Effect of Plant- and Animal-Based Foods on Prostate Cancer Risk

John Shin, MD; Denise Millstine, MD; Barbara Ruddy, MD; Mark Wallace, MD; Heather Fields, MD

From the Division of Hematology in the Department of Internal Medicine and the Department of Medical Oncology at the Mayo Clinic in Rochester, Minnesota (Dr Shin); the Division of Women's Health Internal Medicine (Dr Millstine) and the Division of Community Internal Medicine in the Department of Medicine (Drs Ruddy, Wallace, and Fields) at the Mayo Clinic in Scottsdale, Arizona.

Financial disclosures: None reported.

Support: None reported.

Address correspondence to John Shin, MD, Mayo Clinic, Medical Oncology/Hematology, 200 First St SW, Rochester, MN, 55905-0001. Email: shin.john@mayo.edu

Submitted November 28, 2019; final revision received April 29, 2019; accepted May 10, 2019.

Context: Many studies have explored whether plant and animal-based food consumption is associated with prostate cancer (PCa) risk, but there is much discordance.

Objective: To perform an updated review of the literature that further investigates the association of plant- and animal-based food consumption with PCa risk.

Methods: This review was conducted by using 3 databases and produced a total of 550 references. The search was limited to a publication date range of 2006 to February 2017, English language, and humans. After case reports, comments, letters, editorials, and duplicate references were removed, 297 citations remained for review. Articles that did not investigate the association of dietary patterns or a major component of diet with PCa were excluded.

Results: Of the 297 references found, 47 were eligible for inclusion in this review. The authors identified 2 very large cohort studies (≥100,000 participants), 6 large cohort studies (≥40,000 participants), 11 medium cohort studies (≥10,000 participants), 10 small cohort studies (<10,000 participants), 13 case-control studies, 4 meta-analyses, and 1 population study investigating diet and PCa risk. Most studies showed that plant-based foods are associated with either decreased or unchanged risk of PCa, whereas animal-based foods, particularly dairy products, are associated with either increased or unchanged risk of PCa.

Conclusion: This review of the literature suggests that consumption of higher amounts of plant-based foods may be associated with decreased PCa risk, and consumption of higher amounts of dairy products may be associated with increased PCa risk.

J Am Osteopath Assoc. 2019;119(11):736-746. Published online October 21, 2019. doi:10.7556/jaoa.2019.123

Keywords: animal-based foods, dairy, plant-based foods, prostate cancer

In the United States, the lifetime risk of prostate cancer (PCa) is 11.6%,[1] which has the highest incidence and second highest mortality rate of all cancers in men.[2] Previous studies[3-6] have shown that increased consumption of animal products is associated with increased PCa risk. One 2001 review[3] found that 16 of 22 studies showed a positive correlation between meat intake and PCa risk. Eight studies in this review assessed red meat intake separately, and all but 1 showed a correlation with increased risk of PCa. Other studies[4-6] have shown a correlation between dairy consumption and increased PCa risk.

These associations are likely related to a multitude of factors. With regard to meat, the formation of heterocyclic amines during high-temperature cooking, hormonal effects,[7] other nutrient components,[3,8] and the relatively lower levels of anticarcinogenic compounds found in meats compared with plants are all likely implicated. Many of these factors may also be implicated in dairy products. For instance, animal protein and dairy intake is associated with elevated insulinlike growth factor 1, which is associated with elevated PCa risk.[9-16] Additionally, dairy has implications distinct from other animal products. Prostate cancer cellular proliferation and invasiveness is inhibited by calcitriol,[17] but increased calcium intake suppresses the formation of calcitriol. Increased calcium intake and low levels of vitamin D are associated with increased PCa risk.[18] Dairy products are the primary source of calcium in Western countries.[19] In countries in which the intake of dairy products is high, PCa rates are high.[20] In Asian countries, in which intake of dairy products is low, PCa rates are low.[21]

A growing body of evidence suggests there may be an association between plant-based diets and decreased PCa risk. The decreasing mortality rates in the United States for several common cancers, including PCa, coincides with decreased meat and dairy intake and increased plant-based food consumption.[22] The widespread implementation of cancer-screening initiatives such as prostate-specific antigen testing possibly contributes to this decrease in mortality but is unlikely to be the sole explanation for the trend. A large epidemiologic study[23] in 1981 estimated that 35% of all cancer could be attributed to dietary causes, and a 2015 review[24] of this landmark report found its estimates to be generally true in the 21st century. One randomized clinical trial[25] studied men with known low-grade PCa who declined standard therapy. The trial found that after being exposed to a year of lifestyle interventions consisting of a vegan diet, exercise, and stress management techniques, the prostate-specific antigen of men in the experimental group decreased, whereas it increased in the control group. Studies reviewed by Kristal and Lampe[26] showed an association between increased consumption of certain vegetables and decreased PCa risk. It is because of these correlations that we sought to review the current literature for the association of dietary patterns and PCa risk.

Methods

We searched Ovid MEDLINE, PubMed, and Embase databases with the following keywords: prostate cancer, dairy products, milk, yogurt, vegetarian diet, vegan diet, lacto-ovo-vegetarian, semi-vegetarian, pesco-vegetarian, and plant-based diet. We used the following search criteria: date range from 2006 to February 2017, English language, and human participants. We found 550 relevant articles and then removed case reports, comments, letters, editorials, and duplicate citations. A total of 297 references remained for review. References and abstracts were divided among authors for review, and articles that did not investigate the association of dietary patterns or a major component of diet with PCa were excluded. The initial decision to exclude an article was made by the reviewing author, and this decision was upheld if all authors agreed. Examples of excluded articles included those studying silibinin, milk thistle, prostate stromal protein 20, soy protein isolate, phytanic acid, meroterpenoids, acai juice, vitamin K, choline, and dietary flavonoids such as cranberry proanthocyanidins. Finally, data were grouped according to study design (prospective cohort vs case-control) and study size (very large, ≥100,000; large, 40,000-99,999; medium, 10,000-39,999; and small, <10,000 participants) for analysis.

