Proceeding paper

Ultra-Processed Food and Risk of Colorectal, Breast and Prostate Cancer: Meta-Analysis †

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Abstract: Cancer is a significant global public health issue. Various dietary factors have been investigated for their possible link with cancer. We aimed to assess the risk of colorectal, breast and prostate cancer associated with high consumption of ultra-processed food. Meta-analyses were done producing a pooled Hazard Ratio (HR) with 95% Confidence Interval (95%CI). High consumption of ultra-processed food was significantly associated with the risk of colorectal cancer (HR = 1.26, 95%CI 1.14-1.39, $p < 0.00001$). The risk for breast cancer was increased but not significantly (HR = 1.14, 95%CI 0.99-1.32, $p = 0.08$) in persons consuming ultra-processed food, while the risk was not increased for prostate cancer (HR = 0.98, 95%CI 0.84–1.15, $p = 0.82$).

Keywords: cancer; ultra-processed food; risk; meta-analysis

1. Introduction

Approximately 19.3 million people were diagnosed with cancer and about 10 million people died of cancer in 2020 [1]. Breast, colorectal and prostate cancer are among the top 4 most commonly diagnosed cancers and among the top 8 leading causes of cancer deaths worldwide [1].

The evaluations of the International Agency for Research on Cancer on carcinogenic risks have identified several carcinogens so far, but the etiology of cancer is still not sufficiently elucidated [2]. According to the Pan American Health Organization, foods are categorized based on the processing extent and group 4 is ultra-processed foods [3]. Ultra-processed foods are high in fat, sodium, refined carbohydrates, they contain additives and their packaging and preparation process can lead to formation of harmful chemical substances [3]. The nutritional composition of ultra-processed food and worldwide increase in its consumption have prompted research into its impact on health. So far, studies have shown an association between the consumption of ultra-processed foods and cardiovascular diseases, obesity, diabetes, depression and all-cause mortality [3].

The aim of this study was to assess the risk of colorectal, breast and prostate cancer associated with high consumption of ultra-processed food.

2. Materials and Methods

This meta-analysis was performed following the Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA) guidelines [4].

2.1. Literature Search and Eligibility Criteria

A comprehensive literature search of PubMed database was done. The following keywords were used: "ultra-processed food" and "cancer". Abstracts and full-texts of papers

were screened for inclusion. There were no language restrictions. Studies conducted in humans and designed as case-control or cohort studies were included. Exclusion criteria were: studies not done in humans, reviews, case-reports. In addition, we also searched the references of review articles. Exposure of interest was high level of consumption of ultra-processed food. Outcome of interest was occurrence of cancer (colorectal, breast, prostate).

2.2. Data Extraction and Quality Assessment of Studies

We extracted the following data from the studies: author, year of publication, study design, sample size, population characteristics, risk estimates. Estimates were extracted from models which were adjusted for most variables.

Methodological quality of included studies was assessed by I.I. and M.I. using the Joanna Briggs Institute Critical Appraisal Tools for cohort and case-control studies [5]. Any disagreements were resolved through discussion.

2.3. Statistical Analysis

Meta-analyses were performed using the generic inverse variance method. Extracted estimates were pooled to produce a pooled Hazard Ratio (HR) with 95% confidence interval (95% CI). Heterogeneity was estimated using the I^2 statistic, with values of 30-60%, 50-90% and 75-100% representing moderate, substantial and considerable heterogeneity, respectively [6]. DerSimonian and Liard random effects model was applied. Results of meta-analyses were presented graphically using forest plots. Diamond on the forest plot represents the pooled estimate, while its width represents the confidence interval of this estimate. Publication bias was assessed using a funnel plot. All analyses were done in Review manager, version 5.4.1 [7].

