Sugar sweetened and artificially sweetened beverages, fruit and vegetable juices and cancer risk: a World Cancer Research Fund International Global Cancer Update Programme (CUP Global) systematic literature review and meta-analysis

Ahmad Jayedi[1], Georgios Markozannes[1,2], Sayada Zartasha Kazmi[1], Margarita Cariolou[1], Rita Vieira[1], Sonia Kiss[1], Katia Balducci[1], Eirini Pagkalidou[1,2], Sofia Cividini[1], Dagfinn Aune[1,3,4,] Darren C Greenwood[5], Laure Dossus[6], Emma Fontvieille[6], Nahid Ahmadi[6], Yahya Mahamat-Saleh[6], Amanda J. Cross[7], Marc J. Gunter[8], Shalini Jayasekar Zürn[9], Christian C. Abnet[10], Pietro Ferrari[11], Vanessa L.Z. Gordon-Dseagu[12], Kristy Maskell[12], Christelle Clary[12], Helen Croker[12], Panagiota Mitrou[12], Elio Riboli[12], Monica Baskin[13], Rajiv Chowdhury[14], Mia Gaudet[15], Edward Giovannucci[16], Ellen Kampman[17], Sarah J. Lewis[18], Anne M. May[19, 20], Yikyung Park[21], Tobias Pischon[22], Gianluca Severi[23], Lynette Hill[24], Matty P. Weijenberg[25], John Krebs[26], Konstantinos K Tsilidis[1,2*], Doris S.M. Chan[1*]

[1] Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London
[2] Department of Hygiene and Epidemiology, University of Ioannina Medical School, Ioannina, Greece
[3] Department of Nutrition, Oslo New University College, Oslo
[4] Department of Research, The Cancer Registry of Norway, Oslo, Norway
[5] Leeds Institute for Data Analytics, University of Leeds, Leeds, UK
[6] Nutrition and Metabolism Branch, International Agency for Research on Cancer, Lyon, France
[7] Department of Surgery and Cancer, Imperial College London, London, UK
[8] Cancer Epidemiology and Prevention Research Unit, School of Public Health, Imperial College London, London, UK
[9] Knowledge, Advocacy and Policy, Union for International Cancer Control, Geneva, Switzerland
[10] Metabolic Epidemiology Branch (MEB), Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Rockville, MD 20850, United States
[11] Head, Nutrition and Metabolism Branch, International Agency for Research on Cancer, Lyon, France
[12] World Cancer Research Fund International, London, UK
[13] Massey Comprehensive Cancer Center, USA
[14] Department of Global Health, Florida International University, Miami, Florida, USA
[15] Trans-Divisional Research Program (TDRP), Division of Cancer Epidemiology Genetics (DCEG), National Cancer Institute (NCI), National Institutes of Health, Rockville, MD 20850, United States
[16] Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA
[17] Division of Human Nutrition and Health, Wageningen University & Research, Wageningen, The Netherlands
[18] Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK
[19] University Medical Centre Utrecht, Julius Centre for Health Sciences and Primary Care, Utrecht, The Netherlands
[20] Netherlands Cancer Institute, Division of Psychosocial Research & Epidemiology, PO Box 90203, 1006 BE Amsterdam, The Netherlands |
[21] Division of Public Health Sciences, Washington University School of Medicine, Washington University in St.Louis, St Louis, USA
[22] Molecular Epidemiology Research Group, Max Delbrück Center for Molecular Medicine, Berlin, Germany
[23] CESP U1018, U.Paris-Saclay, UVSQ, INSERM, France

[24] Public Representative
[25] Department of Epidemiology, Maastricht University, Maastricht, The Netherlands
[26] Department of Biology, University of Oxford, Oxford, UK

* Shared last co-authors

Corresponding authors: Konstantinos K Tsilidis, Doris S.M. Chan
Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London
d.chan@imperial.ac.uk; k.tsilidis@imperial.ac.uk

Main text word count: 4816 / Abstract word count: 298 / Figures: 4

Summary

Background: Sugar sweetened beverages (SSBs), artificially sweetened beverages (ASBs), and fruit and vegetable juices are consumed worldwide, yet their associations with cancer remain unclear.

Methods: Within World Cancer Research Fund International's Global Cancer Update Programme (CUP Global), we conducted a systematic review by searching PubMed and Embase until September 2024 for cohort studies of SSBs, ASBs, and juices and cancer risk. Meta-analyses were conducted to calculate the relative risks (RRs) and 95% CIs per 1 serving/day (355 mL for SSBs/ASBs; 177 mL for juices). Evidence was graded by the CUP Global Expert Panel. The CUP Global standard protocol was registered at: https://osf.io/7utbm/.