Results

We selected 47 articles for inclusion in this review based on the criteria described in the Methods section. These articles included 2 very large cohort studies (XL), 6 large cohort studies (L), 11 medium cohort studies (M), 10 small cohort studies (S), 13 case-control studies, 4 meta-analyses, and 1 population study. All

Table.
Breakdown of the 28 Included Prostate Cancer and Food Consumption Cohort Studies Listed According to Size

Studies	Cohort Size	PCa Cases (n)	Mean Follow-up, y
Very Large Cohort Studies (≥100,000)			
Park et al[59] (2007)	293,888	10,180	6
Gonzalez et al[29] (2010)	153,457	2727	8.7
Large Cohort Studies (≥40,000)			
Stram et al[34] (2006)	82,486	3922	7
Park et al[58] (2007)	82,483	4404	8
Giovannucci et al[75] (2006)	47,750	3544	16
Wu et al[69] (2006)	47,725	3002	14
Takachi et al[35] (2010)	43,475	339	7.4
Kurahashi[52] (2008)	43,435	329	7.5
Medium Cohort Studies (≥10,000)			
Kirsh et al[32] (2007)	29,361	1338	4.2
Mitrou et al[57] (2007)	29,133	1267	17
Butler et al[74] (2010)	27,293	298	11
Egeberg et al[38] (2011)	26,691	1081	12
Tantamango-Bartley et al[30] (2016)	26,346	1079	7.8
Song et al[53] (2013)	21,660	2806	28
Key et al[28] (2014)	15,594	457	14.9
Umesawa et al[37] (2014)	15,471	143	16
Key et al[27] (2009)	12,230	235	10
Neuhouser et al[47] (2007)	12,025	890	11
Koh et al[56] (2006)	10,011	815	10
Small Cohort Studies (<10,000)			
Gilsing et al[31] (2016)	4465	399	20.3
Pettersson et al[60] (2012)	3918	229 (PCa deaths)	7.6
Rohrmann et al[48] (2007)	3892	199	13
Diallo et al[36] (2016)	3313	139	12.6
Kesse et al[54] (2006)	2776	69	7.7
van der Pols et al[61] (2007)	2159	41	65
Chan et al[33] (2006)	1202	392 (PCa progression)	6
Wilson et al[67] (2016)	971	94	3
Yang et al[55,70] (2015)	926	56 (PCa deaths)	9.9

Abbreviation: PCa, prostate cancer.

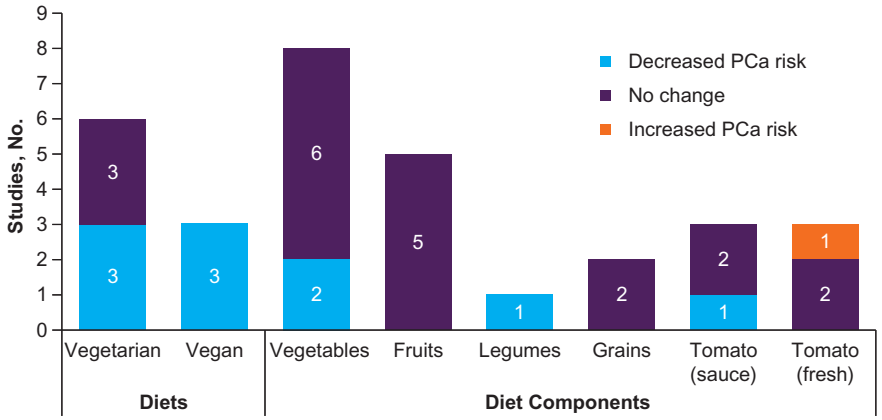

Figure 1.
Associations between various plant-based foods and prostate cancer risk based on 28 cohort study findings.
Abbreviation: PCa, prostate cancer.

CIs displayed are at the 95% level. The breakdown of the included cohort studies is listed according to size in the **Table**.

Plant-Based Foods

Ten prospective cohort studies, 5 case-control studies, and 1 meta-analysis were reviewed for the effect of plant-based foods on PCa risk. These results are summarized in **Figure 1** and **Figure 2**. Of the 5 prospective cohort studies that investigated the effects of a vegetarian diet, 2 showed an association with decreased incidence of all cancers, which included PCa (relative risk [RR], 0.89; 95% CI, 0.83-0.96, M study)[27,28] while 3 showed no change in risk.[29-31] Three studies[27,28,30] also examined vegan diets, and all 3 found an association with decreased PCa risk (RR, 0.81; 95% CI, 0.66-0.98, M study)[27,28] (hazard ratio [HR], 0.64; 95% CI, 0.48-0.83, M study).[30]

Many cohort studies investigated the effects of specific plant-based food elements. For example, 8 studies[28,29,32-37] examined the effects of overall vegetable consumption, and 2 studies[28,32] found an

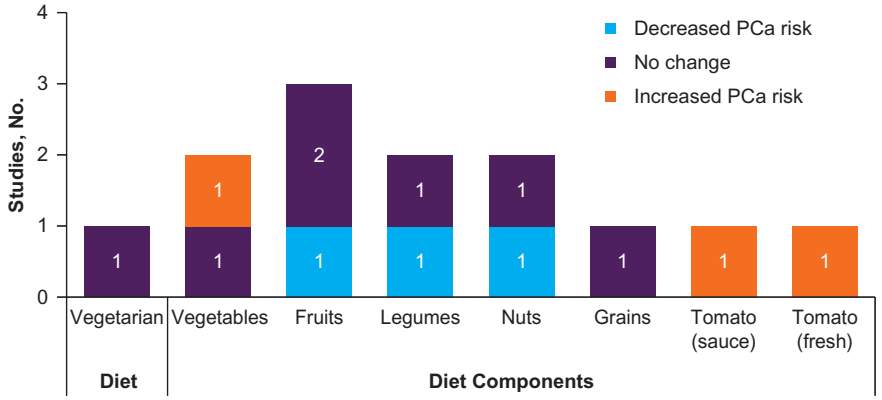

Figure 2.
Associations between various plant-based foods and prostate cancer risk based on case-control studies.
Abbreviation: PCa, prostate cancer.

