed an increased risk of prostate cancer among men with a history of gonorrhea or syphilis (45).

- **Vasectomy:** Vasectomy, the most common male contraception method in the US, is significantly associated with the development of prostate cancer. Some research has found that vasectomy may increase the risk of prostate cancer by up to 70% (46)(47).

Prevention

Non-modifiable risk factors like family history, age, and race cannot be controlled. However, lifestyle changes can reduce the risk of developing prostate cancer. Controlling dietary intake, body weight, and physical activity has been suggested as possible ways of lowering the risk of developing the disease. Men who are obese or overweight are predisposed to developing prostate cancer, with higher mortality rates (48). Increased physical activity helps to reduce body weight and is therefore imperative in lowering the risk of prostate cancer. Certain vitamins, minerals, and supplements such as lycopene, selenium, and soy protein have been recommended for reducing the risks of prostate cancer but further studies are needed. While low doses of certain vitamin supplements may prevent prostate cancer, the risk is increased with higher intakes of vitamins A, B, folic acid, and zinc. Vitamin E supplementation is contraindicated in prostate cancer (49).

CONCLUSION

While race and age are the two major risk factors for prostate cancer, socioeconomic status (SES) is known to affect the mortality rate of the disease. Both the incidence rates and the likelihood of surviving prostate cancer increase with increasing SES. This may be due to greater access to screening, early diagnosis, and quality health care in more affluent communities. Mississippi, with a poverty rate of 19.7%, is ranked the poorest state in the nation. It also has the lowest median household income of any state at $45,792 (51). The low SES combined with poor lifestyle and food choices may be exacerbating the prostate cancer prevalence and mortality among men in Mississippi. In contrast to a Mediterranean diet, the southern diet common in Mississippi and other southern states of the US is low in healthy foods such as whole grains, fresh fruits, and leafy vegetables but high in processed food with added fat, fried food, eggs, and sugary beverages. A good understanding of the association between nutritional status, socioeconomic status (SES), and prostate cancer will be valuable to public health authorities in policy and decision-making. It can also help to identify vulnerable populations to be targeted for prevention and intervention programs. The best guidance for reducing the risk of prostate cancer is to:

- Get early screening.
- Maintain healthy eating habit, which includes a variety of colorful fruits and vegetables and whole grains, and avoid or limit red and processed meats, sugar-sweetened beverages, and highly processed foods.
- Maintain healthy body weight.
- Keep physically active by engaging in regular mild to moderate exercise.

Statement of Competing Interests

The authors have no competing interests

REFERENCES

1. Sung, H., Ferlay, J., Siegel, R., Laversanne, M., Soerjomataram, I., Jemal, A., Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries, CA Cancer J Clin., 71(3). 209-249, May 2021
2. Elflein, J., "Prostate Cancer - Statistics & Facts,"March 2021. (online) Available Statistica: https://www.statista.com/

topics/4379/ prostate-cancer-in-the-us/# dossierKeyfigures (Accessed May 16, 2022)

3. Mississippi State Department of Health (MSDH). "Comprehensive Cancer Control"Nov 2020," (Online) Available: msdh.gov: https://msdh.ms.gov/msdhsite/_static/43,0,292.html (Accessed May 16, 2022)

4. Moolgavkar, Suresh H et al., "Impact of reduced tobacco smoking on lung cancer mortality in the United States during 1975-2000." J Natl Cancer Inst vol., 104,7. 541-8. 2012 (online) Available: https://pubmed.ncbi.nlm.nih.gov/22423009/(Accessed May 16, 2022)

5. MSDH "Burden of Cancer – Mississippi," Nov 2014 (online) Available: https://msdh.ms.gov/msdhsite/ _static/resources/ 6191.pdf (accessed May 17 2022)

6. American Cancer Society, "Cancer Facts & Figures," 2021 (online)Available: https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2021.html

7. MSDH, Burden of Cancer-Mississippi (online) Available: https://msdh.ms.gov/msdhsite/_static/resources/6191.pdf (accessed May 17 2022)

8. Chan JM, Gann PH, Giovannucci EL,"Role of diet in prostate cancer development and progression," J Clin Oncol. 23(32):8152–8160. Sep 2016. Available: https://ascopubs.org/doi /10.1200/JCO.2005.03.1492 (Accessed; May 17, 2022)