Findings: We identified 158 publications from 51 cohorts. There was evidence of a probable causal positive association for SSBs, including carbonated SSBs, with pancreatic cancer incidence (RR 1.09 [95% CI 1.01–1.16]; I^2=8%, n=18 studies), and for SSBs with colorectal cancer incidence (RR 1.07 [95% CI 1.00–1.14]; I^2=41%, n=13). Limited suggestive evidence supported positive associations of SSBs with ovarian (RR 1.61 [95%CI 1.03–2.53]; I^2=0%, n=2), endometrial (RR 1.21 [95%CI 1.03-1.42]; I^2=0%, n=3), and postmenopausal breast cancer incidence (RR 1.05 [95%CI 1.00-1.10] ; I^2=0%, n=6), and of carbonated ASBs with leukaemia incidence (RR 1.29 [95%CI 1.01-1.64]; I^2=0%, n=2). There was evidence of a probable causal positive association for orange juice with different types of skin cancer including melanoma (RR 1.21 [95%CI 1.08-1.34]; I^2=0%, n=4), and basal (RR 1.12 [95%CI 1.06-1.17]; I^2=46%, n=2) and squamous cell carcinoma (RR 1.13 [95%CI 1.04-1.24]; I^2=0%, n=2). An interactive evidence platform is available at: https://teacup.cc.ic.ac.uk/soft-drinks-cancer.html.

Interpretation: This review provides evidence supporting probable causal associations of SSBs with pancreatic and colorectal cancers, and of orange juice with skin cancers, with additional

suggestive evidence for SSBs with other obesity-related cancers, extending concerns about sugary drink consumption beyond cardiometabolic health to cancer risk.

Funding: World Cancer Research Fund network of charities (American Institute for Cancer Research; World Cancer Research Fund; Wereld Kanker Onderzoek Fonds).

Introduction

The intake of sugar sweetened beverages (SSBs) has increased worldwide over recent decades.[1] Between 1990 and 2018, global consumption of SSBs rose by 0.68 servings/week among children and adolescents[2] and by 0.37 servings/week in adults,[3] resulting in an average weekly intake of 3.6 servings for children and adolescents and 2.7 servings for adults in 2018. These beverages represent the predominant source of added free sugars in the diet while providing minimal nutritional value.[4]

A growing body of evidence suggests that high consumption of added free sugars from SSBs contributes to weight gain, promotes de novo lipogenesis and ectopic fat accumulation, and exacerbates insulin resistance and low-grade systemic inflammation[5] and is therefore linked to higher risks of type 2 diabetes [6] and heart disease.[7] These concerns may encourage consumers to seek alternatives perceived as healthier.[8] Artificially sweetened beverages (ASBs) and fruit juices are commonly consumed as substitutes for SSBs.[9] However, potential adverse effects of ASBs on the gut microbiome, appetite regulation, sweet taste perception, and fat storage have been raised.[10] In addition, commercially produced juice products (e.g., juice drinks and nectars) may contain added free sugars, fruit juice concentrates or other sweetening ingredients, further increasing their overall free sugar content. [11] Pure juices contain certain nutrients and are included in dietary guidelines in several countries, where modest consumption (e.g., half or one glass of unsweetened 100% fruit or vegetable juice) contributes to recommended fruit and vegetable intake.[12] However, even 100% juices are low in fibre and relatively high in free sugars and energy-dense, and excessive consumption may promote weight gain.[13]

Epidemiological evidence linking SSBs consumption to cancer risk remains inconsistent and inconclusive [14-16]. For ASBs, a meta-analysis of cohort studies suggested a positive association for leukaemia,[16] while a recent umbrella review found no association for gastrointestinal cancers and total cancer mortality.[17] Evidence for fruit juice is also inconsistent. [15,16] These findings, however, are limited by the inclusion of case-control studies and by heterogeneous exposure definitions,

including the combination of different beverage types and lack of distinction between pure and commercially produced juices. Such heterogeneity complicates interpretation and limits the ability to draw conclusions about specific beverage types.

In 2018, the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) Third Expert Report[18] issued 10 evidence-based recommendations for cancer prevention, including limiting SSBs intake, largely based on evidence linking SSBs to weight gain. At that time, however, epidemiologic evidence directly linking SSBs, ASBs, and fruit and vegetable juices to cancer risk was limited. To address these gaps, WCRF International's Global Cancer Update Programme (CUP Global) prioritised [19] SSBs, ASBs, and fruit and vegetable juices for an updated systematic literature review to complement the conclusions of the Third Expert Report. This work presents the results of a systematic literature review examining the associations between different types of soft drinks and juices and the risks of site-specific cancer incidence in adults, and alongside a companion review on sedentary behaviour and cancer risk (Markozannes et al, unpublished) contributes to a series of CUP Global reviews examining lifestyle-related exposures and cancer risk that will inform the Fourth Expert Report which will be developed by WCRF International in the coming years.

