Journal of Prostate Cancer

Review Article Open Access

# Prostate Cancer, Farming and Other Risk Factors: A Mini Review

**Sharma M, Lawson J, Karunanayake C, Dosman JA and Punam P***

*Canadian Centre for Health and Safety in Agriculture (CCHSA), University of Saskatchewan, Saskatoon, Saskatchewan, Canada*

**Abstract**

Prostate cancer is the fourth most common cancer and is the second most frequently diagnosed cancer among men. Studies have suggested that an increased risk of prostate cancer among men may be associated with age, race/ethnicity and family history of cancer. The etiology of prostate cancer is not precisely known with respect to other putative risk factors such as farming, exposure to pesticides and lifestyle factors. Therefore, the purpose of this paper was to review the published literature to identify some of the potential risk factors of prostate cancer.

**Keywords:** Prostate cancer; Epidemiology; Etiology; Risk factors; Farming; Exposure to pesticides

## Introduction

Globally, cancer is a primary cause of morbidity and mortality accounting for 14 million incident cases and 8.2 million deaths related to cancer in 2012 [1]. It is estimated that over the next two decades, the number of incident cases will rise by nearly 70% [1]. Overall of all cancer types, prostate cancer is the fourth most common cancer and is the second most frequently diagnosed cancer among men [2]. Prostate cancer starts in the cells of the prostate gland which is a part of the male reproductive system and can also spread to nearby organs. It usually grows slowly and can be detected early using a Prostate Specific Antigen (PSA) test and a Digital Rectal Exam [3,4]. Due to widespread use of PSA testing the incidence rates of prostate cancer has increased since 1980 [5].

Despite its high morbidity, the etiology of prostate cancer remains obscure. So far, the known risk factors associated with the development of prostate cancer are advancing age, race and a positive family history of prostate cancer [6-8]. Some of the suspected putative risk factors include farming occupation [6,9-12], occupational exposures to pesticides [13-17], wood dust [18,19], grain dust [18,19], asbestos dust [18,19], personal smoking history [20-26], diet [27-29], obesity [30,31] and physical activity [32-33].

Much attention has been given to farming occupation and exposure to pesticides to investigate its relationship with prostate cancer. However, the results provide inconsistencies in the published literature. In an epidemiologic review conducted by Parent and Siemiatycki [9], the authors suggested that it is important to study the occupation and its related exposures when investigating the potential risk for any cancer. So far, some of the literature has indicated an association between farming and its exposure to pesticides at workplace and prostate cancer [11,13-17]. In an Australian study, a statistically significant increased risk in prostate cancer mortality was observed among men living in rural areas compared with urban areas [34]. The development of prostate cancer shows intricate interactions between environmental and genetic factors [6]. Therefore, the purpose of this paper was to review some of the important risk factors of prostate cancer.

## Identification of Literature

The purpose of the review was to determine the risk factors associated with prostate cancer. The following literature review includes a description of the epidemiology of prostate cancer, mortality and incidence rates and its well established and suspected risk factors. The whole search was conducted using Medline database and Google scholar. The search included articles from 1991 to 2016 and was completed in the month of August, 2016. Additional literature searches were completed periodically in order to update the article lists. Search terms or keywords included but were not limited to "prostate cancer", "risk factors", "epidemiology", "rural", "age", "ethnicity", "race", "pesticides", "fungicides", "herbicides", "insecticides", "farming", "family history", "smoking", "diet", "physical activity" and "obesity". Combinations of these terms were used to explore the literature. This literature review was limited to publications in the English language and in relation to human studies only.

