Nutrition and prostate cancer: review of the evidence

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ABSTRACT

Objectives: Of the possible causes of cancer, nutritional factors are supposed to play a major role in preventable cancers. Regarding prostate cancer, nutritional data remain contradictory. This article aims to review current evidence on the relation between nutrition and prostate cancer.

Material and methods: A systematic literature search for meta-analyses, systematic reviews, and pooled analyses was conducted in the PubMed database from its inception to September 2019. Eligible studies had to assess the association between nutrition and risk of prostate cancer.

Results: Generally, no evidence was found for an association between most food items or groups, including fruit, vegetables, meat, tea, coffee, and risk of prostate cancer. There was an inconsistent and weak positive association between milk and dairy foods and prostate cancer. Carbohydrates, vitamins, and minerals were not associated with prostate cancer. Furthermore, no association was found with dietary patterns such as vegetarian or pesco-vegetarian, but increased adherence to a Mediterranean diet seemed to have a protective effect. In general, large heterogeneity between studies was observed. Studies included in meta-analyses were mostly observational, and therefore prone to several inherent biases.

Conclusions: The evidence on any potential association between diet and prostate cancer is weak. The reductionist approach considering individual nutritional factors is not suitable, and conducting more observational studies or small randomised trials evaluating the impact of individual nutritional factors on prostate cancer will not bring further answers. Large, well-designed, randomised, controlled trials are mandatory in order to clarify the relationship between nutrition and prostate cancer.

KEY WORDS: diet, prostate cancer, review, nutrition, dietary patterns, dietary factors, dietary supplements.

INTRODUCTION

In the 1980s, nutrition was estimated to contribute to the development of more than one third of cancers (35%) in Western countries [1], which made nutrition the second most important preventable cause of cancer, after smoking.

According to the latest burden of disease study, almost 530,000 deaths in 2016 in the US were attributed to dietary factors [2], which corresponds to approximately 19.3% of the total number of deaths in the United States of America (USA).

Prostate cancer is the second most commonly diagnosed cancer in men: almost 1.3 million men in the world were projected to be diagnosed with prostate cancer in 2018 [3]. Moreover, with an estimated number of associated deaths of 359,000 in 2018, prostate cancer is the fifth leading cause of death from cancer in men [3].

While prostate cancer aetiology remains mostly unknown, an association with nutritional factors is plausible; since prostate cancer presents a long latency, diet and nutrition might have an impact on its pro-
gression at several stages of the life cycle. Nonetheless, existing evidence supporting this association is mainly inconsistent [4–6].

Therefore, the aim of this article was to review the current evidence of the impact of several dietary factors on the risk of prostate cancer.

METHODS

A systematic literature search was conducted to identify meta-analyses or systematic reviews assessing the association between nutrition and prostate cancer. The literature search was restricted to articles published in English in the PubMed database from its inception to September 2019. A combination of key words and MeSH index terms was used including “prostate cancer” or “prostate neoplasm”, “diet” or “dietary” or “dietary intake” and “meta-analysis” or “pooled analysis”. Complementary searches were also conducted; more details are reported in the supplementary material (Appendix 1).

Eligible articles had to 1) present a meta-analysis or a pooled analysis of retrospective or prospective studies, and 2) report a summary estimate on risk of prostate cancer associated with either a measurement of food intake (dietary intake or supplementation) or with a measurement of the adherence to a dietary pattern.

Titles and abstracts were screened for eligibility. Full copies of eligible articles were retrieved and fully read.

For each article, the following information was extracted: the number and the design (cohort, case-control, or randomised controlled trial) of the included studies, total number of prostate cancer cases, sample size of the study, mean follow-up period, and the summary estimate with its corresponding confidence interval (CI). Moreover, information on the publication bias (type of assessment and results with p-value) as well as on the between-study heterogeneity (I² or p-value) were also extracted.

RESULTS

The literature search yielded 68 published meta-analyses investigating the association between nutrition and prostate cancer risk. The nutritional topics that were investigated were: vitamins and minerals (11 articles); fruit, vegetables, and carotenoids (11 articles); fat and fatty acids (10 articles); meat (11 articles); milk and dairy (seven articles); carbohydrates (four articles) and other dietary items (seven articles). Also, seven articles reported on the association between dietary patterns and risk of prostate cancer. Results in terms of strength and direction of the association are summarised in Table 1.

VITAMINS AND MINERALS

Eleven meta-analyses assessed the relationship between vitamins and/or minerals dietary intake or supplementation and risk of prostate cancer [7–17] (Appendix 2).

Overall, there was no statistically significant association between vitamin intake or supplementation and risk of prostate cancer, regardless of the type of vitamin and the study design. Only one meta-analysis of 18 observational studies found a significant decrease of 11% in prostate cancer risk when comparing highest and lowest dietary intake levels of vitamin C, with low to moderate heterogeneity (I² = 39.4%) and no evidence of publication bias [7]. An earlier published meta-analysis [9], including two randomised, controlled trials (RCTs), compared vitamin C supplementation with placebo and found no association (summary relative risk [SRR] = 0.98 [95% CI: 0.91, 1.06]).

Five meta-analyses investigated the association between folic acid intake and risk of prostate cancer. Meta-analyses of observational studies did not suggest an association when comparing highest and lowest intakes of folate, with reported SRRs ranging from 0.83

![TABLE 1. Summary of found evidence](image-url)
(95% CI: 0.57, 1.20) to 1.02 (95% CI: 0.95, 1.09). Low to moderate amounts of heterogeneity were observed, with higher heterogeneity in case-control (I² = 57.7%) compared to cohort studies (I² = 0%). Summary relative risks were higher in RCTs compared to observational studies, but in two out of three meta-analyses, the association between intake of folate and risk of prostate cancer was not statistically significant. On the other hand, a meta-analysis of five RCTs found a significantly increased risk of 24% in patients randomised to folic acid compared to those randomised to placebo.

There was no association between zinc intake and risk of prostate cancer in two meta-analyses [10, 12], but the results remained heterogeneous (I² of 23.8 and 90%, respectively), and were based on a limited number of studies included in the analyses.

The results of studies investigating selenium intake and prostate cancer risk were inconsistent. A recently published Cochrane review of 21 observational studies found a statistically significant risk reduction of 16% when comparing highest and lowest selenium intake levels [14], with low heterogeneity across studies and no evidence of publication bias. However, the same review reported no association between selenium intake and prostate cancer risk in an analysis based on four RCTs. Similarly, two other meta-analyses [9, 12] found no association between selenium supplementation and risk of prostate cancer, but included a limited number of studies that were very heterogeneous (I² of 84% and 96%, respectively).

**FRUIT, VEGETABLES, AND CAROTENOIDs**

Eleven meta-analyses reported on the association between fruit, vegetable, and carotenoid intake or supplementation and prostate cancer risk [9, 12, 18-26] (Appendix 3).

Two meta-analyses investigated concomitantly the relationship between fruit and vegetable intake and prostate cancer [22, 23], both finding no association between fruit intake and prostate cancer, with no significant heterogeneity and no evidence of publication bias. Moreover, a more recent meta-analysis found no association with prostate cancer when comparing highest and lowest quartiles of apple consumption. No association was found between vegetable intake and risk of prostate cancer.

Three meta-analyses reported on the association between raw and cooked tomato intake and risk of prostate cancer [18, 20, 24]. The most recent and largest one, published by Rowles et al. [24], reported a significantly reduced risk of prostate cancer when comparing highest and lowest intakes of total tomato, tomato foods, and cooked tomato and sauces, with corresponding SRRs of 0.81 (95% CI: 0.71, 0.92), 0.84 (95% CI: 0.72, 0.98), and 0.84 (95% CI: 0.73, 0.99), respectively. However, heterogeneity between studies remained high (I² of 73.1%, 76.7%, and 57.4%, respectively) and statistical tests suggested publication bias.

On the other hand, five meta-analyses of observational studies examined the association between lycopene intake – a carotenoid found in particularly large amounts in tomatoes and associated products – and risk of prostate cancer [18-20, 25, 26]. An overall reduced risk of prostate cancer was observed with increasing consumption of lycopene, with risk reductions ranging from 3 to 12% across these studies.