Methods

The present systematic review and meta-analysis have been conducted in accordance with a pre-registered CUP Global standard protocol (https://osf.io/7utbm/) and is reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (**Supplementary Table 1**).[20]

Search strategy and selection criteria

We searched PubMed and Embase until 1st September 2024 using a prespecified standard CUP Global strategy (**Supplementary Text 1**), supplemented by reference screening. In brief, eligible studies included randomised controlled trials (RCTs), cohort studies, Mendelian randomisation (MR) studies, and pooled analyses of such studies, on soft drinks or juices intake and adult cancer

incidence or mortality that reported multivariable adjusted risk estimates (more information provided in **Supplementary Text 2)**.

We classified beverages into four main groups including 1) SSBs; 2) ASBs; 3) juices , and 4) soft drinks (unspecified non-alcoholic sweetened drinks, assumed to be a combination of SSBs and ASBs) (**Supplementary Text 3).** Risk of bias was assessed using a modified Risk of Bias for Nutrition Observational Studies (RoB-NObs) tool,[21] originally developed by the U.S Department of Agriculture (USDA) Nutrition Evidence Systematic Review based on Cochrane's Risk of bias In Non-randomised Studies of Interventions (ROBINS-I),[22] and further adapted and validated by the CUP Global team at Imperial College London for lifestyle-disease associations (**Supplementary Text 4**). The RoB domains and criteria to rate studies in relation to each domain are listed in **Supplementary Tables 3-4**.

The characteristics and the results of the studies were extracted into the CUP Global database. Whenever possible, we preferentially extracted multivariable adjusted models excluding adiposity measures to avoid overadjustment for sugary beverages (SSBs, juices and soft drinks), while adiposity-adjusted models were used for ASBs (**Supplementary Text 5)**. The list of information extracted from MR studies is provided in **Supplementary Text 6**. Article selection, data extraction, and risk of bias assessment were double-checked in at least 10% of the records by a second reviewer. Any disagreement between reviewers was resolved with the review coordinator.

Data analysis

Our primary analyses were linear dose-response meta-analyses when two or more cohort studies provided sufficient information. When dose-response meta-analysis was not possible or when more than a third of the included studies did not have sufficient information for inclusion in a dose-response meta-analysis, a supporting categorical high versus low analysis was conducted. When a meta-analysis was not possible, the studies were descriptively reviewed. Non-linear dose-response

meta-analyses were conducted when at least five primary studies provided sufficient information (**Supplementary Text 7**). Meta-analyses were conducted separately for incidence and mortality, with additional combined analyses for high-fatality cancers (pancreas, liver, lung, and gallbladder). Hamling's method was used to pool results reported by cancer subtypes (e.g., colon and rectal cancer) to account for common denominators in risk estimates.[23] Each reported exposure was reviewed and analysed only once, however, we conducted additional analyses combining studies which reported on all SSBs with studies which reported only on carbonated SSBs, as carbonated SSBs constitute the predominant component of SSBs and this approach would increase statistical power. A similar approach was decided for carbonated ASBs and ASBs. We also combined orange juice with overall citrus fruit juice since orange juice is a good representative for citrus juice. A similar approach was used for pure fruit juice and fruit juice (**Supplementary Text 7**).

A DerSimonian-Laird random effects model[24] was used for linear dose-response and categorical meta-analyses. The increment units for the linear dose-response meta-analyses were 355 mL (12 US fluid oz)/day for SSBs, ASBs, and soft drinks,[25] and 177 ml (6 US fluid oz)/day for fruit or vegetable juices.[26] The proportion of total variability in effect estimates attributable to heterogeneity between studies was assessed by the I^2 metric.[27] Potential sources of heterogeneity were explored by pre-specified subgroup analyses (**Supplementary Text 7**), when at least two studies reported the results for the same subgroup. Leave-one-out sensitivity analyses were conducted to assess the impact of individual studies on the summary estimate.[28] Non-linear dose-response meta-analyses were conducted by one-stage mixed effects models [29,30] using restricted cubic splines with three knots placed at fixed percentiles (10th, 50th, and 90th) of the exposure distribution. [31] The potential for small study effects, including publication bias, was evaluated using the Egger's test[32] and by visually inspecting the funnel plots for asymmetry, when at least 10 studies were available. Analyses were conducted in Stata version 16.1. We also assessed MR studies for completeness of evidence and reviewed them descriptively, but it is likely that these results are not fully credible, as the biological relevance of the genetic variants associated with these exposures is unclear.[33]

Grading the evidence

An Expert Panel convened by WCRF International interpreted and graded the quality of the evidence as *convincing***,** *probable*, *limited suggestive, limited no conclusion*, or *substantial effect on risk unlikely*, following predefined evidence-grading criteria designed to evaluate the likelihood of causality **(Supplementary Table 5)**. Evidence of biological plausibility in humans was also considered by the Expert Panel and assessed separately using a structured framework (REF) and reviewed by CUP Global collaborators at International Agency for Research on Cancer (IARC).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

The systematic search identified 17 309 unique records, of which 633 were selected for full text review. Subsequently, 457 publications were excluded, resulting in 176 publications that were deemed potentially eligible (**Figure 1**). We additionally excluded 17 publications based on the reasons presented in **Supplementary Table 6** and added two additional publications found in a complementary search. Finally, 161 publications met the eligibility criteria, including 158 from 51 prospective observational cohort studies **(Supplementary Tables 7-10)** [26,34-190] and three MR studies [191-193], with no RCTs identified. A detailed list of exposure-outcome pairs assessed in each of the 51 cohort studies included in the systematic review is presented in (**excel file: Soft drinks and juices_Cohorts**).