## Incidence and Mortality

The international patterns in prostate cancer incidence and mortality rates vary hugely [2]. According to the GLOBOCAN cancer fact sheet, worldwide in the year 2012, it was the second most common cancer diagnosed among men with 1.1 million new cases (15% of cancer diagnosed in men) [2]. Approximately 70% (i.e., 759,000) of the registered cases of prostate cancer arise in developed countries [2]. A review conducted by Baade et al. [35] confirmed that prostate cancer was prevalent in more developed nations such as the United States of America (USA) and the Scandinavian countries. According to recent data compiled in United States, of all sites, 220,800 (26%) were new cases of prostate cancer [36]. In some of the developing regions for example Caribbean (approximately 79.8 per 100,000), South America (approximately 60.1 per 100,000), Southern Africa (approximately 61.8 per 100,000) fairly high incidence rates were reported [2]. In South-Central Asia (4.5 per 100,000), estimated age-standardized incidence rate was lowest in the world [2]. In the year 2012, worldwide, prostate cancer was the fifth most common cause of death (307,000 deaths, 6.6% of the total men deaths) [2]. The mortality rates did not differ much worldwide and constitutes almost the same number of deaths in both developed and developing nations [2]. In general, in the year 2012, mortality rates were high in largely African-American populations (Caribbean: 29 per 100,000 and sub-Saharan Africa age-standardized

***Corresponding author:** Pahwa P, Canadian Centre for Health and Safety in Agriculture (CCHSA), University of Saskatchewan, Saskatoon, Saskatchewan, Canada, Tel: 306-966-8300; E-mail: pup165@mail.usask.ca

**Received:** July 27, 2016; **Accepted:** August 22, 2016; **Published:** August 31, 2016

**Citation:** Sharma M, Lawson J, Karunanayake C, Dosman JA, Punam P (2016) Prostate Cancer, Farming and Other Risk Factors: A Mini Review. J Pros Canc 1: 109.

**Copyright:** © 2016 Sharma M, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

rates (ASR): 19-24 per 100,000), very low in Asian populations (ASR: 2.9 per 100,000 in south central Asia) [2]. The mortality rates were highest in Sweden (approximately 25 per 100,000) followed by Zimbabwe, Netherlands and USA [37].

In 2000, Grover et al. [38] projected that (i) in the 1997 cohort of 5.8 million Canadian men between 40 and 80 years old (non-cases), prostate cancer would be diagnosed in 12.1% of Canadian men over their life-time and would be fatal in 3% to 4% cases and (ii) lifetime costs of care will total $9.76 billion. They also estimated a total cost of $286 million to be annually associated with treating prostate cancer in this cohort in 2022. Quon et al. [39] estimated that in future, incidence rates will increase from 25,355 new cases in 2009 to 35,121 new cases by 2021.

## Risk factors and etiology

To date, only three potential risk factors have been well established including age generally over 65 years, race particularly African-Americans and family history of prostate cancer [6,7,40]. According to the Canadian Cancer Society, not every adult male having these risk factors necessarily develops prostate cancer but having these risk factors means it increases the chance of developing it [40]. It can be said that all three established risk factors are non-modifiable risk factors. Given that there are very few well established risk factors of prostate cancer, environmental/farming related exposures and lifestyle factors requires further investigation [10]. The literature calls for more research on the relationship between farming and cancer to identify environmental carcinogens and specific high-risk groups. Both environmental and genetic factors may play a role in the development of prostate cancer [6].

**Age:** Age is known to be a significant risk factor for prostate cancer. As cited by Quinn and Babb [37], globally three-quarters of cases occurred in men aged ≥ 65 years. Very few people aged younger than 50 years are diagnosed with prostate cancer [8,35,41]. The mean age of prostate cancer cases is 72-74 years and nearly 85% of cases are diagnosed after 65 years of age [7]. The incidence rates of prostate cancer increases with advancing age [6]. In countries like USA, Australia, Sweden, UK, Italy, Japan, Hong Kong and China, incidence rates rose exponentially with advancing age [41]. As cited by Fradet et al. [42] in the year 2008 the rate of prostate cancer diagnoses in Canada was approximately 100 per 100,000 in men aged 50 to 54, 500 per 100,000 men aged 60 to 64 and greater than 700 per 100,00 in men over the age of 80. The incidence rates began to rise in 45-49 years of age group and sharply continued to increase until 65-69 years of age group after which the rates were more or less similar in the age groups after age 70 [42].