association between increased vegetable intake and decreased PCa risk (RR, 0.81; 95% CI, 0.66-0.98, M study),[28] (RR, 0.41; 95% CI, 0.22-0.74, M study)[32] whereas 6 studies[29,33-37] found no difference in risk. Five studies[32-36] looked at the effects of fruit intake and found no significant difference in PCa risk. One cohort study[36] examined legumes and found an association with increased intake and decreased PCa risk (HR, 0.53; 95% CI, 0.34-0.85, S study). Two studies[33,38] looked at grains specifically and found no change in PCa risk. Three studies[33,34,36] looked at the effects of tomato sauce. One of these studies[33] found an association with increased intake of tomato sauce and decreased risk of PCa (HR, 0.56; 95% CI, 0.38-0.82, S study), and 2 studies[34,36] found no change in risk. These same studies[33,34,36] also looked at the effects of fresh tomatoes: 2 studies[34,36] found no difference in PCa risk, and 1 study[33] found an association of fresh tomato consumption with increased PCa risk (HR, 1.58; 95% CI, 1.10-2.25, S study). One meta-analysis[39] found that increased intake of soy was associated with reduced PCa risk (RR, 0.74; 95% CI, 0.63-0.89).

Of the case-control studies[40-44] reviewed, 1 study[40] found an association with decreased PCa risk and increased fruit consumption (odds ratio, [OR], 0.65; 95% CI, 0.45-0.92), and the other study[41] showed an association with decreased PCa risk and increased legume (OR, 0.4; 95% CI, 0.22-0.74) and nut (OR, 0.43; 95% CI, 0.22-0.85) consumption. One study[42] showed an association with increased risk of PCa and the consumption of vegetables (OR, 1.25; 95% CI, 1.05-1.50), tomato sauce, and fresh tomatoes (OR, 1.25; 95% CI, 0.99-1.59). Three studies[42-44] showed no significant change in PCa risk with the consumption of a vegetarian diet,[43] vegetables in particular,[44] fruits,[42,44] legumes,[42] nuts,[42] or grains.[42]

Meat

Six prospective cohorts, 4 case-control studies, 1 meta-analysis, and 1 population study were reviewed regarding the effect of meat and fish on PCa risk. A summary of these data along with the data for eggs and dairy are found in **Figure 3** and **Figure 4**. In a large population study,[45] meat intake was associated

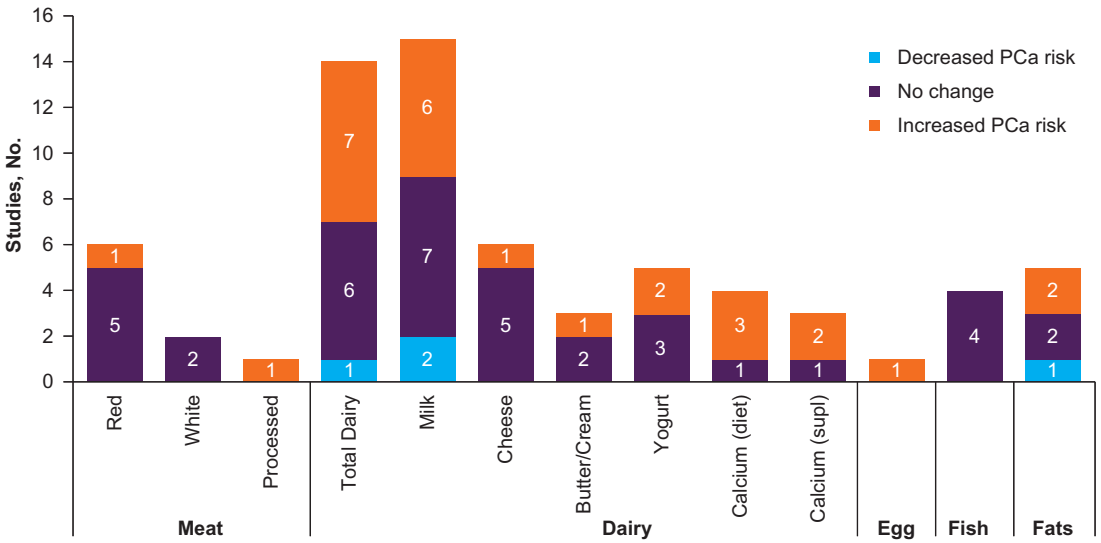

Figure 3.
Associations between various animal-based foods and prostate cancer risk based on cohort studies.
Abbreviation: PCa, prostate cancer

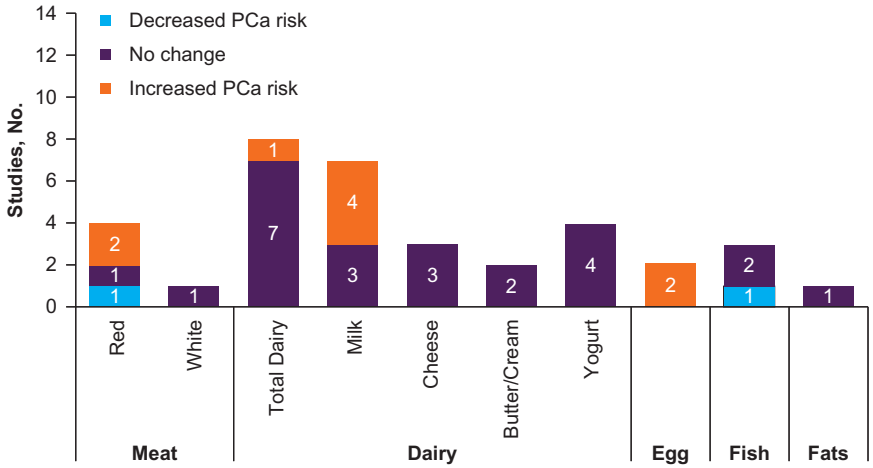

Figure 4.
Associations between various animal-based foods and prostate cancer risk based on case-control studies.
Abbreviation: PCa, prostate cancer.

with increased PCa mortality. Two prospective cohorts[28] showed no significant effect of eating meat on PCa incidence.