3. Results

3.1. Literature Search

Literature search yielded 51 records. In total, three studies comprising 2005 colorectal cancer cases, 2225 breast cancer cases and 3153 prostate cancer cases were included in the meta-analysis. Figure 1 shows the flow diagram of literature search. Characteristics of included studies are shown in Table 1.
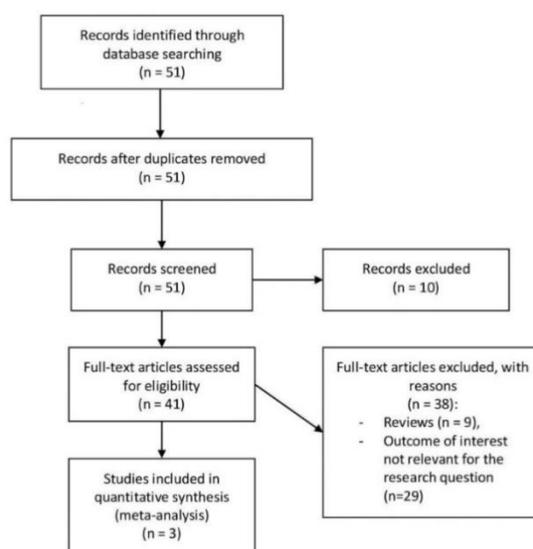

Figure 1. Flow diagram of literature search.

Table 1. Characteristics of included studies.

Author, Year [ref.]	Study Design	No of Participants (Total)	No of Participants (High Consumption of Ultra-Processed Food)	Estimated Risk for Cancer (95% CI)	Assessed Quality Score [1]
Ro-maguera, 2021 [8]	Case-control	Colorectal cancer – 1852; Breast cancer – 1486; Prostate cancer -953; Controls - 3543	/[2]	Colorectal cancer – OR=1.30 (1.11-1.51); Breast cancer – OR=1.15 (0.95-1.40); Prostate cancer – OR=1.06 (0.84-1.34)	10
Trudeau, 2020 [9]	Case-control	Prostate cancer – 1919; Controls - 1991	Prostate cancer – 516; Controls - 497	OR=0.92 (0.72-1.17)	9
Fiolet, 2018 [10]	Cohort study	Colorectal cancer – 153, Non-cases – 104827; Breast cancer – 739, Non-cases – 81420; Prostate cancer – 281, Non-cases - 22540	Colorectal cancer – 26, Non-cases – 23219; Breast cancer - 111, Non-cases – 20429; Prostate cancer – 30, Non-cases - 5675	Colorectal cancer – HR=1.23 (1.08-1.40); Breast cancer – HR=1.13 (0.89-1.42); Prostate cancer – HR=0.93 (0.61-1.40)	11

[1]According to the Joanne Briggs Institute Critical Appraisal Tools – the number indicates how many "yes" answers there were (out of 11 for cohort studies and out of 10 for case-control studies). [2]The study did not report the number of cases and controls in the high consumption of ultra-processed group separately from the low consumption group in the models adjusted for the most variables.

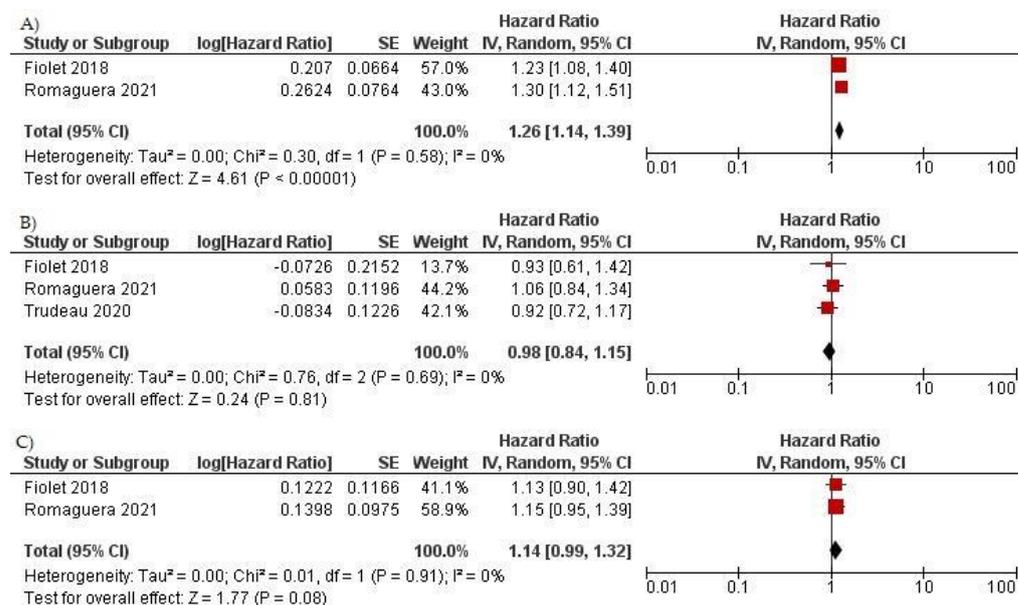*3.2. High consumption of Ultra-Processed Food and Cancer Risk*