Based on evidence from the scientific literature, prostate cancer is very rare among men aged <50 years. However, an American study with large sample size identified some cases of prostate cancer in these men [43]. It consisted of men aged 35-74 years diagnosed with prostate cancer between 1988 and 2003 and identified 1,673 cases (that included grade-low, intermediate and high; Stage I or II, III and IV) of prostate cancer in the youngest age group of 35-44 years. Even though the number was small as compared to the total number (181,099) of men in the age group 65-74 years, it suggested that the investigators must consider this youngest age group seriously in the future studies.

**Race:** The risk of developing prostate cancer is dramatically higher among African-American men compared to men of any other race [7]. This population has the highest incidence rates in the world, nearly 60 times greater than the men in Shanghai, China where rates are lowest [41].

For the period 2009-2013, race-specific incidence rates in the United States ranged from 203.5 per 100,000 for African-American, 121.9 per 100,000 for Caucasians, 106.9 per 100,000 for Hispanics, 68.9 per 100,000 for Asian/Pacific Islanders, and 63.9 per 100,000 for American/Alaskan natives [44].

African Americans have approximately twice the mortality than that of Caucasians. It is yet uncertain whether the differences in death rates can be clarified by differences in stage at diagnosis, socio-economic status or biology of prostate cancer among men from different races. It appears that the interactions between genetic and environmental factors could elucidate these biological explanations [45].

Consumption of dietary fat is also under scrutiny as it is higher among African Americans [46]. As cited by Bostwick et al. [46] the rates of prostate cancer shift toward those of the host country. For instance, Japanese men who consume a low fat diet have low incidence rates of prostate cancer in their country. However, the incidence and mortality risk increases when they move to United States.

**Family history of prostate cancer:** One of the most consistent and strongest risk factors that have been associated with an increased risk of prostate cancer is family history of prostate cancer. The risk of early onset of prostate cancer is considered to be strongly affected by the number of relatives with prostate cancer and their age at diagnosis [47]. Numerous studies have reported familial congregation, showing men who have first-degree male relatives (father, brother, son) with a positive history of prostate cancer have 2 to 3 fold elevated risk [6]. Epidemiological studies provide an indication that inherited susceptibility genes cause 5% to 10% of all prostate cancer cases, and 30% to 40% of early onset disease [47]. In a population based case-control study of prostate cancer, cases and controls were interviewed as to their family history of prostate cancer. The study provided further evidence of familial congregation and suggested the possibility that part or all of such clustering could be related to inherited genetic patterns [48].

As cited by Fradet et al. [42] according to the United States National Institutes of Health in 2008, men whose fathers had prostate cancer before age 60 years have a 20% chance of developing prostate cancer as compared with 8% of men without this history. A slightly greater risk was observed for men whose brothers had prostate cancer than for those whose fathers had prostate cancer. A population based case-control study was conducted among Caucasians, African-Americans and Asian-Americans in United States of America and Canada. The results of this study suggested that in each of the ethnic groups, positive family history was associated with 2 to 3 fold statistically significant increased risk [49]. A study consisted of 44,788 twin pairs who were listed in Swedish, Danish and Finnish twin registries found that these inherited factors made a small contribution to susceptibility to prostate cancer. It also indicated that environment played the crucial role in causing sporadic cancer [42].

Race/ethnicity has been widely used in conducting research involving genetics [50]. Biological explanations of the difference between ethnic groups could involve genetic factors [45]. Pahwa et al. [51] suggested that race/ethnicity correlates with increased genetic homogeneity among people of similar identity. A review by Powell indicated that compared to European-American men, prostate cancer is biologically and genetically more aggressive in African-Americans [52].