Red meat (beef, pork, or lamb) intake has been associated with increased PCa incidence.[46] Five studies[33,41,44,47,48] showed no effect. One prospective cohort[31] showed increased incidence of advanced PCa when eating meat once weekly compared with eating meat 6 to 7 days per week (HR, 1.75; 95% CI, 1.03-2.97, S study) but no association for all PCa. In one case-control study,[42] red meat intake was associated with decreased PCa (OR, 0.83; 95% CI, 0.70-0.99). Two case-control studies[40,49] found an increase in PCa among men in the highest tertile of red meat consumption compared with those in the lowest tertile of daily red meat consumption (OR, 1.68; 95% CI, 1.18-2.38 and RR, 1.43; 95% CI, 1.11-1.84, respectively).

Processed meat (eg, salted or smoked) was not associated with an increase in PCa in a meta-analysis of 4 prospective cohorts.[44] Regular sausage intake was associated with an increase in advanced PCa in a US cohort (HR, 2.83; 95% CI, 1.34-5.99, S study),[48] but no increase in PCa was found in a Canadian population.[41]

White meat, generally poultry, was not associated with increased PCa in 1 meta-analysis of 4 prospective cohorts,[44] 2 prospective cohorts,[31,48] and 1 case-control study.[41] Fish intake was not associated with change in incidence or outcomes in PCa in a meta-analysis of 4 prospective cohorts,[44] 4 prospective studies,[27,28,33,48] and 1 case-control study.[42] Another case-control study[41] showed a decrease in the incidence of PCa with fish intake in Canada (OR, 0.54; 95% CI, 0.30-0.97).

Dairy

Two meta-analyses, 14 prospective cohorts, and 8 case-control studies assessed the association of total dairy intake and PCa risk. Meta-analyses from Aun et al[50] and Qin et al[51] showed increased correlation with PCa (RR, 1.07; 95% CI, 1.02-1.12 and RR, 1.13; 95% CI, 1.02-1.24, respectively). Seven prospective cohorts were associated with increased risk (HR, 1.32; 95% CI, 1.01-1.72, XL study[29]; HR, 1.65; 95% CI, 1.02-2.66, S study[48]; RR, 1.63; 95% CI, 1.14-2.32, L study[52]; HR, 1.12; 95% CI, 0.93-1.35, M study[53]; RR, 1.35; 95% CI, 1.02-1.78, S study[54]; and HR, 1.76; 95% CI, 1.21-2.55, S study).[55] One study[38] reported no point estimate or CI. Six prospective cohorts[47,56-60] showed no correlation, and 1 prospective

cohort[61] showed a decreased risk when dairy was consumed during childhood (OR, 0.34; 95% CI, 0.11-1.04, S study). One case-control study[41] showed increased risk (OR, 2.19; 95% CI, 1.22-3.94), and 7 case-control studies[21,40,42,44,49,62,63] showed no association.

Increased risk of PCa with total milk consumption was found in 3 of 4 meta-analyses (RR, 1.03; 95% CI, 1.00-1.07,[50] RR, 1.13; 95% CI, 1.02-1.24,[51] and RR, 1.50; 95% CI, 1.03-2.17[64]); 6 of 15 prospective cohorts (RR, 1.34; 95% CI, 1.04-1.71, M study[5]; HR, 2.03; 95% CI, 1.12-3.70, S study[48]; RR, 1.53; 95% CI, 1.07-2.19, L study[52]; HR, 1.19; 95% CI, 1.06-1.33, M study[53]; HR, 1.76; 95% CI, 1.21-2.55, S study[55]; and RR, 1.23; 95% CI, 0.99-1.54, XL study[59]); and 4 of the 7 case-control studies (OR, 1.73; 95% CI, 1.16-2.39,[21]; OR, 2.01; 95% CI, 1.42-2.82[40]; OR, 2.27; 95% CI, 1.25-4.09[41]; and OR, 1.43; 95% CI, 1.09-1.88[62]). Two prospective cohorts[47,61] found a decreased risk of PCa (HR, 0.59; 95% CI, 0.40-0.85, M study[47] and OR, 0.34; 95% CI, 0.11-1.04, S study[61]), and the remaining studies that analyzed dairy consumption and PCa risk[44,49,54,57,58,60,63] found no association.

One of 2 meta-analyses (RR, 1.23; 95% CI, 0.94-1.61),[64] and 1 of 6 prospective cohort studies (HR, 1.43; 95% CI, 1.01-2.03, S study)[48] found increased risk of PCa with increased cheese intake. Five cohorts[52,54,57,58,60] and 3 case-control studies[41,44,62] showed no association. The case-control studies[41,44,62] that evaluated cheese and PCa risk found no association. One meta-analysis[64] showed no association between butter, cream, or yogurt and PCa risk. One cohort study[57] found increased risk for PCa with butter and cream consumption (RR, 1.11; 95% CI, 0.93-1.33, M study), and 2 cohort studies[58,60] found no association. Two cohort studies found an increased risk for PCa with yogurt consumption (RR, 1.52; 95% CI, 1.10-2.12, L study[52]; RR, 1.61; 95% CI, 1.07, 2.43, S study[54]), and 3 cohort studies[57,58,60] showed no association. No effect on PCa risk was found in the case-control studies that evaluated consumption of butter and cream[21,41] and yogurt.[21,41,44,62]

Eggs

Although 2 case-control studies (OR, 2.43; 95% CI, 1.70-3.48[40]; OR, 1.89; 95% CI, 1.15-3.10[65]) showed an association between egg consumption and PCa incidence and mortality, a review[66] of 9 cohort studies and 11 case-control studies performed prior to July 2012 did not find evidence to support an association. However, later studies (OR, 2.43; 95% CI, 1.70-3.48[40]; OR, 1.98; 95% CI, 1.08-3.63, S,[67]; and RR, 1.14; 95% CI, 1.01-1.28[68]) suggested an association between a higher intake of eggs and a higher risk of advanced PCa.