In the most recent meta-analysis, based on 25 observational studies, the decreased risk was statistically significant (SRR = 0.88 [95% CI: 0.78, 0.98]), when comparing highest and lowest categories of lycopene intake. However, there was significant between-study heterogeneity (I² = 56.7%, p = 0.001) and Begg’s test suggested potential publication bias. When stratified by study design (e.g. cohort vs case-control studies), the association remained significant only for cohort studies, with a higher pooled estimate (SRR = 0.93 [95% CI: 0.79, 0.99]), when compared to case-control studies (SRR = 0.83 [95% CI: 0.67, 1.02]). Between-study heterogeneity was higher in case-control studies (65.5%) when compared to cohort studies (11%).

Fewer meta-analyses reported on the association between other carotenoids and prostate cancer risk. When comparing highest and lowest intake levels of α-carotene from 12 observational studies, we found a borderline significant reduction of 13% in prostate cancer risk. On the other hand, no association was found between β-carotene dietary intake and/or supplementation and risk of prostate cancer in observational studies and RCTs [9, 12, 26], with SRRs ranging from 0.90 to 1.18.

**FAT AND FATTY ACIDS**

Ten meta-analyses reported on the association between fat and/or fatty acids intake and risk of prostate cancer [27-36] (Appendix 4).

Two meta-analyses examined the relationship between total, saturated, and unsaturated fat intake and prostate cancer risk [32, 35]. Both found no association between saturated or unsaturated fat and risk of prostate cancer. However, results were divergent for total fat, with one meta-analysis finding a significantly increased risk (SRR = 1.17 [95% CI: 1.10, 1.25]), and the other finding no association (SRR = 1.00 [95% CI: 0.99, 1.01]).

Concerning fatty acids, seven meta-analyses reported on the association between intake of alpha-linolenic acid (ALA) and prostate cancer. Only two meta-analyses found an increased risk of prostate cancer associated with ALA intake [28, 32]. In the other five meta-analyses, there was no association between ALA intake and risk of prostate cancer, with SRRs varying from 0.95 to 1.30,
which were higher in case-control studies compared to cohort studies. Overall, there was no evidence of publication bias, and heterogeneity ranged from 0 to 90%.

Regarding intake of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), current evidence suggests there is no association with prostate cancer risk, with SRRs ranging from 0.99 to 1.11. There were low to large amounts of heterogeneity ($I^2$ ranging from 0 to 61%) and most studies lacked reporting of publication bias.

There seemed to be no evidence of an association between linoleic acid intake in two meta-analyses reporting relevant data, with SRRs ranging from 0.83 to 1.27, which were larger in analyses based on case-control studies compared to analyses based on cohort studies.

Of note, in most analyses, the reporting on publication bias and heterogeneity was incomplete, and the number of included studies was limited.

### MEAT, FISH, SEAFOOD, ALTERNATIVES TO MEAT, AND EGGS

Eleven meta-analyses reported on the association between meat, alternatives to meat, fish, seafood, and/or egg intakes and risk of prostate cancer [37-47] (Appendix 5).

Three meta-analyses suggested there was no association between red meat intake and risk of prostate cancer, regardless of the type of red meat (processed or unprocessed), with SRRs ranging from 0.99 to 1.06. In most analyses, funnel plots and publication bias tests suggested potential publication bias, and between-study heterogeneity ranged from 0 to 61%. Also, based on pooled results from 15 cohort studies, there was no evidence of an association between poultry or seafood and prostate cancer risk [44].

Szymanski et al. [43] investigated the relationship between fish consumption and prostate cancer separately in 12 case-control and 12 cohort studies and found divergent results, with SRRs of 0.85 (95% CI: 0.72, 1.00) and 1.01 (95% CI: 0.90, 1.14), respectively.

Based on four meta-analyses of cohort and case-control studies, higher intakes of tofu and/or soy food were generally associated with a significantly lower risk of prostate cancer, in comparison with lower intakes, with corresponding SRRs ranging from 0.65 to 0.75. The most recent meta-analysis published by Applegate et al. [38] reported risk reductions of 19% and 17% when comparing highest and lowest consumption of total soy food and tofu, respectively.

No association was found between isoflavones (generally found in soy) and risk of prostate cancer [38, 47].

Results from three meta-analyses suggested no association between intake of eggs and risk of prostate cancer, regardless of the study design (cohort vs case-control) and the quantification of eggs intake. There was no evidence of publication bias, and heterogeneity was low to moderate ($I^2$ ranging from 0 to 52.2%). However, based on four studies, Keum et al. [41] found a significantly increased risk of fatal prostate cancer associated with egg intake (SRR = 1.47 [95% CI: 1.01, 2.14]) with moderate heterogeneity ($I^2 = 40\%$).

More generally, there was no association between protein intake and risk of prostate cancer [42].

### MILK, DAIRY PRODUCTS, AND SOURCES OF CALCIUM

Seven meta-analyses investigated the association between milk, dairy, and/or calcium dietary intakes and supplementation and risk of prostate cancer [48-54] (Appendix 6).

In the most complete meta-analysis of cohort studies, Aune et al. [48] suggested that high intakes of total dairy, milk, low-fat milk, cheese, total calcium, dietary calcium, and dairy calcium were associated with increased risk of prostate cancer, when compared to lower intakes. Corresponding SRRs varied from 1.07 to 1.18, with low to moderate between-study heterogeneity ($I^2$ ranging from 0 to 53%). Conversely, high intakes of whole milk were associated with an 8% decrease in prostate cancer risk, when compared to lower intakes. There was no significant association between other types of dairy products such as yoghurt, non-dairy calcium, and supplemental calcium intakes and prostate cancer risk. Overall, results from other meta-analyses of observational studies were consistent with those of Aune et al. [48].

However, in a meta-analysis of seven RCTs, Bristow et al. [49] found a significant 46% reduction in prostate cancer risk when comparing calcium supplementation and placebo.

### CARBOHYDRATES, DIETARY FIBRE, GLYCAEMIC LOAD, AND GLYCAEMIC INDEX

Four meta-analyses reported on the association between carbohydrates, dietary fibre, and whole grain intake and risk of prostate cancer [55-58] (Appendix 7). One meta-analysis also investigated the relationship between glycaemic index (GI), glycaemic load (GL), and prostate cancer [57].

Based on 17 studies, Sheng et al. [56] found a decrease in the risk of prostate cancer when comparing highest and lowest dietary fibre intakes, with significant heterogeneity ($I^2 = 53.6\%, p = 0.005$). No evidence of publication bias was observed. When stratifying the analysis by study design, the reduced risk was statistically significant in case-control studies, with no heterogeneity, but not significant in cohort studies, with very large heterogeneity.

Wang et al. [57] investigated the potential association between dietary fibre intake, whole grains, carbohydrates, glycaemic index (GI), and glycaemic load (GL) and risk of prostate cancer in a systematic review.
of 27 studies. The authors found no clear evidence of a relationship with prostate cancer risk. Funnel plot inspection and Egger’s and Begg’s tests suggested no evidence of publication bias. Heterogeneity was generally moderate, ranging from 39.5 to 69.5% for dietary fibre intake and GI, respectively.

Based on five cohorts and 16 case-control studies, Fan et al. [55] found no association between carbohydrate intake and prostate cancer risk. Funnel plot inspection and statistical tests indicated no evidence of publication bias. Significant heterogeneity among included studies was observed (I^2 = 62.7%). Results were not altered when the analysis was stratified by study design (data not shown); however, larger heterogeneity was observed in case-control studies when compared to cohorts (68.3% vs 7.8%). Results published in a previous meta-analysis are also consistent [58].

**OTHER DIETARY ITEMS**

Seven meta-analyses reported on the association between intake of other dietary items or food groups and risk of prostate cancer [59-65]. Dietary items/groups assessed were various and included tea, and coffee, flavonoids, fried food, and dietary acrylamide (Appendix 8).

Based on seven cohort studies, there was no association between tea consumption and risk of prostate cancer. Results regarding coffee intake were inconsistent: when comparing highest and lowest intakes, two meta-analyses of 13 and five prospective studies reported significant protective effects of coffee, with risk reductions of 10% [59] and 21% [64], respectively. Conversely, another meta-analysis of 12 observational studies found a significant harmful effect of coffee [62].