Detailed characteristics of the cohort studies on SSBs, ASBs, juices, and soft drinks are presented in **Supplementary Tables 11-17**. In brief, 20 studies (38%) (87 publications) were from North America,[34,37-39,41,42,46,48,50-52,54-60,62,63,71,72,74,75,77,79-82,86-89,93,94,98,102,105,108,109,113-116,119-123,128-131,135,138,141,143-145,148,150,151,153,157,158,160-163,168,170-175,177,178,183-190] 16 studies (30%) (45 publications)

were from Europe,[35,36,40,43,44,47,49,53,61,65-69,78,83,90,95,96,99,104,107,110-112,118,124,126,127,133,136,137,142,146,147,152,156,159,164-167,179-181] eight (15%) (16 publications) were from Southeast/East Asia,[45,76,84,85,97,100,101,103,106,125,132,134,149,154,169,176] two were from Australia,[70,73] and eight pooled analyses from a combination of the above-mentioned regions.[26,64,91,92,117,139,155,182]

A summary of associations that received an evidence grading is presented in **Figures 2-4.** Summaries of all associations investigated across various exposure groups, including results for biological (e.g., molecular, histological, and clinical) subtypes and anatomical subsites and cancer mortality, are presented in **Supplementary Figures 1-7**, and summaries of associations across major cancer sites are presented in **Supplementary Figures 8-17.** Supporting results showing the categorical highest versus lowest comparisons are presented in **Supplementary Figures 18-69.** A brief overview of the results is provided below, with all estimates relating to cancer incidence, unless otherwise stated, and expressed per 1 serving/day (355 mL for SSBs and ASBs; 177 mL for juices). Results for cancer mortality and descriptive synthesis are detailed in **Supplementary Texts 8-16**, and single-study associations in **Supplementary Tables 18-21**.

Thirty-nine studies (61 publications, including 10 pooled analyses) examined SSBs and cancer risk across 18 anatomical sites, encompassing 89 exposure-outcome pairs (64 incidence, 25 mortality) (**Supplementary Tables 11**).[34,36-40,42,44-47,53,64,66,70,72,74,75,78-82,84,85,90,97-101,105,106,108,109,113,114,122,126-131,135,145,146,150,157,168,169,172,173,177,178,180,182,184,186-188] Forest plots indicating meta-analyses are indicated in **Supplementary Figures 70-104**, a summary of all associations in **Supplementary Figures 2-3**, and a summary of the associations that received grading in **Figure 2**.

There was a positive association between SSBs and ovarian (RR 1.61 [95%CI 1.03-2.53]; I^2=0%) (2 studies, 228 cases)[38,70] (**Supplementary Figure 70**) and endometrial cancer risk (RR 1.21 [95%CI 1.03-1.42]; I^2=0%) (3 studies, 931 cases)[38,70,74] (**Supplementary Figure 71**), as well as between SSBs and carbonated SSBs combined and pancreatic cancer risk (RR 1.09 [95%CI 1.01-1.16]; I^2=8%) (18 studies, 5 publications including one pooled analysis of 14 cohorts, 4914

cases)[39,45,64,127,131] (**Supplementary Figures 72-75).** There was also a positive association between SSBs and colorectal cancer risk (RR 1.07 [95%CI 1.00-1.14]; I^2=41%) (13 studies, 11 publications, 12,649 cases)[38,40,44,70,81,97,101,108,129,135,168] (**Supplementary Figure 76**), with little evidence of association for colorectal cancer anatomical subsites (**Supplementary Figures 77-82**). Of note, substituting SSBs with ASBs (per 1 serving/day) was associated with a lower risk of proximal colon cancer risk (RR 0.84 [95%CI 0.77-0.95]) (2 studies, 1 publication, 1275 cases)[178] (**Supplementary Figure 83**).

There was also an indication of a positive association between SSBs and breast cancer risk (RR 1.07 [95%CI 0.98-1.18]; I^2=56%) (8 studies, 7 publications, 15 855 cases)[38,44,97,108,128,145,146] (**Supplementary Figure 84**) and premenopausal breast cancer risk (RR 1.26 [95%CI 0.95-1.68]; I^2=64%) (5 studies, 4 publications, 3970 cases),[38,44,128,145] although CIs included the null. The association was more evident for postmenopausal breast cancer risk (RR 1.05 [95%CI 1.00-1.10]; I^2=0%) (6 studies, 5 publications, 10 774 cases)[38,44,70,130,145] (**Supplementary Figure 85**). A positive association but with a CI crossing the null value was also observed between SSBs and carbonated SSBs combined and kidney cancer risk (RR 1.11 [95%CI 0.97-1.28]; I^2=33%) (6 studies, 5 publications, 1598 cases)[66,70,98,100,173] (**Supplementary Figures 87-88).** Little evidence of an association was observed for other investigated exposure-outcome pairs (**Supplementary Figures 89-104)**. Non-linear dose-response meta-analysis of colorectal, breast, and postmenopausal breast cancers indicated no evidence of departure from linearity (**Supplementary Figures 105-107**).