Mixed Diets

Studies examining whole dietary patterns have been limited and inconsistent. In one study,[69] Western dietary patterns (eg, processed and red meats, high-fat dairy, and refined grains) were not associated with increased PCa incidence, whereas another study[43] found an increased risk (OR, 1.82; 95% CI, 1.15-2.87). One cohort study[70] found an association of Western dietary patterns with a higher risk of PCa mortality (HR, 2.53; 95% CI, 1.00-6.42, S study). Prudent dietary patterns (vegetables, fruits, fish, legumes, whole grains) have not been associated with changes in incidence of PCa[69,43] nor PCa mortality.[70] Mediterranean diet patterns (whole grains, fruits, vegetables, low fat dairy, nuts, poultry, legumes, fish, olive oil) were not associated with PCa incidence in one study[42] but were associated with a lower incidence in another study[71] (OR, 0.22; 95% CI, 0.08-0.58).

Discussion

Our review of the literature found that the majority of prospective cohort studies investigating plant-based food consumption showed either no significant association or an association with decreased risk of PCa (**Figure 1**). This finding held true when a subset that included only the larger cohort studies (>10,000 participants) was considered. Only 1 study[33] showed a small elevation of PCa risk with the consumption of plant-

based food, specifically fresh tomatoes. However, this was an isolated finding, and other studies[72,73] indicated that tomato products, particularly when cooked, are associated with decreased PCa risk.

With regard to animal-based foods, the majority of prospective cohort studies demonstrated an association with either no change in risk or an increased risk of PCa (**Figure 3**). This finding was true for dairy products, and the pattern held when a subset of only the larger cohort studies were considered. In addition, 3 meta-analyses showed an association between dairy products and increased PCa risk.[50,51,64] Furthermore, increased intake of calcium also appeared to be associated with increased PCa risk.[18,57,74,75] Since dairy products are rich in calcium, this raises the possibility of calcium playing an important role in the link between dairy and PCa.

Strengths

This large review evaluated 47 studies comprising more than 1,000,000 participants. It was a comprehensive review of all available data since 2006 to get a broad perspective of the effects of current dietary patterns on PCa. We also looked at the effects of subsets of food categories, such as fruits, vegetables, nuts, legumes, whole grains, red meats, processed meats, white meats, milk, cheese, butter/cream, yogurt, and eggs. Many of the studies attempted to control for confounding nondietary lifestyle factors, such as smoking, exercise, and sun exposure by using multivariate Cox regression.[27,28,30,34] The systematic reviews attempted to control for publication bias and small study effects using funnel plot analysis via the Begg rank correlation test and the Egger regression test.[39,50,51,64]

Limitations

Our study had a number of limitations. First, despite the broad search and detailed method of data extraction, we did not include a meta-analysis with our systematic review because the significant heterogeneity found among the studies preclude meaningful quantitative analysis. Not only were several types of studies included (eg, systematic reviews, prospective cohorts, and case-control studies), but there was also significant heterogeneity within each subset. Second, epidemiologic data cannot prove causation, so any change in risk for PCa is by association and subject to confounding factors. For instance, people who follow more prudent diets are also less likely to smoke or drink alcohol and more likely to exercise. As with most observational nutrition studies, the presented data were primarily collected by dietary recall, which has inherent flaws. The effect of diet on PCa is also difficult to study because of the inherent indolence of the disease and variability in staging. Some of the studies looked at PCa incidence, whereas others looked at PCa mortality. Very few studies[47] tried to determine associations of diet with more aggressive forms of PCa. Even if more studies had looked at this factor, we would likely find the definition of aggressive cancer to be variable as well.

Future Research

One of the biggest obstacles in the field of dietary research is the lack of standardized methods for capturing and reporting diet and lifestyle data. However, despite the heterogeneity in methods and discordant conclusions found in the literature, our review shows that, in general, plant-based foods may be associated with a decreased risk of PCa, whereas dairy products may be associated with an increased risk of PCa. It would be helpful to test the validity of these findings through more randomized controlled trials such as the one conducted by Ornish et al.[25] There is also a need to better understand the possible effect of nondietary lifestyle factors, such as smoking and exercise, on PCa risk so that future dietary studies can better control for these factors.

Conclusion

Our review of the literature suggests that consumption of higher amounts of plant-based foods may be associated with decreased PCa risk, and the consumption of higher amounts of dairy products may be associated with

increased PCa risk. There does not appear to be a clear association between increased PCa risk and increased consumption of other types of animal-based foods, including red, white, or processed meat, fish, and eggs.