**Cigarette smoking:** Smoking is considered to be a risk factor for several cancers. However, the association between smoking and prostate cancer remains a debatable matter [20,21]. As reviewed by Huncharek et al. [21], in a meta-analysis of 24 prospective cohort studies, the authors concluded that with more than 26,000 prostate

cancer cases, 9% to 30% increase in both new and mortality specific prostate cancer was associated with smoking. On the contrary, no association was observed between current or former smoking status and prostate cancer incidence [22,23].

Data from large epidemiological studies observed that cigarette smoking is related to prostate cancer mortality [20,21,23]. Moreover, some evidence showed a dose-response relationship between cigarette smoking and prostate cancer mortality [24]. Smokers who smoked more than 40 cigarettes per day had 51% increased prostate cancer mortality risk. In another prospective cohort study, compared with non-smokers, current smokers had 61% increased risk of dying from prostate cancer [25].

Another study that examined whether cigarette smoking affected the risk of prostate cancer was a prospective US cohort study [20]. The study population consisted of men aged 50 to 71 years. Prostate cancer cases were classified into one of the three groups namely non-advanced, advanced and fatal. The results of the study suggested that current smoking and former smoking had decreased risk of non-advanced prostate cancer. However, when compared with non-smokers, current smokers seemed to be associated with an increased risk of fatal prostate cancer.

Another case-control study investigated the relationship between smoking at the time of diagnosis and risk of prostate cancer death [26]. A population based cohort of prostate cancer cases aged 40-64 years were included in the study. After adjusting for age, race, education etc., the study found that compared to the cases who never smoked, cases who smoked at the time of diagnosis had a 2.66 relative hazard of prostate cancer-specific mortality.

**Farming occupation and pesticide exposure:** One of the probable factors that are under scrutiny in literature includes occupation and occupational exposures. In the past, some studies have found associations between occupation and prostate cancer incidence and mortality [11,53]. Of these, farming has received greater attention [9,12]. In 1999, the occupational cancer patterns among males in British Columbia who died of prostate cancer between 1950 and 1984 were investigated. This included a review of 216 occupations and 88 industries. One of the findings of this study suggested that farmers were at higher risk of developing prostate cancer [49]. However, a review article suggested that it cannot be affirmed with certainty that farmers have an increased risk of developing prostate cancer [9]. An elevated risk of prostate cancer among farmers has been investigated in some studies, however no specific associations with agricultural chemicals (pesticides) have been found. The results of one study stated that, as compared to unexposed farmers, farmers who were exposed to pesticides had a two-fold excess risk [13].

Some of the studies that found a positive association between prostate cancer and farming related exposures such as pesticides are discussed in this paragraph. A recent study has shown that workplace exposure to insecticides and fungicides together were associated with prostate cancer in rural Saskatchewan population, Canada [54]. A retrospective cohort study of Canadian men found a statistically significant association with herbicides and prostate cancer mortality among farmers [55]. An Italian study evaluated the relationship among rural farmers and found that farmers who were exposed to organochlorine insecticides and acaricides were at a high risk of developing prostate cancer [14]. Therefore, it is possible that such pesticides could contribute to the increased risk and should be further investigated in a different population [14]. A recent population based case-control study [15] in California investigated the association between environmental pesticide/fungicide exposure and prostate cancer. California is considered the most productive agricultural state in the United States of America and each year the use of agricultural pesticides in California exceeds 250 million pounds of active ingredients. The study provided the evidence that in and around homes in huge agricultural settings, an association between prostate cancer and ambient pesticide exposure to methyl bromide and organochlorines was observed. The researchers also suggested that the associations seem precise to compounds (methyl bromide, capton and organochlorines) with a possible biologic role in prostate carcinogenesis [15]. The considerable association between prostate cancer and farming related exposure (such as DDT, simazine and lindane) was observed among farmers in British Columbia [16]. A review conducted by Mink et al. [17] suggested that, of eight cohorts and five case-control studies none of them were able to illustrate an increase in risk to support a causal relationship between agricultural pesticide exposure and prostate cancer. Few other studies including systematic reviews have concluded that a possible association exists between prostate cancer risk and exposure to pesticides such as organophosphate insecticides, organochlorine insecticide Aldrin and chlorinated pesticides [56-58]. Some important interactions between family history and pesticides have also been observed [56,59]. Based on the scientific literature, farming and its occupational exposures such as insecticides, herbicides and fungicides might be related to prostate cancer.