Increased intake of flavonoids was also associated with significant increases in risk of prostate cancer. However, results seemed to be driven by one large study; after its removal from the analysis, the pooled estimate lost statistical significance.

Also, fried food seemed to increase the risk of prostate cancer, but the limited number as well as the case-control design of the included studies imply caution when interpreting these results.

Finally, no association was found between intake of dietary acrylamide and prostate cancer.

**DIETARY PATTERNS**

Seven meta-analyses assessed the relationship between different dietary patterns and risk of prostate cancer [66-72] (Appendix 9).

When comparing highest and lowest adherence to healthy dietary patterns, two meta-analyses found no association with prostate cancer [67, 69]. On the other hand, Fabiani et al. [67] reported a significantly increased risk of prostate cancer associated with highest adherence to western and carbohydrate dietary patterns (considered unhealthy), with corresponding increases in risk of 34% and 64%, respectively. Based on seven case-control studies, Grosso et al. [69] reported a similar estimate, with a 44% increase in risk associated with higher adherence to unhealthy dietary patterns. Nonetheless, this association was not observed in cohort studies.

No association with risk of prostate cancer was found when comparing vegetarian, pesco-vegetarian, and semi-vegetarian diets to a non-vegetarian diet, based on results pooled from four, four, and two cohort studies, respectively [69].

The most recent meta-analysis investigating the Mediterranean diet – high in vegetables, olive oil, complex carbohydrates, lean meats, and antioxidants – was found to decrease the risk of prostate cancer by 5%, with no heterogeneity. However, this decrease was not statistically significant, and the authors suggested potential publication bias. Results from two other previously published meta-analyses were also consistent [71, 72].

Furthermore, a meta-analysis of seven cohort studies suggested that adherence to the World Cancer Research Fund and American Institute for Cancer Research (CRF/AICR) dietary recommendations was associated with a significantly lower risk of prostate cancer. These dietary recommendations included: limiting the consumption of energy-dense foods and avoiding sugar-sweetened beverages, eating mostly foods of plant origin, reducing consumption of red meat and avoiding that of processed meat, and limiting alcoholic beverages [70].

**DISCUSSION**

The relationships between nutrition and prostate cancer risk have been the subject of a myriad systematic reviews, and this article provides a comprehensive overview of these publications.

Current evidence does not support an association between carbohydrates, fat and fatty acids, fruit and vegetables, meat and alternatives for meat, vitamins, minerals, and tea and risk of prostate cancer.

Several meta-analyses of observational studies suggested a positive association between milk and dairy and prostate cancer risk. Regarding calcium, results were inconsistent between observational studies and randomised trials, the latter suggesting a protective effect of calcium when compared to placebo. These contradictory results among types of dairy products and sources of calcium suggest that other elements instead of fat and calcium might be responsible for the increase in risk of prostate cancer.

Conversely, a potentially beneficial role of lycopene was detected in observational studies. Lycopene is found in high concentration in the prostate and is the most potent antioxidant among the carotenoids [73, 74]. It is thought that through its antioxidant powers, lycopene could reduce DNA damage in the prostate.
Overall, evidence for associations was at best probable, but in most of the cases it remained suggestive/limited; however, this is part of a much bigger picture: generally, studies investigating associations between malignancies and nutritional ingredients are based on weak evidence [77]. Also, one problematic aspect of observational studies on nutrition is that they measure dietary intake only once (e.g. at baseline); however, dietary intake during follow-up are not necessarily reflected by the baseline measured consumption [79]. Measuring food intake or adherence to dietary patterns more than once could be more appropriate.

The lack of association and the inconclusiveness of results might also be a result of weakness of evidence, small effect sizes, and nutritional studies’ flawed assessment of dietary intake.

Based on existing evidence, it remains difficult to draw conclusions regarding the relationship between diet and prostate cancer. It is disappointing to see that despite the great number of published studies, very few associations stand out. Another myriad of observational studies or small randomised trials will not bring further answers [80]. More specifically, large, well-designed, randomised, controlled trials, are required in order to obtain stronger levels of evidence and attempt to better clarify the associations between dietary factors and prostate cancer risk. Orienting future research towards other nutrition-related topics (e.g. food security, climate change as a consequence of food production, differential food access due to social inequalities, etc.) would potentially help better comprehend ways in which nutrition influences cancer, and more specifically, prostate cancer.

DISCLOSURE

The authors report no conflict of interest.

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AUTHORS’ CONTRIBUTIONS
MD, PB prepared research concept and design. MD collected data, analysed them and wrote the article. PM critically revised the article. All authors contributed to preparing the final publication.
Appendix 1. Detailed literature search queries

**MAIN LITERATURE SEARCH**

("prostate cancer" OR ("prostate" and "cancer") OR "Prostate Neoplasms"[MeSH] OR "prostate carcinoma" OR "prostatic cancer" OR ("prostatic" AND "cancer") OR ("prostatic" AND "neoplasms"))

AND

("diet" OR Diet[MeSH] or "dietary" or "dietary intake" or "nutrition")

AND

("meta-analysis"[Publication Type] OR “meta-analysis as topic”[MeSH] OR “meta-analysis” OR "pooled analysis”)

**OTHER COMPLEMENTARY LITERATURE SEARCHES**

**VITAMIN D**

("prostate cancer" OR ("prostate" and "cancer") OR "Prostate Neoplasms"[MeSH] OR "prostate carcinoma" OR "prostatic cancer" OR ("prostatic" AND "cancer") OR ("prostatic" AND "neoplasms"))

AND

("Vitamin D"[Mesh] OR “vitamin D” OR "Ergocalciferols"[Mesh] OR "ergocalciferol" OR "Cholecalciferol"[Mesh] OR "Cholecalciferol")

AND

("meta-analysis"[Publication Type] OR “meta-analysis as topic”[MeSH] OR “meta-analysis” OR "pooled analysis”)

**RED MEAT**

("prostate cancer" OR ("prostate" and "cancer") OR "Prostate Neoplasms"[MeSH] OR "prostate carcinoma" OR "prostatic cancer" OR ("prostatic" AND "cancer") OR ("prostatic" AND "neoplasms"))

AND

("red meat" or "meat")

AND

("meta-analysis"[Publication Type] OR “meta-analysis as topic”[MeSH] OR “meta-analysis” OR "pooled analysis”)


Appendix 2. Characteristics of meta-analyses investigating the association between vitamins and minerals and prostate cancer risk