Author Contributions

All authors provided substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; all authors drafted the article or revised it critically for important intellectual content; all authors gave final approval of the version of the article to be published; and all authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Cancer stat facts: prostate cancer. National Cancer Institute website. https://seer.cancer.gov/statfacts/html/prost.html. Accessed August 29, 2019.
2. Chan JM, Jou RM, Carroll PR. The relative impact and future burden of prostate cancer in the United States. *J Urol*. 2004;172(pt 2): S13-S17. doi:10.1097/01.ju.0000142068.66876.53
3. Kolonel LN. Fat, meat, and prostate cancer. *Epidemiologic reviews* 23, 72-81 (2001).
4. Gao X, LaValley MP, Tucker KL. Prospective studies of dairy product and calcium intakes and prostate cancer risk: a meta-analysis. *J Natl Cancer Inst*. 2005;97(23):1768-1777. doi:10.1093/jnci/dji402
5. Chan JM, Stampfer MJ, Ma J, Gann PH, Gaziano M, Giovannucci EL. Dairy products, calcium, and prostate cancer risk in the Physicians' Health Study. *Am J Clin Nutr*. 2001;74(4):549-554. doi:10.1093/ajcn/74.4.549
6. Qin LQ, Xu JY, Wang PY, Kaneko T, Hoshi K, Sato A. Milk consumption is a risk factor for prostate cancer: meta-analysis of case-control studies. *Nutr Cancer* 2004;48(1):22-27. doi:10.1207/s15327914nc4801_4
7. Sato T. Chronic diseases suspected to arise through the enhanced activity of growth hormone by excessive intake of animal protein, IV: the cancer and the hypertrophy of the prostate. *Bull Public Health*. 1963;12:222-228.
8. Ghosh J, Myers CE. Arachidonic acid stimulates prostate cancer cell growth: critical role of 5-lipoxygenase. *Biochem Biophys Res Comm*.1997;235(2):418-423. doi:10.1006/bbrc.1997.6799
9. Ma J, Giovannucci E, Pollak M, et al. Milk intake, circulating levels of insulin-like growth factor-I, and risk of colorectal cancer in men. *J Natl Cancer Inst*. 2001;93(17):1330-1336. doi:10.1093/jnci/93.17.1330
10. Qin LQ, He K, Xu JY. Milk consumption and circulating insulin-like growth factor-I level: a systematic literature review. *IntJ Food Sci Nutr*. 2009;60(suppl 7):330-340. doi:10.1080/09637480903150114
11. Allen NE, Appleby PN, Davey GK, Key TJ. Hormones and diet: low insulin-like growth factor-I but normal bioavailable androgens in vegan men. *Br J Cancer*. 2000;83:95-97. doi:10.1054/bjoc.2000.1152
12. Cohen P, Peehl DM, Lamson G, Rosenfeld RG. Insulin-like growth factors (IGFs), IGF receptors, and IGF-binding proteins in primary cultures of prostate epithelial cells. *J Clin Endocrinol Metab*. 1991;73 (2):401-407. doi:10.1210/jcem-73-2-401
13. Cohen P, Peehl DM, Rosenfeld RG. The IGF axis in the prostate. *Horm Metab Res*. 1994;26(2):81-84. doi:10.1055/s-2007-1000777
14. Allen NE, Key TJ, Appleby PN, et al. Serum insulin-like growth factor (IGF)-I and IGF-binding protein-3 concentrations and prostate cancer risk: results from the European Prospective Investigation into Cancer and Nutrition. *Cancer Epidemiol Biomarkers Prev*. 2007;16 (6):1121-1127. doi:10.1158/1055-9965.epi-06-1062
15. Chan JM, Stampfer MJ, Giovanucci E, et al. Plasma insulin-like growth factor-I and prostate cancer risk: a prospective study. *Science*. 1998;279(5350):563-566. doi:10.1126/science.279.5350.563
16. Roddam AW, Allen NE, Appleby P, et al. Insulin-like growth factors, their binding proteins, and prostate cancer risk: analysis of individual patient data from 12 prospective studies. *Ann Intern Med*. 2008;149 (7):461-471. doi:10.7326/0003-4819-149-7-200810070-00006
17. Schwartz GG, Wang MH, Zang M, Singh RK, Siegal GP. 1 alpha, 25-dihydroxyvitamin D (calcitriol) inhibits the invasiveness of human prostate cancer cells. *Cancer Epidemiol Biomarkers Prev*. 1997;6 (9):727-732.
18. Giovannucci E. Dietary influences of 1,25(OH)2 vitamin D in relation to prostate cancer: a hypothesis. *Cancer Causes Control*. 1998;9 (6):567-582.
19. Ganmaa D, Li XM, Wang J, Qin LQ, Wang PY, Sato A. Incidence and mortality of testicular and prostatic cancers in relation to world dietary practices. *Int J Cancer*. 2001; 98(2):262-267. doi:10.1002/ijc.10185
20. Torniainen S, Hedelin M, Autio V, et al. Lactase persistence, dietary intake of milk, and the risk for prostate cancer in Sweden and Finland. *Cancer Epidemiol Biomarkers Prev*. 2007;16(5):956-961. doi:10.1158/1055-9965.EPI-06-0985
21. Kimura T. East meets West: ethnic differences in prostate cancer epidemiology between East Asians and Caucasians. *Chinese J Cancer*. 2012;31(9):421-429. doi:10.5732/cjc.011.10324
22. Wynder EL, Cohen LA. Correlating nutrition to recent cancer mortality statistics. *J Natl Cancer Inst*. 1997;89(4):324-324. doi:10.1093/jnci/89.4.324
23. Doll R, Peto R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. *J Natl Cancer Inst*. 1981;66(6):1191-1308.
24. Blot WJ, Tarone RE. Doll and Peto's quantitative estimates of cancer risks: holding generally true for 35 years. *J Natl Cancer Inst*. 2015;107 (4). doi:10.1093/jnci/djv044
25. Ornish D, Weidner G, Fair WR, et al. Intensive lifestyle changes may affect the progression of prostate cancer. *J Urol* 2005;174 (3):1065-1070. doi:10.1097/01.ju.0000169487.49018.73
26. Kristal AR, Lampe JW. Brassica vegetables and prostate cancer risk: a review of the epidemiological evidence. *Nutr Cancer* 2009;42(1):1-9. doi:10.1207/S15327914NC421_1
27. Key TJ, Appleby PN, Spencer EA, Travis RC, Roddam AW, Allen NE. Cancer incidence in vegetarians: results from the european prospective investigation into cancer and nutrition (EPIC-Oxford). *Am J Clin Nutr*. 2009;89(5):1620S-1626S. doi:10.3945/ajcn.2009.26736M
28. Key TJ, Appleby PN, Crowe FL, Bradbury KE, Schmidt JA, Travis RC., Cancer in British vegetarians: updated analyses of 4998 incident cancers in a cohort of 32,491 meat eaters, 8612 fish eaters, 18,298

vegetarians, and 2246 vegans. *Am J Clin Nutr.* 2014;100 (1):378S-385S. doi:10.3945/ajcn.113.071266