**Other modifiable factors:** The role of diet as an individual risk factor in the development of prostate cancer has been investigated in the past [27-29,60,61]. Some studies [29,60,61] but not all [27,62,63] provide evidence suggesting such relationship. A typical western diet having an increased fat deposits and cholesterol levels increases development of prostate cancer [7,32,60]. Consumption of processed meat and fish [61], dairy products especially milk [29,64], fat from red meat [65] increased the risk of prostate cancer. Heavy alcohol drinkers and binge drinkers may be at a higher risk of prostate cancer [66,67]. Other large cohort studies did not find the similar association between alcohol and prostate cancer [68,69] and other beverages including tea and cola consumption [70]. According to Parent and Siemiatycki [9], lifestyle and occupation of an individual are linked together. For instance, in farming occupation Iowa farmers had different lifestyles including smoking, alcohol drinking and consumption of calories etc. as compared to non-farmers. Therefore, researchers propose considering lifestyle as a confounding issue to estimate the risk of prostate cancer [9].

Systematic reviews and meta-analyses have shown a positive link between obesity and advanced prostate cancer [30,31]. Increased body mass index has been associated with risk of prostate cancer [31,71-73]. Allott et al. [30] reviewed this epidemiologic association and suggested that increased weight is dangerous for prostate cancer and encouraged weight loss counselling with incident cases for overweight and obese men.

On the contrary, other studies observed no such associations with body mass and physical activity [32,33]. A prospective cohort study of U.S. men observed no difference in risk of prostate cancer between men who engaged in the highest level of recreational physical activity and those who reported no recreational physical activity [33].

Diet including fat intake, consumption of alcohol and other beverages, obesity and physical activity has been extensively investigated in relation to prostate cancer, yet conclusions on the direction of the association seem oblique.

## Conclusion

Prostate cancer is a major public health problem and its burden will continue to increase in future. Age, race/ethnicity, family history of cancer is the well-established risk factors of prostate cancer. Identifying other risk factors such as lifestyle (for example smoking) and occupation (for example farming) will help direct investigation into the underlying etiology of prostate cancer and help focus future prevention efforts.