| First author, year | Dietary item assessed | Analysis conducted | No. of studies and design (CC, CH, RCT) | Total cases | Sample size (range) | Mean FU (95% CI) | Publication bias (type of assessment and results with p-value) | Heterogeneity (I² or p-value) |
|-------------------|----------------------|--------------------|-----------------------------------------|-------------|---------------------|----------------|---------------------------------------------------------------|--------------------------|
| **Vitamins**      |                      |                    |                                         |             |                     |                |                                                              |                          |
| Bai, 2015         | Vitamin C            | Highest vs lowest  | 18 (6 CH, 12 CC)                       | 15,926      | 103,658             | 0.89 (0.83, 0.94) | pEgger = 0.295, pBegg = 0.173, funnel plot inspection did not suggest PB | 39.4%, 0.045             |
| Jiang, 2010       | Vitamin C            | Vs placebo         | 2 RCT                                   | 2,346       | 44,002              | 0.98 (0.91, 1.06) | NR                                                            | 0%, 0.47                 |
|                   | Vitamin E            | Vs placebo         | 5 RCT                                   | 3,580       | 85,549              | 0.96 (0.85, 1.08) | NR                                                            | 64%, 0.03                |
| Gilbert, 2011     | Vitamin D            | Per 1000 IU increase | 4 CH, 2 NCC                             | 5,997       | 116,061             | 1.14 (0.98, 1.31) | Funnel plot inspection suggested PB                           | 0%, 0.572                |
|                   | Vitamin D            | Per 1000 IU increase | 5 CC                                    | 2,725       | 5,726              | 0.83 (0.28, 2.43) | Funnel plot inspection suggested PB                           | 49.2%, 0.097             |
| Stratton, 2011    | Vitamin E            | Vs no vitamin E supplementation | 10 (5 CH, 2 CC, 3 RCT) | 21,608 | 501,292 | 5.7* 1.02 (0.89, 1.16) | NR | 93%, 0.00001 |
|                   | Multivitamins        | Vs no multivitamin supplementation | 5 (2 CH, 2 CC, 1 RCT) | 3,837 | 305,851 | 10.6* 1.11 (0.95, 1.29) | NR | 65%, 0.03 |
| Folic acid        |                      |                    |                                         |             |                     |                |                                                              |                          |
| Tio, 2014         | Folate               | Highest vs lowest  | 11 (5 CH, 6 CC)                        | 15,336      | 146,782             | 0.97 (0.89, 1.06) | pEgger = 0.22                                                     | 41.9%, 0.07              |
|                   | Highest vs lowest    | 5 CH                | 12,898                                 | 140,428     | NR                  | 1.00 (0.96, 1.05) | pEgger = 0.67                                                     | 0%, 0.88                 |
|                   | Highest vs lowest    | 6 CC                | 2,438                                  | 6,354       | NA                  | 0.83 (0.57, 1.20) | pEgger = 0.95                                                     | 57.7%, 0.04              |
| Wang, 2014        | Folate               | Highest vs lowest  | 5 CH                                    | 2,725       | 5,726              | NA             |                                                              | 0%, 0.00001             |
| Qin, 2013         | Folic acid           | Vs control          | 5 RCT                                   | 508         | 27,065              | 1.17 (0.84, 1.62) | NR                                                            | 54.3%, 0.07              |
| Vollset, 2013     | Folic acid           | Vs placebo          | 12 RCT                                  | 656         | 44,177              | 1.15 (0.94, 1.41) | NR                                                            | NR                       |
| Wien, 2012        | Folic acid           | > 0.4 g/day vs control | 5 RCT                                   | 632         | 25,738              | 1.24 (1.03, 1.49) | NR                                                            | 17%, 0.31                |
| **Minerals**      |                      |                    |                                         |             |                     |                |                                                              |                          |
| Vinceti, 2018     | Selenium             | Highest vs lowest  | 4 RCT                                    | 1,020       | 18,942             | 1.01 (0.90, 1.14) | NR                                                            | 0%                       |
| Mahmoud, 2016     | Zinc                 | Highest vs lowest  | 21 observational studies               | 576,667     | 14,950             | 0.84 (0.75, 0.95) | Funnel plot inspection did not suggest PB                     | 35%                      |
| Stratton, 2011    | Zinc                 | Vs no zinc supplementation | 3 (1 CH, 2 CC)                  | 2,930       | 40,082             | 1.18 (0.71, 0.96) | NR                                                            | 90%, 0.00001             |
|                   | Selenium             | Vs no selenium supplementation | 2 (1 CC, 1 RCT)               | 2,249       | 20,923             | 1.57 (0.68, 3.61) | NR                                                            | 96%, 0.00001             |
| Jiang, 2010       | Selenium             | Vs placebo          | 2 RCT                                   | 912         | 18,700             | 0.78 (0.41, 1.48) | NR                                                            | 84%, 0.01                |

CC – case-control, NCC – nested case-control, CH – cohort, RCT – randomised controlled trial, FU – follow-up, CI – confidence interval, NA – not applicable, NR – not reported, PB – publication bias, PCa – prostate cancer, * mean FU computed with FU values of cohort studies and/or RCTs, ** mean FU for all included studies including several cancer sites was abstracted, § I² represents the percentage of heterogeneity between studies not explained by chance
### Appendix 3. Characteristics of meta-analyses investigating the association between fruit, vegetables, and carotenoids and prostate cancer risk

| First author, year | Dietary item assessed | Analysis conducted | No. of studies and design (CC, CH, RCT) | Total cases | Sample size | Mean FU (range) | SRR (95% CI) | Publication bias (type of assessment and results with \(p\)-value) | Heterogeneity (\(I^2\) or \(p\)-value) |
|-------------------|----------------------|--------------------|----------------------------------------|-------------|-------------|----------------|--------------|-------------------------------------------------|-----------------------------|
| **Fruit and vegetables** |                     |                    |                                        |             |             |                |              |                                                 |                             |
| Rowles, 2018      | Total tomato intake  | Highest vs lowest  | 26 (5 CH, 2 NCC, 19 CC)               | 22,555      | 266,037     | NR             | 0.81 (0.71, 0.92) | pEgger = 0.011, pBegg = 0.003                   | 73.1%, 0.000                |
|                   | Raw tomato intake    | Highest vs lowest  | 10 (3 CH, 1 NCC, 6 CC)                | 9808        | 170,085     | NR             | 0.95 (0.84, 1.09) | pEgger = 0.568, pBegg = 0.592                   | 55.6%, 0.016                |
|                   | Tomato foods intake  | Highest vs lowest  | 18 (4 CH, 1 NCC, 13 CC)               | 14,215      | 211,841     | NR             | 0.84 (0.72, 0.98) | pEgger = 0.037, pBegg = 0.053                   | 76.7%, 0.000                |
|                   | Cooked tomato and sauces intake | Highest vs lowest | 10 (3 CH, 1 NCC, 6 CC) | 13,925 | 166,535 | NR | 0.84 (0.73, 0.99) | pEgger = 0.019, pBegg = 0.020 | 57.4%, 0.012 |
| Petimar, 2017     | Fruit intake         | Highest vs lowest  | 15 CH                                  | 52,680      | 842,149     | 9-22           | 1.01 (0.98, 1.04) | NR                                                | 0.69                         |
|                   | Vegetables intake    | Highest vs lowest  | 15 CH                                  | 52,680      | 842,149     | 9-22           | 0.99 (0.96, 1.02) | NR                                                | 0.55                         |
| Fabiani, 2016     | Apple intake         | Highest vs lowest  | 2 CC                                   | 1,344       | 8,073       | NA             | 0.93 (0.79, 1.09) | NR                                                | 0.0% 0.664               |
| Meng, 2014        | Fruit intake         | Highest vs lowest  | 14 CH                                  | 26,297      | 1,078,471   | 11.1 (3-33)**  | 1.02 (0.98, 1.07) | pEgger = 0.092, pBegg = 0.511, funnel plot inspection did not suggest PB | 0%, 0.929          |
|                   | Vegetables intake    | Highest vs lowest  | 12 CH                                  | 27,223      | 869,758     | 11.1 (3-33)**  | 0.97 (0.93, 1.01) | pEgger = 0.549, funnel plot inspection did not suggest PB | 0%, 0.505          |
| Chen, 2013        | Raw tomato intake    | Highest vs lowest  | 3 CH                                   | 2,292       | 84,525      | 5              | 0.81 (0.38, 0.95) | NR                                                | 74%, 0.02                 |
|                   | Cooked tomato intake | Highest vs lowest  | 2 CH                                   | 3,819       | 70,996      | 8              | 0.85 (0.69, 1.06) | NR                                                | 64%, 0.09                 |
| Etminan, 2004     | Raw tomato intake    | Highest vs lowest  | 9 (2 CH, 7 CC)                         | 6,459       | 60,333      | NR             | 0.89 (0.80, 1.00) | Funnel plot inspection did not suggest PB               | 0.05                       |
|                   | Cooked tomato intake | Highest vs lowest  | 6 (1 CH, 5 CC)                         | 5,747       | 53,905      | NR             | 0.81 (0.71, 0.92) | NR                                                | 0.90                       |
| **Carotenoids**   |                     |                    |                                        |             |             |                |              |                                                 |                             |
| Rowles, 2017      | Lycopene intake      | Highest vs lowest  | 25 (8 CH, 1 NCC, 16 CC)               | 36,336      | 443,815     | 10’          | 0.88 (0.78, 0.98) | pEgger = 0.130, pBegg = 0.032                   | 56.7%, 0.001                |
| Chen, 2015        | Lycopene intake      | Highest vs lowest  | 13 (2 CH, 3 NCC, 8 CC)                | 13,180      | 171,468     | 10’          | 0.91 (0.82, 1.01) | NR                                                | 45.5%, 0.037                |
|                   | Lycopene intake      | Per 5 mg/day       | 13 (2 CH, 3 NCC, 8 CC)                | 13,180      | 171,468     | 10’          | 0.97 (0.93, 1.01) | pEgger = 0.22, pBegg = 0.20                   | 50.2%, 0.020                |
| Wang, 2015        | Lycopene intake      | Highest vs lowest  | 13 (4 CH, 9 CC)                       | 7,327       | 178,643     | 6.8’         | 0.88 (0.76, 1.02) | NR                                                | 23.6%, 0.02                 |
|                   | Alpha-carotene       | Highest vs lowest  | 12 (4 CH, 8 CC)                       | 6,492       | 159,026     | 10.1’        | 0.87 (0.76, 0.99) | NR                                                | 15.5%, 0.16                 |
|                   | Beta-carotene        | Highest vs lowest  | 19 (8 CH, 11 CC)                      | 10,164      | 209,075     | 12’          | 0.90 (0.81, 1.01) | NR                                                | 26%, 0.10                  |
| Chen, 2013        | Lycopene intake      | Highest vs lowest  | 5 (3 CH, 2 NCC)                       | 8,350       | 141,359     | 8             | 0.93 (0.86, 1.01) | Funnel plot inspection did not suggest PB               | 18%, 0.30                 |
| Stratton, 2011    | Beta-carotene        | vs no beta-carotene supplementation | 3 (1 CH, 1 CC, 1 RCT) | 2,886 | 43,060 | 5.4’ | 1.18 (0.61, 2.30) | NR                                                | 95%, < 0.00001               |
| Jiang, 2010       | Beta-carotene        | vs placebo         | 3 RCT                                  | 2,332       | 61,656      | 7.4          | 0.97 (0.90, 1.05) | NR                                                | 0%, 0.37                   |
| Etminan, 2004     | Lycopene intake      | Highest vs lowest  | 10 (3 CH, 7 CC)                       | 5,241       | 111,912     | NR           | 0.89 (0.81, 0.98) | Funnel plot inspection did not suggest PB               | 0.23                       |