9. Willis MS, Wians FH,"The role of nutrition in preventing prostate cancer: a review of the proposed mechanism of action of various dietary substances," Clin Chim Acta. 330(1-2):57–83. 2003

10. American Cancer Society, "Key Statistics for Prostate Cancer," (online) Available:https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html. (Accessed May 20, 2022)

11. Stratton MR, Campbell PJ, Futreal PA., "The cancer genome," Nature9;458(7239):719-24. Apr 2009

12. American Cancer Society, "Cancer statistics center: Mississippi at a Glance," 2022, (online) Available:https:// cancerstatisticscenter. cancer.org/#!/state/Mississippi (Accessed May 20, 2022)

13. American Cancer Society, "Key Statistics for Prostate Cancer," Jan 2022, (online) Available:https: //www.cancer. org/cancer/prostate-cancer/about/key-statistics.html (Accessed May 20, 2022)

14. Panigrahi GK, Praharaj PP, Kittaka H, Mridha AR, Black OM, Singh R, Mercer R., et al. "Exosome proteomic analyses identify inflammatory phenotype and novel biomarkers in African American prostate cancer patients," Cancer Med.8(3):1110-1123 Mar 2019

15. American Cancer Society, "Causes Risk Factors, and Prevention," 2019. (online) Available: https://www.cancer.org/ cancer/prostate-cancer/causes-risks-prevention/what-causes.html# (Accessed May 20, 2022)

16. Dagnelie PC, Schuurman AG, Goldbohm RA, Van den Brandt PA,"Diet, anthropometric measures and prostate cancer risk: a review of prospective cohort and intervention studies," BJU Int. 2004;93(8):1139–1150. May 2004

17. Kolonel LN, Altshuler D, Henderson BE,"The multiethnic cohort study: exploring genes, lifestyle and cancer risk," Nat Rev Cancer;4(7):519–527. Jul 2004

18. Kolonel LN, "Fat, meat, and prostate cancer,"Epidemiol Rev;23(1):72–81.2001

19. Mettlin CJ, Schoenfeld ER, Natarajan N,"Patterns of milk consumption and risk of cancer."Nutr Cancer;13(1-2):89–99. Jan 1990

20. Tat D, Kenfield SA, Cowan JE, Broering JM, Carroll PR, Van Blarigan EL, et al.,"Milk, and other dairy foods in relation to prostate cancer recurrence: data from the cancer of the prostate strategic urologic research endeavor (CaPSURE™) Prostate;78(1):32–39. Jan 2018

21. Coates RJ, Weiss NS, Daling JR, et al.,"Serum levels of selenium and retinol and the subsequent risk of cancer," Am J Epidemiol, 128 (3): 515-523 Sep1998

22. Gann PH, Ma J, Giovannucci E, et al., "Lower prostate cancer risk in men with elevated plasma lycopene levels: results of prospective analysis," Cancer Res., 59 (6) 1225-1230. Jan 1999

23. Goodman GE, Schaffer S, Omenn GS, et al., "The association between lung and prostate cancer risk, and serum micronutrients: results and lessons learned from Beta-Carotene and Retinol Efficacy Trial". Cancer Epidemiol Biomarkers Prev.;12(6):518–526. Jun 2003

24. Xie, L., Song, Y., Lin, T., et al., "Association of plasma retinol levels with incident cancer risk in Chinese hypertensive adults: A nested case-control study", British Journal of Nutrition, 122(3), Jul 2019

25. Gill JK, Franke AA, Steven Morris J, et al., "Association of selenium, tocopherols, carotenoids, retinol, and 15-isoprostane F(2t) in serum or urine with prostate cancer risk: the Multi-ethnic Cohort", Cancer Causes Control,;20(7):1161–1171. Feb 2009

26. Schenk JM, Riboli E, Chatterjee N, et al., "Serum retinol and prostate cancer risk: a nested case-control study in the prostate, lung, colorectal, and ovarian cancer screening trial". Cancer Epidemiol Biomarkers Prev. (4):1227-31. Mar 2009.