Subgroup analyses by study and participant's characteristics are presented in **Supplementary Table 19** and **Supplementary Figures 108-154**. Of note, there was no heterogeneity in the subgroup analyses by potential presence of biases due to confounding and deviation from intended exposure and by frequency of dietary assessment (baseline vs repeated). The positive association between carbonated SSBs and pancreatic cancer was consistent across subgroups defined by BMI, alcohol

consumption, and physical activity (**Supplementary Figure 139**). There were indications of heterogeneity by geographical location, where studies conducted in Europe indicated positive associations between SSBs and colorectal (RR 1.82 [95%CI 1.04-3.16]; I^2=0%; n=2) (**Supplementary Figure 109**) and breast cancer risk (RR 2.07 [95%CI 1.27-3.38]; I^2=0%; n=2) (**Supplementary Figure 140**), while studies conducted in the North America and East/Southeast Asia showed weaker or no association (P group differences = 0.018 and 0.021, respectively) (**Supplementary Table 19)**. Sensitivity analyses showed largely stable results (**Supplementary Figures 155-168**). Test for publication bias was possible for colorectal cancer, which indicated little evidence of small-study effects (P Egger's test = 0.13) (**Supplementary Figure 169**).

Fifteen studies (26 publications, including seven pooled analyses) examined ASBs and cancer risk across 18 anatomical sites, covering 66 exposure-outcome pairs (47 incidence, 19 mortality) (**Supplementary Tables 12**).[39,44,49,66,70,72,74,75,78,79,98,109,113,114,126,127,140,144,145,150,151,168,177,180,186,187] Linear dose-response meta-analyses are indicated in **Supplementary Figures 191-209**, a summary of all associations in **Supplementary Figure 4,** and a summary of the associations that received grading in **Figure 3**. A positive association was seen between carbonated ASBs and leukaemia risk (RR 1.29 [95%CI 1.01-1.64]; I^2=0%) (2 studies, 1 publication, 339 cases)[150] (**Supplementary Figure 191**), and between ASBs (RR 1.05 [95%CI 1.00-1.10]; I^2=23%) (3 studies, 10 896 cases)[39,113,127] and ASBs and carbonated ASBs combined (RR 1.03 [95%CI 1.01-1.05]; I^2=0%) (5 studies, 4 publications, 11,275 cases)[39,113,127,151] and pancreatic cancer incidence/mortality (**Supplementary Figures 192-194**). Little evidence of an association was observed for other investigated exposure-outcome pairs (**Supplementary Figures 195-209)**. There was no evidence of heterogeneity in the subgroup analyses (**Supplementary Table 20**, **Supplementary Figures 210-220**). The main results did not change materially in the influence analyses (**Supplementary Figures 221-228**).

Forty studies (93 publications, including 13 pooled analyses) examined juices and cancer risk across 18 anatomical sites, encompassing 187 exposure-outcome pairs (167 incidence, 20 mortality) (**Supplementary Tables 13**).[26,36,38,41,43,44,47,49,51,52,54-60,62,63,65,66,69,72,74,76-79,81,83,84,86-94,98,103,104,107,108,110-112,115-118,120,121,123-125,127,131,133,134,136,138,139,141,142,147-149,152-156,158-162,164-167,170,171,174-176,179,181,183,185,188] Forest plots presenting meta-analyses are indicated in **Supplementary Figures 242-291**, a summary of all associations in **Supplementary Figures 5-7,** and a summary of the associations that received an Expert Panel grading is shown in **Figure 4**.

In general, there was little evidence of an association between fruit juices and cancer incidence, except for positive associations between fruit juice (RR 1.09 [95%CI 1.03-1.14]; I^2=75%) (2 studies, 1495 cases)[89,108] and fruit juice and pure fruit juice combined (RR 1.09 [95%CI 1.03-1.14]; I^2=54%) (3 studies, 1786 cases)[44,89,108] and prostate cancer risk (**Supplementary Figures 242-246**). Based on a pooled analysis of 15 studies with 52 680 cases, there was a positive association between fruit and vegetable juice and risk of prostate cancer (RR 1.03 [95%CI=1.01-1.05]) and its subtypes including localised, high grade, and especially advanced restricted prostate cancer (RR 1.11 [95%CI=1.02-1.21]) (**Supplementary Figure 247**).[139]