**CC** – case-control, **NCC** – nested case-control, **CH** – cohort, **RCT** – randomised controlled trial, **FU** – follow-up, **CI** – confidence interval, **NA** – not applicable, **NR** – not reported, **PB** – publication bias, **PCa** – prostate cancer, ‘*’ mean FU computed with FU values of cohort studies, ‘**’ mean FU for all studies (fruit and vegetables), ‘§’ represents the percentage of heterogeneity between studies not explained by chance.
| First author, year | Dietary item | Analysis conducted | No. of studies and design | Total cases | Sample size | Mean FU (range) | SRR (95% CI) | Publication bias (type of assessment and results with p-value) | Heterogeneity (I² or p-value) |
|-------------------|--------------|-------------------|--------------------------|-------------|-------------|----------------|---------------|---------------------------------------------------------------|-----------------------------|
| Xu, 2015          | Total fat    | Per 28.35 g (1 ounce) | 13 CH                    | 36,144      | 692,771     | 9.5 (2-17.4)  | 1.00 (0.99, 1.01) | Publication bias (type of assessment and results with p-value) | 5.0% (0.34)                  |
|                   | Unsaturated fat | Per 28.35 g (1 ounce) | 10 CH                    | 34,644      | 648,764     | 9.2 (2-17.4)  | 1.00 (0.99, 1.01) | Publication bias (type of assessment and results with p-value) | 4.8% (0.40)                  |
|                   | Saturated fat | Per 28.35 g (1 ounce) | 9 CH                     | 33,983      | 625,789     | 9.6 (2-17.4)  | 1.00 (0.99, 1.01) | Publication bias (type of assessment and results with p-value) | 4.9% (0.67)                  |
|                   | Monounsaturated fat | Per 28.35 g (1 ounce) | 14 CH                    | 104,944     | 2,09,771    | 9.6 (2-17.4)  | 1.00 (0.99, 1.01) | Publication bias (type of assessment and results with p-value) | 9.9% (0.01)                  |
|                   | Total fat    | Per 28.35 g (1 ounce) | 15 CH                    | 117,120     | 2,34,271    | 9.6 (2-17.4)  | 1.00 (0.99, 1.01) | Publication bias (type of assessment and results with p-value) | 9.9% (0.01)                  |
|                   | Unsaturated fat | Per 28.35 g (1 ounce) | 14 CH                    | 104,944     | 2,09,771    | 9.6 (2-17.4)  | 1.00 (0.99, 1.01) | Publication bias (type of assessment and results with p-value) | 9.9% (0.01)                  |
|                   | Saturated fat | Per 28.35 g (1 ounce) | 9 CH                     | 33,983      | 625,789     | 9.6 (2-17.4)  | 1.00 (0.99, 1.01) | Publication bias (type of assessment and results with p-value) | 9.9% (0)                    |
|                   | Monounsaturated fat | Per 28.35 g (1 ounce) | 14 CH                    | 104,944     | 2,09,771    | 9.6 (2-17.4)  | 1.00 (0.99, 1.01) | Publication bias (type of assessment and results with p-value) | 9.9% (0)                    |
|                   | Total fat    | Per 28.35 g (1 ounce) | 15 CH                    | 117,120     | 2,34,271    | 9.6 (2-17.4)  | 1.00 (0.99, 1.01) | Publication bias (type of assessment and results with p-value) | 9.9% (0)                    |
|                   | Unsaturated fat | Per 28.35 g (1 ounce) | 14 CH                    | 104,944     | 2,09,771    | 9.6 (2-17.4)  | 1.00 (0.99, 1.01) | Publication bias (type of assessment and results with p-value) | 9.9% (0)                    |
|                   | Saturated fat | Per 28.35 g (1 ounce) | 9 CH                     | 33,983      | 625,789     | 9.6 (2-17.4)  | 1.00 (0.99, 1.01) | Publication bias (type of assessment and results with p-value) | 9.9% (0)                    |
|                   | Monounsaturated fat | Per 28.35 g (1 ounce) | 14 CH                    | 104,944     | 2,09,771    | 9.6 (2-17.4)  | 1.00 (0.99, 1.01) | Publication bias (type of assessment and results with p-value) | 9.9% (0)                    |
### Characteristics of meta-analyses investigating the association between meat, fish, seafood, alternatives to meat, eggs, and proteins and prostate cancer risk

