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Post-diagnosis dietary patterns among cancer survivors in relation to all-cause mortality and cancer-specific mortality: a systematic review and meta-analysis of cohort studies

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## **ABSTRACT**

This study aims to synthesize the latest evidence regarding the association of *a priori* and *a posteriori* dietary patterns with robust outcome measures, such as total mortality and cancer-specific mortality, expanding our search chronologically, including more databases, implementing robust risk of bias tools and focusing exclusively on the post-diagnosis period. A systematic literature review will be conducted and all cohort studies will be evaluated. The methodological rigour of the included studies was critically appraised using the ROBINS-I (Risk Of Bias In Nonrandomized Studies of Interventions) tool, which is proposed for non-randomized studies of interventions/exposures.

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- Objective: To synthesize the latest evidence regarding the association of *a priori* and *a posteriori* dietary patterns with robust outcome measures, such as total mortality and cancerspecific mortality.
- 2 Eligibility criteria: Studies will be eligible to be included if: (i) they have a cohort design, prospective or retrospective, (ii) examine the association of a priori or a posteriori dietary pattern or patterns after cancer diagnosis with at least one of the primary endpoints of interest, all-cause mortality and cancer-specific mortality, (iii) the study population consists of cancer survivors, defined as women and men aged 18 years and older with a diagnosis of primary cancer (from the time of diagnosis through the remainder of their lives), (iv) the minimum sample size is 100 participants, (v) the length of follow-up is at least six months, and (vi) provide a measure of association, such as Hazard Ratio (HR), and the corresponding 95% confidence intervals (CIs), or sufficient information for their calculation, for the comparison between the highest versus the lowest category of adherence to one a priori or a posteriori dietary pattern. The search will exclude editorials, letters to the Editor, comments, conference abstracts, systematic reviews and metaanalyses and it will be limited to English articles.
- Literature search: The literature search will be performed in three electronic databases MEDLINE, Scopus and Web of Science from January 2000 up to 09 October 2022. Reference lists of previous meta-analyses and systematic reviews, as well as, from the identified articles in the present review, will be also hand-searched in order to retrieve any additional relevant articles.
- Data extraction: The following data will be extracted: first author, publication year, study location, cancer site, cancer stage (where available), sample size, age and sex distribution, follow-up duration, outcome assessed (all-cause mortality and cancer-specific mortality), types of dietary patterns and dietary assessment method used, increments or categories used for the analysis of dietary patterns

(i.e. values from quartiles/quintiles used to define the highest category and the lowest category taken as reference), adjustment covariates and the reported measures of associations (i.e HR with associated 95% CIs).

- Risk of bias: The risk of bias in the included cohort studies will be evaluated with the ROBINS-I tool, which takes into account seven domains of bias: confounding, selection of participants into the study, classification of exposures, deviations from intended exposures during follow-up, missing data, outcome measurement, and selection of reported result.
- Data analysis: The pooled estimate for the association of the highest vs. the lowest categories of adherence to post-diagnosis *a priori*and *a posteriori* dietary patterns, grouped by cancer site and overall, with each of the outcomes of interest, i.e. all-cause and cancer-specific mortality, will be estimated by random effects meta-analysis models to take into account the between-study heterogeneity. The between-studies variance will be estimated using the approach by Der Simonian and Laird. Heterogeneity will be assessed by the I<sup>2</sup> statistic, with values > 50% considered as substantial heterogeneity, and graphically by Galbraith plots. Publication bias will be assessed by funnel plots and Egger's test will investigate the asymmetry in the case of more than 10 studies in the meta-analyses. We will further apply subgroup analysis among studies by their assessment of the overall risk of bias. A cumulative meta-analysis by year of publication will be also performed for all-cause mortality and cancer-specific mortality. A sensitivity analysis with influence plots investigating the impact of a priori dietary patterns on overall mortality and cancer mortality by omitting one study at a time and assessing its effect on the overall estimate will be also applied.