Orange juice was associated with a higher risk of melanoma (RR 1.21 [95%CI 1.08-1.34]; I^2=0%) (4 studies, 3 publications, 2912 cases)[54,110,171] (**Supplementary Figure 269**) and skin basal cell (RR 1.12 [95%CI 1.06-1.17]; I^2=46%) (2 studies, 1 publication, 20 840 cases)[170] (**Supplementary Figure 270**) and squamous cell carcinoma (RR 1.13 [95%CI 1.04-1.24]; I^2=0%) (2 studies, 1 publication, 3544 cases)[170] (**Supplementary Figure 271**). Additional analyses combining studies reporting on citrus juice with those reporting on orange juice showed similar positive associations (**Supplementary Figures 272-274**). Other results indicated evidence of no association between grapefruit juice and risks of skin cancers, citrus juice and vegetables juice and prostate cancer, and fruit and vegetable juice and various cancers (**Supplementary Figures 275-291).** A limited number of subgroup analyses were possible which indicated no evidence of heterogeneity (**Supplementary**

Table 21, **Supplementary Figures 292-299**). The main results did not change materially in influence analyses (**Supplementary Figures 300-307**).

Twenty-six studies reported on total soft drinks (**Supplementary Tables 14**).[26,35,36,39,48-50,61,65-68,71,73,79,85,95,96,102,117-119,125-127,132,136,137,140,143,147,159,163,180,183,189] Meta-analyses were possible for 13 cancers **(Supplementary Figure 1)**, suggesting no clear associations between soft drinks and cancer incidence (**Supplementary Figure 309-325**, **Supplementary Table 22**, **Supplementary Texts 17-19**).

Risk of bias assessments are summarised in **Supplementary Figure 326** and detailed in **Supplementary Text 20**. Most publications (81%) had moderate, 8% serious, and 11% critical risk of bias due to confounding, reflecting incomplete adjustment for key factors such as smoking intensity (for smoking-related cancers), alcohol intake, reproductive factors, race, and skin cancer-related variables. Bias due to departure from intended exposures was frequently rated as critical (74% of publications), primarily due to reliance on single baseline dietary assessments. However, subgroup analyses by assessment frequency and risk of bias did not show important difference between subgroups. Other domains, including exposure classification, missing data, outcome measurement, and selective reporting, were generally of lower concern. Evidence from three MR studies [191-193] on genetically predicted self-reported intake of sweet beverages, [192] SSBs, [191,192]ASBs, [191] and artificial sweeteners added to coffee or tea [193] and various cancer sites are presented in **Supplementary Table 23** and reviewed in **Supplementary Text 21.**

Based on IARC's review findings, the MEC did not identify strong evidence of biological mechanisms linking soft drinks and cancer through insulin- and glucose-related IPs (Fontvieille et al., unpublished). The MEC also acknowledged that furocoumarins may be implicated in biological mechanisms linking citrus fruit juices (including orange juice) to skin cancer; however, further research is required to fully characterise these mechanisms (see **Text Box** (**Panel) 1** for more information).

A summary of the evidence grading agreed by the Expert Panel is presented in the **Text Box (Panel) 2**. The evidence was graded as probable, indicating the likelihood of causality, for a positive association between SSBs and pancreatic and colorectal cancers, and limited suggestive for ovarian, endometrial, kidney, and breast cancer overall and by menopausal status. The evidence was also graded probable for the positive associations between orange juice and citrus juice and orange juice combined and risks of melanoma and skin basal cell and squamous cell carcinomas, and lower evidence grades were concluded for other cancers. An online interactive tool to help explore the evidence can be found at: https://teacup.cc.ic.ac.uk/soft-drinks-cancer.html.

Discussion

In this systematic literature review of 158 publications from 51 cohorts, we assessed associations between SSBs, ASBs, and fruits and vegetable juices and 19 cancer sites. Higher intake of SSBs was positively associated with the incidence of pancreatic, colorectal, ovarian, endometrial, kidney, and breast cancers, although the evidence supporting a causal association varied across cancers, with probable evidence for pancreatic and colorectal cancers, and limited suggestive evidence for ovarian, endometrial, kidney, and breast cancer overall and by menopausal status. ASBs showed mostly null associations, except for limited suggestive evidence supporting a positive association with leukaemia incidence. Among juices, orange juices and orange and citrus juices combined were positively associated with the incidence of melanoma and skin basal and squamous cell carcinomas (probable evidence), and fruit and vegetable juice with prostate cancer (limited suggestive evidence). Most other associations were null.