29. Gonzalez CA, Riboli E. Diet and cancer prevention: contributions from the European Prospective Investigation into Cancer and Nutrition (EPIC) study. *Eur J Cancer*. 2010;46(14):2555-2562. doi:10.1016/j.ejca.2010.07.025
30. Tantamango-Bartley Y, Knutsen SF, Knutsen R, et al. Are strict vegetarians protected against prostate cancer? *Am J Clin Nutr*. 2015;103(1):153-160. doi:10.3945/ajcn.114.106450
31. Gilsing AMJ, Weijenberg MP, Goldbohm RA, Dagnelie PC, van den Brandt PA, Schouten LJ. Vegetarianism, low meat consumption and the risk of lung, postmenopausal breast and prostate cancer in a population-based cohort study. *Eur J Clin Nutr*. 2016;70:723-729. doi:10.1038/ejcn.2016.25
32. Kirsh VA, Peters U, Mayne ST, et al. Prospective study of fruit and vegetable intake and risk of prostate cancer. *J Natl Cancer Inst*. 2007;99(15):1200-1209. doi:10.1093/jnci/djm065
33. Chan JM, Holick CN, Leitzmann MF, et al. Diet after diagnosis and the risk of prostate cancer progression, recurrence, and death (United States). *Cancer Causes Control*. 2006;17(2):199-208. doi:10.1007/s10552-005-0413-4
34. Stram DO, Hankin JH, Wilkens LR, et al. Prostate cancer incidence and intake of fruits, vegetables and related micronutrients: the multiethnic cohort study* (United States). *Cancer Causes Control*. 2006;17(9):1193-1207. doi:10.1007/s10552-006-0064-0
35. Takachi R, Inoue M, Sawada N, et al. Fruits and vegetables in relation to prostate cancer in japanese men: the japan public health center-based prospective study. *Nutr Cancer*. 2010;62(1):30-39. doi:10.1080/01635580903191502
36. Diallo A, Deschasaux M, Galan P, et al. Associations between fruit, vegetable and legume intakes and prostate cancer risk: results from the prospective Supplementation en Vitamines et Mineraux Antioxydants (SU.VI.MAX) cohort. *Br J Nutr*. 2016;115(9):1579-1585. doi:10.1017/S0007114516000520
37. Umesawa M, Iso H, Mikami K, et al. Relationship between vegetable and carotene intake and risk of prostate cancer: the JACC study. *Br J Cancer*. 2014;110:792-796. doi:10.1038/bjc.2013.685
38. Egeberg R, Olsen A, Christensen J, et al. Intake of whole-grain products and risk of prostate cancer among men in the Danish Diet, Cancer and Health cohort study. *Cancer Causes Control*. 2011;22 (8):1133-1139. doi:10.1007/s10552-011-9789-5
39. Yan L, Spitznagel EL. Soy consumption and prostate cancer risk in men: a revisit of a meta-analysis. *Am J Clinl Nutr*. 2009;89 (4):1155-1163. doi:10.3945/ajcn.2008.27029
40. Deneo-Pellegrini H, Ronco AL, De Stefani E, et al. Food groups and risk of prostate cancer: a case-control study in Uruguay. *Cancer Causes Control*. 2012;23(7):1031-1038. doi:10.1007/s10552-012-9968-z
41. Raimondi S, Mabrouk JB, Shatenstein B, Maisonneuve P, Ghadirian P. Diet and prostate cancer risk with specific focus on dairy products and dietary calcium: a case-control study. *Prostate*. 2010;70 (10):1054-1065. doi:10.1002/pros.21139
42. Moller E, Galeone C, Andersson TML, et al. Mediterranean Diet Score and prostate cancer risk in a Swedish population-based case-control study. *J Nutr Sci*. 2013;2:e15. doi:10.1017/jns.2013.2
43. Ambrosini GL, Fritschi L, de Klerk NH, Mackerras D, Leavy J. Dietary patterns identified using factor analysis and prostate cancer risk: a case control study in Western Australia. *Ann Epidemiol*. 2008;18 (5):364-370. doi:10.1016/j.annepidem.2007.11.010
44. Lane JA, Oliver SE, Appleby PL, et al. Prostate cancer risk related to foods, food groups, macronutrients and micronutrients derived from the UK Dietary Cohort Consortium food diaries. *Eur J Clin Nutr*. 2017;71(2):274-283. doi:10.1038/ejcn.2016.162
45. Colli JL, Colli A. International comparisons of prostate cancer mortality rates with dietary practices and sunlight levels. *Urol Oncol*. 2006;24 (3):184-194. doi:10.1016/j.urolonc.2005.05.023
46. Giovannucci E, Rimm EB, Colditz GA, et al. A prospective study of dietary fat and risk of prostate cancer. *J Natl Cancer Inst*. 1993;85 (19):1571-1579. doi:10.1093/jnci/85.19.1571
47. Neuhouser ML, Barnett MJ, Kristal AR, et al. (n-6) PUFA increase and dairy foods decrease prostate cancer risk in heavy smokers. *J Nutr*. 2007;137(7):1821-1827. doi:10.1093/jn/137.7.1821
48. Rohrmann S, Platz EA, Kavanaugh CJ, Thuita L, Hoffman SC, Helzlsouer KJ. Meat and dairy consumption and subsequent risk of prostate cancer in a US cohort study. *Cancer Causes Control*. 2007;18 (1):41-50. doi:10.1007/s10552-006-0082-y
49. Wright JL, Neuhouser ML, Lin DW, et al. AMACR polymorphisms, dietary intake of red meat and dairy and prostate cancer risk. *Prostate*. 2011;71 498-506, doi:10.1002/pros.21267
50. Aune D, Navarro Rosenblatt DA, Chan DSM, et al. Dairy products, calcium, and prostate cancer risk: a systematic review and meta-analysis of cohort studies. *A J Clin Nutr*. 2015;101(1):87-117. doi:10.3945/ajcn.113.067157
51. Qin LQ, Xu JY, Wang PY, Tong J, Hoshi K. Milk consumption is a risk factor for prostate cancer in Western countries: evidence from cohort studies. *Asia Pac J Clin Nutr*. 2007;16(3):467-476.
52. Kurahashi N, Inoue M, Iwasaki M, Sasazuki S, Tsugane S. Dairy product, saturated fatty acid, and calcium intake and prostate cancer in a prospective cohort of Japanese men. *Cancer Epidemiol Biomarkers Prev*. 2008;17(4):930-937. doi:10.1158/1055-9965.EPI-07-2681
53. Song Y, Chavarro JE, Cao Y, et al. Whole milk intake is associated with prostate cancer-specific mortality among U.S. male physicians. *J Nutr*. 2013;143(2):189-196. doi:10.3945/jn.112.168484
54. Kesse E, Bertrais S, Astorg P, et al. Dairy products, calcium and phosphorus intake, and the risk of prostate cancer: results of the French prospective SU.VI.MAX (Supplementation en Vitamines et Mineraux Antioxydants) study. *Brit J Nutr*. 2006;95(3):539-545. doi:10.1079/BJN20051670
55. Yang M, Kenfield SA, Van Blarigan EL, et al. Dairy intake after prostate cancer diagnosis in relation to disease-specific and total mortality. *Int J Cancer*. 2015;137(10):2462-2469. doi:10.1002/ijc.29608
56. Koh KA, Sesso HD, Paffenbarger RS Jr, Lee IM. Dairy products, calcium and prostate cancer risk. *Brit J Cancer*. 2006;95:1582-1585. doi:10.1038/sj.bjc.6603475
57. Mitrou PN, Albanes D, Weinstein SJ, et al. A prospective study of dietary calcium, dairy products and prostate cancer risk (Finland). *Int J Cancer*. 2007;120(11):2466-2473. doi:10.1002/ijc.22553
58. Park SY, Muprhy SP, Wilkens LR, Stram DO, Henderson BE, Kolonel LN. Calcium, vitamin D, and dairy product intake and prostate cancer