### References

1. http://www.who.int/mediacentre/factsheets/fs297/en/
2. http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx
3. http://www.cancer.ca/en/cancer-information/cancer-type/prostate/overview/?region=sk
4. http://www.cancer.ca/en/cancer-information/cancer-type/prostate/finding-cancer-early/?region=sk
5. http://www.cancer.ca/en/cancer-information/cancer-type/prostate/statistics/?region=sk
6. Hsing AW, Chokkalingam AP (2006) Prostate cancer epidemiology. Front Biosci 11: 1388-1413.
7. Grönberg H (2003) Prostate cancer epidemiology. The Lancet 361: 859-864.
8. Crawford ED (2003) Epidemiology of prostate cancer. Urology 62: 3-12.
9. Parent ME, Siemiatycki J (2001) Occupation and prostate cancer. Epidemiol Rev 23: 138-143.
10. Sass-Kortsak AM, Purdham JT, Kreiger N, Darlington G, Lightfoot NE (2007) Occupational risk factors for prostate cancer. Am J Ind Med 50: 568-576.
11. Aronson KJ, Siemiatycki J, Dewar R, Gérin M (1996) Occupational risk factors for prostate cancer: results from a case-control study in Montreal, Quebec, Canada. Am J Epidemiol 143: 363-373.
12. van der Gulden J, Vogelzang P (1996) Farmers at risk for prostate cancer. Br J Urol 77: 6-14.
13. Parent ME, Desy M, Siemiatycki J (2009) Does exposure to agricultural chemicals increase the risk of prostate cancer among farmers? McGill J Med 12: 70-77.
14. Settimi L, Masina A, Andrion A, Axelson O (2003) Prostate cancer and exposure to pesticides in agricultural settings. Int J Cancer 104: 458-461.
15. Cockburn M, Mills P, Zhang X, Zadnick J, Goldberg D, et al. (2011) Prostate cancer and ambient pesticide exposure in agriculturally intensive areas in California. Am J Epidemiol 173: 1280-1288.
16. Band PR, Abanto Z, Bert J, Lang B, Fang R, et al. (2011) Prostate cancer risk and exposure to pesticides in British Columbia farmers. Prostate 71: 168-183.
17. Mink PJ, Adami HO, Trichopoulos D, Britton NL, Mandel JS (2008) Pesticides and prostate cancer: a review of epidemiologic studies with specific agricultural exposure information. Eur J Cancer Prev 17: 97-110.
18. Coble J, Hoppin JA, Engel L, Elci OC, Dosemeci M, et al. (2002) Prevalence of exposure to solvents, metals, grain dust, and other hazards among farmers in the Agricultural Health Study. J Expo Anal Environ Epidemiol 12: 418-426.
19. Fritschi L, Glass DC, Tabrizi JS, Leavy JE, Ambrosini GL (2007) Occupational risk factors for prostate cancer and benign prostatic hyperplasia: a case-control study in Western Australia. Occup Environ Med 64: 60-65.
20. Watters JL, Park Y, Hollenbeck A, Schatzkin A, Albanes D (2009) Cigarette smoking and prostate cancer in a prospective US cohort study. Cancer Epidemiol Biomarkers Prev 18: 2427-2435.
21. Huncharek M, Haddock KS, Reid R, Kupelnick B (2010) Smoking as a risk factor for prostate cancer: a meta-analysis of 24 prospective cohort studies. Am J Public Health 100: 693-701.
22. Butler LM, Wang R, Wong AS, Koh WP, Yu MC (2009) Cigarette smoking and risk of prostate cancer among Singapore Chinese. Cancer Causes Control 20: 1967-1974.
23. Rohrmann S, Genkinger JM, Burke A, Helzlsouer KJ, Comstock GW, et al. (2007) Smoking and risk of fatal prostate cancer in a prospective U.S. study. Urology 69: 721-725.
24. Hsing AW, McLaughlin JK, Hrubec Z, Blot WJ, Fraumeni JF (1991) Tobacco use and prostate cancer: 26-year follow-up of US veterans. Am J Epidemiol 135: 437-441.
25. Kenfield SA, Stampfer MJ, Chan JM, Giovannucci E (2011) Smoking and prostate cancer survival and recurrence. JAMA 305: 2548.
26. Gong Z, Agalliu I, Lin DW, Stanford JL, Kristal AR (2008) Cigarette smoking and prostate cancer-specific mortality following diagnosis in middle-aged men. Cancer Causes Control 19: 25-31.
27. Alexander DD, Mink PJ, Cushing CA, Sceurman B (2010) A review and meta-analysis of prospective studies of red and processed meat intake and prostate cancer. Nutr J 9: 50.
28. Kristal AR, Arnold KB, Neuhouser ML, Goodman P, Platz EA, et al. (2010) Diet, supplement use, and prostate cancer risk: results from the prostate cancer prevention trial. Am J Epidemiol 172: 566-577.
29. Raimondi S, Mabrouk JB, Shatenstein B, Maisonneuve P, Ghadirian P (2010) Diet and prostate cancer risk with specific focus on dairy products and dietary calcium: a case-control study. Prostate 70: 1054-1065.
30. Allott EH, Masko EM, Freedland SJ (2013) Obesity and prostate cancer: weighing the evidence. Eur Urol 63: 800-809.
31. Cao Y, Ma J (2011) Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila) 4: 486-501.
32. Whittemore AS, Kolonel LN, Wu AH, John EM, Gallagher RP, et al. (1995) Prostate cancer in relation to diet, physical activity, and body size in blacks, whites, and Asians in the United States and Canada. J Natl Cancer Inst 87: 652-661.
33. Patel AV, Rodriguez C, Jacobs EJ, Solomon L, Thun MJ, et al. (2005) Recreational physical activity and risk of prostate cancer in a large cohort of U.S. men. Cancer Epidemiol Biomarkers Prev 14: 275-279.
34. Coory MD, Baade PD (2005) Urban-rural differences in prostate cancer mortality, radical prostatectomy and prostate-specific antigen testing in Australia. Med J Aust 182: 112-115.
35. Baade PD, Youlden DR, Krnjacki LJ (2009) International epidemiology of prostate cancer: geographical distribution and secular trends. Mol Nutr Food Res 53: 171-184.
36. Siegel RL, Miller KD, Jemal A (2015) Cancer statistics, 2015. CA Cancer J Clin 65: 5-29.
37. Quinn M, Babb P (2002) Patterns and trends in prostate cancer incidence, survival, prevalence and mortality. Part I: international comparisons. BJU Int 90: 162-173.
38. Grover SA, Coupal L, Zowall H, Rajan R, Trachtenberg J, et al. (2000) The economic burden of prostate cancer in Canada: forecasts from the Montreal Prostate Cancer Model. Can Med Assoc J 162: 987-992.
39. Quon H, Loblaw A, Nam R (2011) Dramatic increase in prostate cancer cases by 2021. BJU Int 108: 1734-1738.
40. http://www.cancer.ca/en/cancer-information/cancer-type/prostate/risks/?region=sk
41. Hsing AW, Tsao L, Devesa SS (2000) International trends and patterns of prostate cancer incidence and mortality. Int J Cancer 85: 60-67.
42. Fradet Y, Klotz L, Trachtenberg J, Zlotta A (2009) The burden of prostate cancer in Canada. Can Urol Assoc J 3: S92.
43. Lin DW, Porter M, Montgomery B (2009) Treatment and survival outcomes in young men diagnosed with prostate cancer: a Population-based Cohort Study. Cancer 115: 2863-2871.
44. http://www.seer.cancer.gov/statfacts/html/prost.html
45. Gann PH (2002) Risk factors for prostate cancer. Rev Urol 4: S3-S10.
46. Bostwick DG, Burke HB, Djakiew D, Euling S, Ho S, et al. (2004) Human prostate cancer risk factors. Cancer 101: 2371-2490.
47. Bratt O (2002) Hereditary prostate cancer: clinical aspects. J Urol 168: 906-913.