For SSBs, the results were indicative of positive associations with several obesity-related cancers, including pancreatic, colorectal, ovarian, endometrial, kidney, and breast cancers, suggesting that high intake of SSBs, partly through their contribution to weight gain, is associated with cancer risk. The evidence was graded as probable for pancreatic cancer, based on consistent findings from many cohort studies evaluating SSBs and carbonated SSBs. Notably, the positive association between

carbonated SSBs and pancreatic cancer persisted across several lower-risk subgroups, including individuals with normal weight, non-alcohol consumers, and those with higher physical activity levels. This consistency strengthens the robustness of the association, reduces concerns about confounding by alcohol or physical inactivity, and suggests potential mechanisms beyond adiposity alone, including inflammation and insulin resistance, which are implicated in pancreatic carcinogenesis. [194] However, mechanistic evaluation within CUP Global did not identify strong evidence supporting insulin- and glucose-related pathways linking SSBs consumption to cancer, reflecting limitations in the available literature. From a public health perspective, excessive intake of SSBs remains a well-established contributor to weight gain, overweight, and obesity, which are recognised risk factors for multiple cancers, as outlined in the WCRF/AICR Third Expert Report in 2018. [18]

Probable evidence was also observed for SSBs and colorectal cancer overall, based on 13 studies with low heterogeneity and risk of bias, supported by a positive association with colorectal cancer mortality. Subgroup analyses by using single versus repeated dietary assessments showed no heterogeneity, supporting the robustness of the findings. In contrast, evidence for colorectal cancer anatomical subsites was largely null, with limited no conclusion for colon cancer and strong evidence of no association for rectal cancer. These discrepancies likely reflect differences in data availability, as colorectal cancer analyses included more recent cohorts or updated dietary data, better capturing SSBs intake given its recent global increase in consumption. [2,3] In contrast, colon cancer estimates relied largely on an older pooled analysis and rectal cancer analysis was based on limited case numbers, underscoring the need for additional contemporary high-quality data.

Evidence for ovarian and endometrial cancers, two other obesity-related cancers,[195] was graded as limited suggestive, based on a small number of studies with limited case numbers, underscoring the need for additional larger studies to strengthen the evidence base and improve certainty. Combined evidence from studies of SSBs and carbonated SSBs were suggestive of a positive association with

kidney cancer, supported by a positive association between SSBs and kidney cancer mortality. Associations with breast cancer were consistently positive overall and by menopausal status, although the association was more evident for postmenopausal breast cancer, which is an established obesity-related cancer.[195] Whilst the wide CIs limited statistical evidence for kidney, breast, and premenopausal breast cancers, the expert panel concluded that the magnitude of the point estimates and consistency in the direction of the associations across included studies supported limited suggestive evidence of a positive association.

There was limited suggestive evidence of a positive association between carbonated ASBs and leukaemia, based on a pooled analysis of two cohorts of health professionals with repeated dietary measurements and low risk of bias due to confounding, with stratified analyses indicating no effect modification by BMI.[150] Experimental evidence in animals[196,197] and re-analysis of long-term cancer studies conducted on rats suggest potential carcinogenicity of aspartame,[198] whereas short-term experimental studies in animals largely support its safety.[199] However, long-term health effects at intakes below established acceptable daily intake remain uncertain.[200] Another possible explanation could involve the shared factors between SSBs and ASBs, such as the additional ingredients found in sodas or the materials used for soda packaging.[201,202] There was also a positive association between ASBs (including carbonated ASBs) and pancreatic cancer risk; however, the evidence was graded as limited no conclusion. This was because more than 95% of the analytical weight was contributed by a single large cohort in the US.[113] In addition, concerns remain regarding confounding by health status (e.g., pre-existing diabetes) and potential reverse causation, whereby individuals may have switched from SSBs to ASBs in response to recent weight gain or metabolic risk. These concerns are further amplified by the reliance of most studies on a single baseline dietary and confounders assessment, limiting the ability to capture changes in beverage consumption over time. Overall, the limited number of studies and inconsistent directions of associations across cancer sites preclude firm conclusions and underscore the need for further research.

Higher intake of orange juice and combined orange/citrus juices was consistently associated with higher risks of melanoma and basal and squamous cell carcinomas of the skin. Low between-study heterogeneity and low risk of bias for confounding and exposure misclassification, together with plausible biological mechanisms reviewed by the MEC, supported probable evidence gradings for skin cancers. Citrus furocoumarins/psoralens absorb ultraviolet radiation and can induce phototoxic skin reactions [203,204] which have lethal, mutagenic, and clastogenic effects.[205] In two pooled US health professionals cohorts, the positive association between orange juice intake and squamous cell carcinoma was restricted to tumours at chronically sun-exposed sites, including the head, neck and extremities, with no association for tumours at truncal sites. [170] Similarly, in the UK Biobank, citrus fruits intake was positively associated with melanoma among individuals with fair skin but inversely associated among those with olive skin, supporting potential effect modification by sun exposure and sensitivity.[110] Whilst the MEC identified the interaction between furocoumarins and sun exposure as a plausible biological mechanism, further research is needed to fully characterise these pathways.