| First author, year | Dietary item assessed | Analysis conducted | No. of studies and design (CC, CH) | Total cases | Sample size | Mean FU (range) | SRR (95% CI) | Publication bias (type of assessment and results with p-value) | Heterogeneity (I² or p-value) |
|-------------------|----------------------|--------------------|-----------------------------------|-------------|-------------|----------------|--------------|---------------------------------------------------------------|-----------------------------|
| **Meat**          |                      |                    |                                   |             |             |                |              |                                                               |                             |
| Wu, 2016          | Total red meat       | > 120 g/day vs 20-40 g/day | 15 CH | 52,683 | 824,149 | 9-22 | 0.99 (0.94, 1.03) | NR | 24%, 0.23 | |
|                   | Unprocessed red meat | >100 g/day vs < 20 g/day | 15 CH | 52,683 | 824,149 | 9-22 | 1.02 (0.98, 1.06) | NR | 2%, 0.43 | |
|                   | Processed red meat   | > 40 g/day vs < 5 g/day | 15 CH | 52,683 | 824,149 | 9-22 | 1.04 (1.01, 1.08) | NR | 0%, 0.61 | |
|                   | Poultry              | > 45 g/day vs < 5 g/day | 15 CH | 52,683 | 824,149 | 9-22 | 1.05 (1.00, 1.09) | NR | 0%, 0.55 | |
| Bylsma, 2015      | Total red meat       | Highest vs lowest   | 10 CH | 23,170 | 411,729 | 11.8 | 1.02 (0.92, 1.12) | pEgger = 0.963, funnel plot suggested slight PB | 61%, 0.006 |
|                   | Fresh red meat       | Highest vs lowest   | 9 CH | 13,007 | 243,396 | 11.8 | 1.06 (0.97, 1.16) | pEgger = 0.001, funnel plot suggested slight PB | 38.3%, 0.113 |
|                   | Processed red meat   | Highest vs lowest   | 11 CH | 27,705 | 568,147 | 12.8 | 1.05 (1.01, 1.10) | pEgger = 0.211 | 3.38%, 0.406 |
| Alexander, 2010    | Red meat             | Highest vs lowest   | 15 CH | NR | NR | NR | 1.00 (0.96, 1.05) | Funnel plot suggested slight PB | 0.264 |
|                   | Processed red meat   | Highest vs lowest   | 11 CH | NR | NR | NR | 1.05 (0.99, 1.12) | pEgger = 0.013, funnel plot suggested PB | 0.088 |
| **Alternatives to meat** | | | | | | | | | | |
| Applegate, 2018    | Total soy food       | Highest vs lowest   | 16 (7 CH, 11 CC) | 11,266 | 209,151 | NR | 0.71 (0.58, 0.85) | pEgger = 0.052, pBegg = 0.300 | 68.9% |
|                   | Non-fermented soy food | Highest vs lowest  | 11 (5 CH, 6 CC) | 5,788 | 81,435 | NR | 0.65 (0.56, 0.83) | pEgger = 0.117, pBegg = 0.161 | 60.3% |
|                   | Tofu                 | Highest vs lowest   | 5 (3 CH, 2 CC) | 865 | 32,618 | NR | 0.73 (0.57, 0.94) | pEgger = 0.093, pBegg = 0.221 | 4.5% |
| Hwang, 2009       | Tofu                 | Highest vs lowest   | 5 (3 CH, 2 CC) | 947 | 32,618 | 28° | 0.73 (0.57, 0.92) | pBegg = 0.079 | 0.428 |
|                   | Total soy food       | Highest vs lowest   | 5 (2 CH, 3 CC) | 2,395 | 65,539 | 21° | 0.69 (0.57, 0.84) | pBegg = 0.295 | 0.544 |
|                   | Non-fermented soy food | Highest vs lowest  | 8 (4 CH, 4 CC) | 2,885 | 48,529 | 25° | 0.75 (0.62, 0.89) | pEgger = 0.047, funnel plot suggested PB | 0.413 |
| Yan, 2009         | Soy food             | Highest vs lowest   | 14 (5 CH, 9 CC) | 9,732 | 171,487 | NR | 0.74 (0.63, 0.89) | pEgger = 0.05, pBegg = 0.16 | NR |
| Yan, 2005         | Non-fermented soy food | Highest vs lowest (and none vs some) | 8 (2 CH, 6 CC) | 4217 | 25,742 | NR | 0.70 (0.59, 0.83) | Authors claim no evidence of PB | NR |
### Appendix 5. Cont.

| First author, year | Dietary item assessed | Analysis conducted | No. of studies and design (CC, CH) | Total cases | Sample size | Mean FU (range) | SRR (95% CI) | Publication bias (type of assessment and results with \( p \)-value) | Heterogeneity (\( I^2 \) or \( p \)-value) |
|--------------------|-----------------------|-------------------|----------------------------------|-------------|-------------|----------------|--------------|---------------------------------------------------------------|----------------------------------|
| **Fish and seafood** |                       |                   |                                  |             |             |                |              |                                                             |                                   |
| Wu, 2016           | Seafood               | > 40 g/day vs < 5 g/day | 15 CH                           | 52,683      | 824,149     | 9-22           | 1.04 (0.98, 1.09) | NR                                                        | 25%, 0.22                        |
| Szymanski, 2010    | Fish                  | Highest vs lowest  | 12 CH                           | 445,820     | 13,924      | NR             | 1.01 (0.90, 1.14) | \( p_{Egger} = 0.84 \), \( p_{Begg} = 0.78 \), funnel plot inspection did not suggest PB | 0.005                            |
|                     | Fish                  | Highest vs lowest  | 12 CC                           | 15,582      | 5777        | NA             | 0.85 (0.72, 1.00) | \( p_{Egger} = 0.62 \), \( p_{Begg} = 0.68 \), funnel plot inspection did not suggest PB | 0.05                             |
| **Eggs**           |                       |                   |                                  |             |             |                |              |                                                             |                                   |
| Wu, 2016           | Eggs                  | > 25 g/day vs < 5 g/day | 15 CH                           | 52,683      | 824,149     | 9-22           | 0.99 (0.96, 1.02) | NR                                                        | 0%, 0.97                         |
| Keum, 2015         | Eggs                  | Per increase of 5 eggs/week | 6                               | 3,655       | NR          | NR             | 1.00 (0.88, 1.14) | \( p_{Egger} = 0.72 \)                                                        | 0%, 0.69                         |
| Xie, 2012          | Eggs                  | Highest vs lowest  | 6 CH                            | 4,087       | 247,432     | NR             | 0.97 (0.87, 1.07) | \( p_{Egger} = 0.401 \), \( p_{Begg} = 0.452 \) | 0%, 0.441                        |
|                     | Eggs                  | Highest vs lowest  | 11 CC                           | 3,714       | 10,779      | NR             | 1.09 (0.86, 1.31) | \( p_{Egger} = 0.151 \), \( p_{Begg} = 0.533 \), funnel plot inspection did not suggest PB | 52.2%, 0.022                     |
| **Isoflavones**    |                       |                   |                                  |             |             |                |              |                                                             |                                   |
| Applegate, 2018    | Isoflavones           | Highest vs lowest  | 6 (2 CH, 1 NCC, 3 CC)           | 11,812      | 133,061     | NR             | 1.03 (0.97, 1.09) | \( p_{Egger} = 0.802 \), \( p_{Begg} = 0.707 \) | 44.9%                            |
| Yan, 2009          | Isoflavones           | Highest vs lowest  | 8 (2 CH, 6 CC)                  | 8,353       | 133,270     | NR             | 0.88 (0.76, 1.02) | Authors claim no evidence of PB                                | NR                               |
| **Protein**        |                       |                   |                                  |             |             |                |              |                                                             |                                   |
| Mao, 2018          | Protein               | Highest vs lowest  | 12 (1 RCT, 8 CH, 3 CC)          | 13,483      | 286,245     | 9.5*           | 0.99 (0.93, 1.06) | \( p_{Egger} = 0.296 \), funnel plot inspection did not suggest PB | 0%, 0.656                        |

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**CC** – case-control, **NCC** – nested case-control, **CH** – cohort, **RCT** – randomised controlled trial, **FU** – follow-up, **CI** – confidence interval, **NA** – not applicable, **NR** – not reported, **PB** – publication bias, **PCa** – prostate cancer, *mean FU computed with FU values of cohort studies;\(^*\) \( I^2 \) represents the percentage of heterogeneity between studies not explained by chance.
Appendix 6. Characteristics of meta-analyses investigating the association between milk, dairy, and calcium and prostate cancer risk