risk: the Multiethnic Cohort Study. *Am J Epidemiol*. 2007;166 (11):1259-1269. doi:10.1093/aje/kwm269

59. Park Y, Mitrou PN, Kipnis V, Hollenbeck A, Schatzkin A, Lietzmann MF. Calcium, dairy foods, and risk of incident and fatal prostate cancer: the NIH-AARP Diet and Health Study. *Am J Epidemiol*. 2007;166(11):1270-1279. doi:10.1093/aje/kwm268
60. Pettersson A, Kasperzyk JL, Kenfield SA, et al. Milk and dairy consumption among men with prostate cancer and risk of metastases and prostate cancer death. *Cancer Epidemiol Biomarkers Prev*. 2012;21(3):428-436. doi:10.1158/1055-9965.EPI-11-1004
61. van der Pols JC, Bain C, Gunnell D, Smith GD, Frobisher C, Martin RM. Childhood dairy intake and adult cancer risk: 65-y follow-up of the Boyd Orr cohort. *Am J Clin Nutr*. 2007;86(6):1722-1729. doi:10.1093/ajcn/86.5.1722
62. Satkunasivam R, Joshi A, Shahabi A, et al. Dairy intake and prostate cancer risk: results from the California collaborative prostate cancer study. *J Urol*. 2014;191(4S):e833. doi:10.1016/j.juro.2014.02.2265
63. Steck SE, et al., Intake of dairy and calcium, NSAIDs and prostate cancer aggressiveness. *FASEB J*. 2011;25(1).
64. Lu W, Chen H, Niu Y, Wu H, Xia D, Wu Y. Dairy products intake and cancer mortality risk: a meta-analysis of 11 population-based cohort studies. *Nutr J*. 2016;15(91). doi:10.1186/s12937-016-0210-9
65. Aune D, De Stefani E, Ronco AL, et al. Egg consumption and the risk of cancer: a multisite case-control study in Uruguay. *Asian Pacific J Cancer Prev*. 2009;10(5):869-876.
66. Xie B, He H. No association between egg intake and prostate cancer risk: a meta-analysis. *Asian Pac J Cancer Prev*. 2012;13 (9):4677-4681. doi:10.7314/apjcp.2012.13.9.4677
67. Wilson KM, Mucci LA, Drake BF, et al. Meat, fish, poultry, and egg intake at diagnosis and risk of prostate cancer progression. *Cancer Prev Res (Phila)*. 2016;9(12)933-941. doi:10.1158/1940-6207.CAPR-16-0070
68. Wu K, Spiegelman D, Hou T, et al. Associations between unprocessed red and processed meat, poultry, seafood and egg intake and the risk of prostate cancer: a pooled analysis of 15 prospective cohort studies. *Int J Cancer*. 2016;138(10).2368-2382. doi:10.1002/ijc.29973
69. Wu K, Hu FB, Willett WC, Giovannucci E. Dietary patterns and risk of prostate cancer in U.S. men. *Cancer Epidemiol Biomarkers Prev*. 2006;15(1):167-171. doi:10.1158/1055-9965.epi-05-0100
70. Yang M, Kenfield SA, Van Blarigan EL, et al. Dietary patterns after prostate cancer diagnosis in relation to disease-specific and total mortality. *Cancer Prev Res*. 2015;8(6):545-551. doi:10.1158/1940-6207.CAPR-14-0442
71. Askari F, Beysaie B, Tehrani A, Parizi MK, Mishekarlou EN, Rashidkhani B. Adherence to Mediterranean-style dietary pattern and risk of prostate cancer: a case-control study in Iran. *Pakistan J Nutr*. 2016;15(4):305-311. doi:10.3923/pjn.2016.305.311
72. Giovannucci E, Rimm EB, Liu Y, Stampfer MJ, Willett WC. A prospective study of tomato products, lycopene, and prostate cancer risk. *J Natl Cancer Inst*. 2002;94(5):391-398. doi:10.1093/jnci/94.5.391
73. Chen J, Song Y, Zhang L. Lycopene/tomato consumption and the risk of prostate cancer: a systematic review and meta-analysis of prospective studies. *J Nutr Sci Vitaminol (Tokyo)*. 2013;59(3):213-223. doi:10.3177/jnsv.59.213
74. Butler LM, Wong AS, Koh WP, Wang R, Yuan JM, Yu MC. Calcium intake increases risk of prostate cancer among Singapore Chinese. *Cancer Res*. 2010;70(12):4941-4948. doi:10.1158/0008-5472.CAN-09-4544
75. Giovannucci E, Liu Y, Stampfer JM, Willett WC. A prospective study of calcium intake and incident and fatal prostate cancer. *Cancer Epidemiol Biomarkers Prev*. 2006;15(2):203-210. doi:10.1158/1055-9965.EPI-05-0586