48. Ghadirian P, Howe G, Hislop T, Maisonneuve P (1997) Family history of prostate cancer: a multi-center case-control study in Canada. Int J Cancer 70: 679-681.

49. Whittemore AS, Wu AH, Kolonel LN, John EM, Gallagher RP, et al. (1997) Family history and prostate cancer risk in black, white, and Asian men in the United States and Canada. Am J Epidemiol 141: 732-740.

50. Sankar P, Cho MK, Mountain J (2007) Race and ethnicity in genetic research. Am J Med Genet A 143 :961-970.

51. Pahwa P, Karunanayake CP, Spinelli JJ, Dosman JA, McDuffie HH (2009) Ethnicity and incidence of Hodgkin lymphoma in Canadian population. BMC Cancer 9: 1.

52. Powell IJ (2011) The precise role of ethnicity and family history on aggressive prostate cancer: a review analysis. Arch Esp Urol 64: 711-719.

53. Buxton JA, Gallagher RP, Le ND, Band PR, Bert JL (1999) Occupational risk factors for prostate cancer mortality in British Columbia, Canada. Am J Ind Med 35: 82-86.

54. Sharma M, Lawson JA, Kanthan R, Karunanayake C, Hagel L, et al. (2016) Factors associated with the prevalence of prostate cancer in rural Saskatchewan: the Saskatchewan rural health study. J Rural Health 32: 125-135.