| First author, year | Dietary item assessed | Analysis conducted | No. of studies and design (CC, CH) | Total cases | Sample size | Mean FU (range) | SRR (95% CI) | Publication bias (type of assessment and results with p-value) | Heterogeneity (I² or p-value) |
|-------------------|----------------------|--------------------|-----------------------------------|-------------|-------------|----------------|--------------|-------------------------------------------------------------|-----------------------------|
| **Milk and dairy** |                      |                    |                                   |             |             |                |              |                                                             |                             |
| Aune, 2015        | Total dairy          | Highest vs lowest  | 15 CH                             | 38,107      | 848,395     | 10.7           | 1.09 (1.02, 1.17) | pEgger = 0.08, pBegg = 0.02 | 43%, 0.04                   |
|                   | Milk                 | Highest vs lowest  | 15 CH                             | 11,392      | 566,146     | 9.7            | 1.11 (1.03, 1.21) | pEgger = 0.06, pBegg = 0.66 | 21%, 0.22                   |
|                   | Whole milk           | Highest vs lowest  | 8 CH                              | 19,664      | 448,719     | 11.6           | 0.92 (0.85, 0.99) | pEgger = 0.04, pBegg = 0.11 | 0%, 0.69                    |
|                   | Low fat milk         | Highest vs lowest  | 6 CH                              | 19,430      | 432,943     | 12.2           | 1.14 (1.05, 1.25) | NR                            | 51%, 0.09                   |
|                   | Cheese               | Highest vs lowest  | 11 CH                             | 22,950      | 887,759     | 11.3           | 1.07 (1.01, 1.13) | pEgger = 0.57, pBegg = 0.44 | 0%, 0.56                    |
|                   | Yoghurt              | Highest vs lowest  | 6 CH                              | 18,351      | 623,112     | 7.4            | 1.12 (0.97, 1.29) | pEgger = 0.45, pBegg = 0.62 | 67%, 0.02                   |
| Huncharek, 2008   | Dairy                | Highest vs lowest  | 11 CH                             | 10,952      | 300,172     | 12.2           | 1.11 (1.03, 1.19) | NR                            | 0.33                        |
|                   | Milk                 | Highest vs lowest  | 11 CH                             | 4,452       | 195,440     | 12.8           | 1.06 (0.91, 1.23) | NR                            | NR                          |
|                   | Cheese               | Highest vs lowest  | 7 CH                              | 7,213       | 211,702     | 12.5           | 1.11 (0.99, 1.25) | NR                            | NR                          |
| Qin, 2007         | Milk or dairy        | Highest vs lowest  | 13 CH                             | 7,546       | 297,119     | 4-23           | 1.13 (1.02, 1.24) | Funnel plot inspection did not suggest PB, pEgger = 0.45 | NR                          |
| Qin, 2005         | Dairy                | Highest vs lowest  | 10 CH                             | 8,383       | 282,887     | 11.2           | 1.11 (1.00, 1.22) | Funnel plot inspection did not suggest PB                 | 28%, > 0.2                  |
| Qin, 2004         | Milk                 | Highest vs lowest  | 11 CC                             | 2,929       | 6,949       | NA             | 1.68 (1.34, 2.12) | NR                            | < 0.05                      |
| **Calcium**       |                      |                    |                                   |             |             |                |              |                                                             |                             |
| Rahmati, 2018     | Total calcium        | Highest vs lowest  | 12 (11 CH, 1 CC)                  | 905,046     | 9.9*        | 1.15 (1.04, 1.27) | pBegg = 0.02 | 59.7%, 0.006                                          |
| Aune, 2015        | Total calcium        | Highest vs lowest  | 9 CH                              | 33,127      | 750,275     | 9.6            | 1.10 (1.01, 1.21) | pEgger = 0.26, pBegg = 0.12 | 50%, 0.04                   |
|                   | Dietary calcium      | Highest vs lowest  | 15 CH                             | 35,493      | 800,879     | 8.9            | 1.18 (1.08, 1.30) | pEgger = 0.11, pBegg = 0.37 | 53%, 0.008                  |
|                   | Dairy calcium        | Highest vs lowest  | 7 CH                              | 10,493      | 479,666     | 10.5           | 1.13 (1.02, 1.24) | pEgger = 0.31, pBegg = 0.13 | 46%, 0.08                   |
|                   | Non-dairy calcium    | Highest vs lowest  | 4 CH                              | 13,067      | 442,796     | 7.5            | 0.91 (0.79, 1.05) | pEgger = 0.92, pBegg = 1.00 | 15%, 0.32                   |
|                   | Supplemental calcium | Highest vs lowest  | 9 (8 CH, 1 RCT)                   | 30,232      | 498,516     | 8.5            | 1.00 (0.95, 1.05) | pEgger = 0.36, pBegg = 0.31 | 0%, 0.68                    |
| Bristow, 2013     | Calcium supplementation | Calcium vs placebo | 7 RCT                             | 48         | 7,693       | 3.9            | 0.54 (0.30, 0.96) | Funnel plot inspection did not suggest PB                 | 0%                          |
| Huncharek, 2008   | Dairy calcium        | Highest vs lowest  | 4 CH                              | 2,282       | 56,327      | 13.1           | 1.18 (1.06, 1.33) | NR                            | 0.02                        |
|                   | Total/dietary calcium| Highest vs lowest  | 5 CH                              | 8,327       | 199,993     | 10.2           | 1.15 (1.02, 1.30) | NR                            | NR                          |
| Gao, 2005         | Calcium              | Highest vs lowest  | 6 CH                              | 7,154       | 222,940     | 7.5            | 1.39 (1.09, 1.77) | Funnel plot inspection did not suggest PB                 | 45%, 0.107                  |

CC – case-control, NCC – nested case-control, CH – cohort, RCT – randomised controlled trial, FU – follow-up, CI – confidence interval, NA – not applicable, NR – not reported, PB – publication bias, PCa – prostate cancer, *mean FU computed with FU values of cohort studies; $I^2$ represents the percentage of heterogeneity between studies not explained by chance.
### Appendix 7. Characteristics of meta-analyses investigating the association between carbohydrates, dietary fibre, and GI/GL and prostate cancer risk

| First author, year | Dietary item assessed | No. of studies and design (CC, CH) | Total cases | Sample size | SRR (95% CI) | Publication bias (type of assessment and results with $p$-value) | Heterogeneity ($I^2$ or $p$-value) |
|-------------------|----------------------|-----------------------------------|-------------|-------------|--------------|---------------------------------------------------------------|---------------------------------|
| **Carbohydrates** |                      |                                   |             |             |              |                                                              |                                 |
| Wang, 2015        | Carbohydrate         | 13 (3 CH, 10 CC)                 | 7,757       | 76,049      | 0.96 (0.81, 1.14) | Funnel plot, $p_{Egger} = 0.598$, $p_{Begg} = 0.428$           | 51.2%, 0.017                     |
| Fan, 2018         | Carbohydrate         | 21 (5 CH, 16 CC)                 | 11,573      | 98,739      | 1.11 (0.98, 1.26) | Funnel plot inspection did not suggest PB, $p_{Egger}$ non-significant | 62.7%, 0.000                     |
| Zhai, 2015        | Carbohydrate         | 5 CH, 13 CC                      | 8,046       | 84,687      | 1.06 (0.93, 1.20) | $p_{Egger} = 0.14$, $p_{Begg} = 0.82$                         | 46.8%, 0.02                      |
|                   | Carbohydrate         | 5 CH                             | 3,679       | 74,115      | 1.06 (0.88, 1.28) | NR                                                            | 24%, 0.261                      |
|                   | Carbohydrate         | 13 CC                            | 4,367       | 10,572      | 1.04 (0.87, 1.23) | NR                                                            | 51.3%, 0.017                     |
| **Dietary fibre** |                      |                                   |             |             |              |                                                              |                                 |
| Sheng, 2015       | Dietary fibre        | 17 (5 CH, 12 CC)                 | 13,484      | 255,026     | 0.89 (0.77, 1.01) | Funnel plot, $p_{Egger} = 0.946$, $p_{Begg} = 0.753$           | 53.6%, 0.005                     |
|                   |                      | 5 CH                             | 9,640       | 247,310     | 0.94 (0.77, 1.11) | NR                                                            | 74.3%, 0.004                     |
|                   |                      | 12 CC                            | 3,844       | 7,716       | 0.82 (0.68, 0.96) | NR                                                            | 17%, 0.277                      |
| Wang, 2015        | Dietary fibre        | 16 (5 CH, 11 CC)                 | 13,330      | 255,670     | 0.94 (0.85, 1.05) | Funnel plot, $p_{Egger} = 0.545$, $p_{Begg} = 0.558$           | 39.5%, 0.053                     |
| **Whole grains**  |                      |                                   |             |             |              |                                                              |                                 |
| Wang, 2015        | Whole grains         | 8 (3 CH, 5 CC)                   | 8,877       | 96,246      | 1.13 (0.98, 1.30) | Funnel plot, $p_{Egger} = 0.475$, $p_{Begg} = 1.000$          | 52.5%, 0.040                     |
| **GI/GL**         |                      |                                   |             |             |              |                                                              |                                 |
| Wang, 2015        | Glycaemic index      | 6 (3 CH, 3 CC)                   | 26,656      | 352,882     | 1.06 (0.96, 1.18) | Funnel plot, $p_{Egger} = 0.299$, $p_{Begg} = 0.260$          | 69.5%, 0.006                     |
|                   | Glycaemic load       | 5 (3 CH, 2 CC)                   | 26,500      | 352,452     | 1.04 (0.91, 1.18) | Funnel plot, $p_{Egger} = 0.247$, $p_{Begg} = 0.221$          | 67%, 0.016                      |