27. Lu QY, Hung JC, Heber D, et al.,"Inverse associations between plasma lycopene and other carotenoids and prostate cancer," Cancer Epidemiol Biomarkers Prev, 10 (7): 749-756. Mar 2001

28. Alison M.l, Joanne L. W, Satu M, Stephanie J. W, Kirk S, Jarmo V, Demetrius A, "Serum Retinol and Risk of Prostate Cancer", American Journal of Epidemiology,173, (7): 813–821. April 2011

29. Grossman DC, Curry SJ, Owens DK, et al., "Screening for prostate cancer: US Preventive services task force recommendation statement". JAMA;319(18):1901–1913. May 2018

30. Jones D, Friend C, Dreher A, Allgar V, Macleod U., "The diagnostic test accuracy of rectal examination for prostate cancer diagnosis in symptomatic patients: a systematic review". BMC Fam Pract.; 19:79. Jun 2018

31. Ahmed HU, Bosaily AE-S, Brown LC, et al.,"Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study". Lancet; 380:1–8. Feb 2017.

32. Cancer Stat Facts: Prostate Cancer (Internet). SEER, 2018. Available from: https://seer.cancer.gov/statfacts/html/prost.html. (Accessed; May 23, 2022)

33. Grant WB, Peiris AN, "Differences in vitamin D status may account for unexplained disparities in cancer survival rates between African and white Americans," Dermatoendocrinol;4(2):85-94. April 2012

34. Wu I, Modlin CS,"Disparities in prostate cancer in African American men: what primary care physicians can do". Cleve Clin J Med.;79(5):313–320. May 2012

35. Hosain GM, Sanderson M, Du XL, Chan W, Strom SS, "Racial/ethnic differences in predictors of PSA screening in a tri-ethnic population," Cent Eur J Public Health;19(1):30–34. Mar 2011.

36. Rawla P. "Epidemiology of Prostate Cancer", World J Oncol;10(2):63-89. Apr 2019

37. Carroll PR, Grossfeld GD, editors. "Prostate cancer", Hamilton, London: Decker Inc.; 2002.

38. Ferris-i-Tortajada J, Garcia-i-Castell J, Berbel-Tornero O, Ortega-Garcia JA.,"Constitutional risk factors in prostate cancer" ActasUrol Esp.;35(5):282–288. May 2011

39. Muller, Roberto L et al., "Association between family history of prostate cancer and positive biopsies in a Brazilian screening program." World journal of urology, 31(5): 1273-8. Oct 2013

40. Demark-Wahnefried W, Moyad MA,"Dietary intervention in the management of prostate cancer". CurrOpin Urol;17(3):168–174. May 2007

41. Greenwald P,"Clinical trials in cancer prevention: current results and perspectives for the future". J Nutr;134(12): 3507S–3512S. Jan 2005

42. Mcbride RB,"Obesity and aggressive prostate cancer bias and biomarkers". Columbia University; 2012.

43. Huncharek M, Haddock KS, Reid R, Kupelnick B,"Smoking as a risk factor for prostate cancer: a meta-analysis of 24 prospective cohort studies". Am J Public Health.;100(4):693–701. Apr 2010

44. Nock NL, Liu X, Cicek MS, Li L, et al.,"Polymorphisms in polycyclic aromatic hydrocarbon metabolism and conjugation genes, interactions with smoking and prostate cancer risk". Cancer Epidemiol Biomarkers Prev.;15(4):756–761. Apr 2006

45. Hayes RB, Pottern LM, Strickler H, et al.,"Sexual behavior, STDs and risks for prostate cancer". Br J Cancer;82(3):718–725. Feb 2000

46. Holt SK, Salinas CA, Stanford JL., "Vasectomy and the risk of prostate cancer". J Urol.;180(6):2565–2567. Oct 2008

47. Cox B, Sneyd MJ, Paul C, Delahunt B, Skegg DC., "Vasectomy and risk of prostate cancer". JAMA;287(23):3110–3115. Jun 2002

48. Freedland SJ, Aronson WJ.,"Examining the relationship between obesity and prostate cancer", Rev Urol;6(2):73-81. 2004

49. Prostate Cancer Research Institute. Supplements for men with prostate cancer. PCRI. September 8. 2017

50. World Population Review, "Poverty Rate by State 2022," (Online). Available: https://worldpopulationreview.com/state-rankings/poverty-rate-by-state. (Accessed 09 June 2022).

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