55. Morrison H, Savitz D, Semenciw R, Hulka B, Mao Y, et al. (1993) Farming and prostate cancer mortality. Am J Epidemiol 137: 270-280.

56. Alavanja MC, Samanic C, Dosemeci M, Lubin J, Tarone R, et al. (2003) Use of agricultural pesticides and prostate cancer risk in the Agricultural Health Study cohort. Am J Epidemiol 157: 800-814.

57. Koutros S, Beane Freeman LE, Lubin JH, Heltshe SL, Andreotti G, et al. (2013) Risk of total and aggressive prostate cancer and pesticide use in the Agricultural Health Study. Am J Epidemiol 177: 59-74.

58. Silva JF, Mattos IE, Luz LL, Carmo CN, Aydos RD (2013) Exposure to pesticides and prostate cancer: systematic review of the literature. Rev Environ Health 2016.

59. Lewis-Mikhael AM, Bueno-Cavanillas A, Ofir Guiron T, Olmedo-Requena R, Delgado-Rodriguez M, et al. (2016) Occupational exposure to pesticides and prostate cancer: a systematic review and meta-analysis. Occup Environ Med 73: 134-144.

60. Llaverias G, Danilo C, Wang Y, Witkiewicz AK, Daumer K, et al. (2010) A Western-type diet accelerates tumor progression in an autochthonous mouse model of prostate cancer. AJP 177: 3180-3191.

61. Vlajinac H, Ilic M, Marinkovic J, Sipetic S (2010) Nutrition and prostate cancer. JBUON 15: 698-703.

62. Key TJ, Silcocks PB, Davey GK, Appleby PN, Bishop DT (1997) A case-control study of diet and prostate cancer. Br J Cancer 76: 678-687.

63. Severson RK, Nomura AM, Grove JS, Stemmermann GN (1989) A prospective study of demographics, diet, and prostate cancer among men of Japanese ancestry in Hawaii. Cancer Res 49: 1857-1860.

64. Chan JM, Stampfer MJ, Ma J, Gann PH, Gaziano JM, et al. (2001) Dairy products, calcium, and prostate cancer risk in the Physicians' Health Study. Am J Clin Nutr 74: 549-554.

65. Giovannucci E, Rimm EB, Colditz GA, Stampfer MJ, Ascherio A, et al. (1993) A prospective study of dietary fat and risk of prostate cancer. J Natl Cancer Inst 85: 1571-1579.

66. Dickerman BA, Markt SC, Koskenvuo M, Pukkala E, Mucci LA, et al. (2016) Alcohol intake, drinking patterns, and prostate cancer risk and mortality: a 30-year prospective cohort study of Finnish twins. Cancer Causes Control 27: 1049-1058.

67. Rizos C, Papassava M, Golias C, Charalabopoulos K (2010) Alcohol consumption and prostate cancer: a mini review. Exp Oncol 32: 66-70.

68. Platz EA, Leitzmann MF, Rimm EB, Willett WC, Giovannucci E (2004) Alcohol intake, drinking patterns, and risk of prostate cancer in a large prospective cohort study. Am J Epidemiol 159: 444-453.

69. Velicer CM, Kristal A, White E (2006) Alcohol use and the risk of prostate cancer: results from the VITAL cohort study. Nutr Cancer 56:50-56.

70. Ellison LF (2000) Tea and other beverage consumption and prostate cancer risk: a Canadian retrospective cohort study. Eur J Cancer Prev 9: 125-130.

71. Discacciati A, Orsini N, Wolk A (2012) Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol 23: 1665-1671.

72. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M (2008) Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. The Lancet 371: 569-578.

73. Gong Z, Agalliu I, Lin DW, Stanford JL, Kristal AR (2007) Obesity is associated with increased risks of prostate cancer metastasis and death after initial cancer diagnosis in middle-aged men. Cancer 109: 1192-1202.