CC – case-control, NCC – nested case-control, CH – cohort, RCT – randomised controlled trial, FU – follow-up, CI – confidence interval, NA – not applicable, NR – not reported, PB – publication bias, PCA – prostate cancer, GI – glycaemic index, GL – glycaemic load. Mean FU was not reported in any of the studies; all studies compared highest and lowest levels of exposure, $I^2$ represents the percentage of heterogeneity between studies not explained by chance.
## Appendix 8. Characteristics of meta-analyses investigating the association between other dietary items and prostate cancer risk

| First author, year | Dietary item assessed | Analysis conducted | No. of studies and design (CC, CH) | Total cases | Sample size | Mean FU (range) | SRR (95% CI) | Publication bias (type of assessment and results with p-value) | Heterogeneity (I² or p-value) |
|-------------------|----------------------|--------------------|-----------------------------------|-------------|-------------|----------------|--------------|---------------------------------------------------------------|-----------------------------|
| **Coffee and tea** |                      |                    |                                   |             |             |                |              |                                                               |                             |
| Grossa, 2017      | Coffee               | Highest vs lowest  | 13 CH                             | 34,105      | 539,577     | NR             | 0.90 (0.85, 0.95) | NR                                                           | 17%                         |
| Zhang, 2014       | Tea                  | Per 1 cup per day increase | 7 CH                             | 4,837       | 187,017     | 7.0-37.0       | 1.02 (0.98, 1.06) | NR                                                           | 62.7%, 0.009                |
|                   |                      | Highest vs lowest  | 7 CH                             | 4,837       | 187,017     | 7.0-37.0       | 1.05 (0.87, 1.27) | NR                                                           | 59.1%, 0.017                |
| Yu, 2011          | Coffee               | Highest vs no coffee/lowest | 5 CH                             | NR          | 63,787      | NR             | 0.79 (0.61, 0.98) | NR                                                           | 57.1%, 0.053                |
| Park, 2010        | Coffee               | Highest vs lowest  | 12 (4 CH, 8 CC)                   | 4,775       | 59,328      | NA             | 1.16 (1.01, 1.33) | pEgger < 0.001, funnel plot suggested PB | 6.9%                        |
|                   |                      | Highest vs lowest  | 4 CH                             | 666         | 49,348      | NR             | 1.06 (0.83, 1.35) | NR                                                           | 0%                          |
|                   |                      | Highest vs lowest  | 8 CC                             | 4,109       | 9,980       | NA             | 1.21 (1.03, 1.43) | NR                                                           | 27.4%                       |
| **Flavonoids**    |                      |                    |                                   |             |             |                |              |                                                               |                             |
| Guo, 2016         | Flavonoids           | Highest vs lowest  | 4 (3 CH, 1 CC)                    | 8,863       | 112,100     | 18*            | 1.12 (1.02, 1.23) | pEgger = 0.476, pBegg = 1.000 | 0%, 0.962                   |
| **Fried food**    |                      |                    |                                   |             |             |                |              |                                                               |                             |
| Lippi, 2015       | Fried food           | Highest vs lowest  | 4 CC                             | 2,579       | 4,856       | NA             | 1.35 (1.17, 1.57) | NR                                                           | 43%                         |
| **Dietary acrylamide** |                  |                    |                                   |             |             |                |              |                                                               |                             |
| Pelucchi, 2015    | Dietary acrylamide   | Per 10 µg/day increase | 6 (4 CH, 2 CC)                   | 13,559      | NR          | NR             | 1.00 (0.99, 1.02) | NR                                                           | 0.74                        |
|                   |                      | Highest vs lowest  | 6 (4 CH, 2 CC)                   | 13,559      | NR          | NR             | 1.00 (0.93, 1.08) | NR                                                           | 0.81                         |

CC – case-control, NCC – nested case-control, CH – cohort, RCT – randomised controlled trial, FU – follow-up, CI – confidence interval, NA – not applicable, NR – not reported, PB – publication bias, PCa – prostate cancer, mean FU computed with FU values of cohort studies; I² represents the percentage of heterogeneity between studies not explained by chance.
### Appendix 9. Characteristics of meta-analyses investigating the association between dietary patterns and prostate cancer risk

| First author, year | Diet/dietary pattern assessed | Analysis conducted | No. of studies and design (CC, CH) | Total cases | Sample size (range) | Mean FU (range) | SRR (95% CI) | Publication bias (type of assessment and results with p-value) | Heterogeneity (I² or p-value) |
|--------------------|--------------------------------|-------------------|-----------------------------------|-------------|---------------------|-----------------|-------------|---------------------------------------------------------------|-----------------------------|
| Godos, 2017        | Vegetarian diet                | Vs non-vegetarian diet | 4 CH                              | 1,935       | 60,391              | 14.3            | 0.83        | (0.63, 1.10) Funnel plot inspection did not suggest PB        | 56%, 0.11                  |
|                    | Pesco-vegetarian diet          | Vs non-vegetarian diet | 4 CH                              | 1,935       | 60,391              | 14.3            | 1.00        | (0.75,1.34) Funnel plot inspection did not suggest PB         | 53%, 0.12                  |
|                    | Semi-vegetarian diet           | Vs non-vegetarian diet | 2 CH                              | 1,478       | 44,797              | 14.1            | 1.18        | (0.95, 1.45) Funnel plot inspection did not suggest PB        | 0%, 0.97                   |
| Jankovic, 2017     | WCRF/AICR diet                 | Per 1 point increase in WCRF/AICR diet score | 7 CH                              | 4,975       | 361,616              | 10-15           | 0.94        | (0.92, 0.97) Funnel plot inspection did not suggest PB        | NR                          |
| Grosso, 2017       | Healthy dietary pattern        | Highest vs lowest   | 7 CC                              | 2,648       | 8,028               | NA              | 0.99        | (0.85, 1.15) Funnel plot inspection did not suggest PB        | NR                          |
|                    | Healthy dietary pattern        | Highest vs lowest   | 3 CH                              | 4,156       | 66,131              | 11.7            | 0.99        | (0.90, 1.08) Funnel plot inspection did not suggest PB        | 0%                          |
|                    | Unhealthy dietary pattern      | Highest vs lowest   | 7 CC                              | 2,648       | 8,028               | NA              | 1.44        | (1.21, 1.71) Funnel plot inspection did not suggest PB        | 62%                         |
|                    | Unhealthy dietary pattern      | Highest vs lowest   | 3 CH                              | 4,156       | 66,131              | 11.7            | 0.87        | (0.71, 1.07) Funnel plot inspection did not suggest PB        | 59%                         |
| Fabiani, 2016      | Healthy dietary pattern        | Highest vs lowest   | 12 (3 CH, 9 CC)                    | 7,410       | 75,718              | 12.1*           | 0.96        | (0.88, 1.04) pEgger = 0.538, pBegg = 0.583                   | 0%, 0.724                  |
|                    | Western dietary pattern        | Highest vs lowest   | 12 (3 CH, 9 CC)                    | 7,410       | 75,718              | 12.1*           | 1.34        | (1.08, 1.65) pEgger = 0.045, pBegg = 0.583                   | 74.6%, 0.0001               |
|                    | Carbohydrate dietary pattern   | Highest vs lowest   | 4 CC                              | 1,888       | 4,118               | NA              | 1.64        | (1.35, 2.00) pEgger = 0.799, pBegg = 1.000                    | 0%, 0.393                  |
| Cheng, 2019        | Mediterranean dietary pattern  | Highest vs lowest   | 10 (5 CH, 5 CC)                    | 33,451      | 403,320             | 13.4*           | 0.95        | (0.90, 1.01) pEgger = 0.770, pBegg = 0.049; asymmetric funnel plot | 12.7%, 0.326               |
| Schwingshackl, 2017| Mediterranean dietary pattern  | Highest vs lowest   | 6 (3 CH, 3 CC)                     | 29,806      | 350,814             | 13.7*           | 0.96        | (0.92, 1.00) Funnel plot inspection did not suggest PB        | 0%                          |
| Schwingshackl, 2014| Mediterranean dietary pattern  | Highest vs lowest   | 5 (4 CH, 1 CC)                     | 29,867      | 425,778             | 13.7*           | 0.96        | (0.92, 0.99) No suggestion of PB (data not shown)            | 0%                          |

CC – case-control, NCC – nested case-control, CH – cohort, RCT – randomised controlled trial, FU – follow-up, CI – confidence interval, NA – not applicable, NR – not reported, PB – publication bias, PCa – prostate cancer, *mean FU computed with FU values of cohort studies, § I² represents the percentage of heterogeneity between studies not explained by chance.