High consumption of ultra-processed food significantly increased the risk for colorectal cancer (HR = 1.26, 95% CI 1.14–1.39, *P* < 0.00001). Risk for prostate cancer was not increased in persons consuming high amounts of ultra-processed food (HR = 0.98, 95% CI 0.84–1.15, *P* = 0.81). Similar results were found for breast cancer (HR = 1.14, 95% CI 0.991.32, *P* = 0.08). Results of meta-analyses are shown in Figure 2. Visual inspection of the funnel plots did not indicate presence of publication bias.

4. Discussion

Our meta-analysis showed that high consumption of ultra-processed food was associated with an increased risk of colorectal cancer, while no significant association was found for prostate and breast cancer.

Investigations into the effects that ultra-processed foods have on health are relatively novel. A large French cohort study found that persons whose diet was characterized by a 10% increase in the consumption of ultra-processed food had a significantly increased risk of overall cancer and breast cancer [10]. Further analyses showed that the risk was higher for postmenopausal breast cancer in women consuming high levels of ultra-processed foods. A Spanish case-control study found a significantly increased risk for breast cancer in a model adjusted for age, study area and educational level, but not in the fully adjusted model or in the stratified analysis by menopausal status or breast cancer subtypes [8]. Notably, the subgroup of women who were former or current smokers and who consumed high levels of ultra-processed food had a significantly increased risk of breast cancer, which points to a possible synergistic effect of these factors [8]. Across studies, the risk for prostate cancer was not increased in persons consuming high level of ultra-processed foods, for either all cases of prostate cancer or high- or low-grade prostate cancer separately [8-10]. A significantly increased risk for colorectal cancer was associated with high intake of ultra-processed food in both sexes combined and for both subtypes (colon cancer and rectal cancer), while the analysis by gender showed the risk was significantly increased in men only [8]. These differences in findings of studies could, at least in part, be explained by different study populations, study design, different definition of high

level of consumption of ultra-processed food. In addition, latest research suggests a significant association between the risk of chronic lymphocytic leukemia (incident cases only) and each 10% increase in ultra-processed food consumption [11].

Figure 2. Forest plot of the risk for **A**) colorectal, **B**) prostate and **C**) breast cancer and high consumption of ultra-processed food.

To the best of our knowledge this is the first meta-analysis which investigated the risk for colorectal, breast and prostate cancer and high level of consumption of ultra-processed food. However, the limitation of the present analysis is the small number of included studies identified using only one database, mainly due to the novelty of the research question. Still, no heterogeneity was detected.

5. Conclusion

This study showed that high consumption of ultra-processed food was associated with a significantly increased risk for colorectal cancer. Further research is necessary in order to fully evaluate the role of ultra-processed food in the occurrence of cancer, and especially its interaction with other dietary and lifestyle factors.

Conflicts of Interest: The authors declare no conflict of interest.

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