Associations for fruit juice and pure fruit juice were largely null, although limited data was available for pure fruit juices. Based on a pooled analysis of 15 cohorts, [139] limited suggestive evidence was found for a positive association between intake of fruit and vegetable juice, including both pure and commercially produced ones, and prostate cancer incidence; the cautious grading from the expert panel for this association is due to a concern of detection bias due to greater health-seeking behaviour and prostate cancer screening among higher consumers. Positive associations between fruit juice and fruit juice and pure fruit juice combined and prostate cancer were also reported, although this finding was largely driven by an observational analysis within a large screening trial in the US,[89] resulting in limited no conclusion grading and highlighting the need for further research.

Several limitations of the available evidence should be considered. Most included cohorts relied on a single baseline dietary assessment, introducing potential exposure misclassification, which is likely non-differential and may have attenuated true associations. In addition, most studies (82%) adjusted for adiposity, a potential mediator of SSBs-cancer associations, which may have further attenuated estimates, as suggested by modestly weaker associations in BMI-adjusted models. Specified substitution analyses were rarely identified as such, although many models in the primary studies adjusted for total energy intake and may partially reflect unspecified isocaloric substitution; [206,207] however, those that performed specified substitution analyses suggested an inverse association for proximal colon cancer when substituting SSBs with ASBs. Nevertheless, further research is needed to evaluate substitution with lower-risk alternatives, particularly water. For ASBs, confounding by weight or underlying health status remains an important consideration to address, and where possible, rule out, as individuals with obesity or type 2 diabetes may preferentially consume these beverages; however, the few studies that examined associations stratified by BMI or diabetes status did not indicate heterogeneity across these subgroups. For juices, data on pure fruit juice were limited, despite its inclusion in dietary recommendations in some countries, underscoring the need for more robust evidence on its potential health effects. [12] In addition, most studies did not distinguish between pure and commercially produced juices, which differ in nutrient composition, particularly in added sugars, thereby limiting definitive conclusions.

This comprehensive evaluation of the evidence provides timely and policy-relevant insights for cancer prevention. Key strengths include the large evidence base, rigorous and harmonised exposure classification that avoided combining heterogeneous beverage types, and the use of multiple complementary analytical approaches, including dose-response meta-analyses, high-versus-low comparisons, and descriptive synthesis where data were limited. Extensive subgroup and sensitivity analyses supported the robustness of the findings. The integration of mechanistic evidence and the use of predefined criteria by an independent expert panel to grade the strength of evidence further strengthen the validity and interpretability of the conclusions. The findings

strengthen the rationale for limiting SSBs consumption, extending concerns beyond obesity and cardiometabolic disease to site-specific cancer risks. Given the global rise in SSBs intake, [2,3] these results support population-level interventions, such as taxation policies, reformulation strategies, and clearer front-of-pack labelling, to reduce consumption. Results from intervention studies suggest that SSBs reduction leads to weight loss.[208] Importantly, our findings also indicate that commonly used substitutes, including ASBs and certain juices, are not necessarily risk-free, underscoring the need for nuanced dietary guidance that differentiates between beverage types rather than promoting simple substitution. The evidence generated in the present review provides a robust foundation to inform future cancer prevention recommendations and highlights the importance of integrating beverage-specific guidance into national and international dietary policies. Specifically, this evidence will form part of the Fourth Expert Report which will be developed by WCRF International in the coming years.

In summary, the present SLR found evidence for a probable causal positive association between SSBs consumption and risk of colorectal and pancreatic cancers, and limited suggestive evidence for ovarian, endometrial, kidney, and breast cancer overall and by menopausal status. Evidence for ASBs was less clear, with limited suggestive evidence of a positive association for leukaemia. For juices, most associations were null, expect for evidence supporting probable causal positive associations between orange and citrus juices and melanoma and skin basal and squamous cell carcinomas. Future studies should focus on repeated measurements during the follow-up, more clear classification of dietary exposures (e.g., pure vs commercially produced fruit or vegetable juices or SSBs vs ASBs), exposure substitution models, and research on less-investigated cancers to generate more specific evidence-based guidelines. Future studies should also prioritise mechanistic research with longitudinal designs and standardised intermediate phenotypes measurement to clarify biological pathways.

Research in context

Evidence before this study

At the time of the WCRF/AICR Third Expert Report (2018), epidemiological evidence linking soft drinks and juices to cancer risk was limited. To prioritise future systematic review topics, CUP Global conducted a data-scanning and prioritisation exercise[19] and searched PubMed (January 2019-February 2024) for meta-analyses, pooled analyses, randomised trials, Mendelian randomisation studies, and large cohort studies using standard CUP Global search strategy and identified soft drinks and juices as one of the prioritised topics for an updated systematic review. Previous reviews found in the prioritisation exercise reported inconsistent associations for SSBs and inconclusive evidence for ASBs and juices, largely due to inclusion of case-control studies and heterogeneous exposure definitions, including combining SSBs with soft drinks (unspecified sweetened drinks, likely the combination of SSBs and ASBs) or grouping pure and commercially produced juices. Consequently, evidence for specific beverage and juice types remained unclear.

Added value of this study

We performed a cancer-wide systematic review and dose-response meta-analysis of 158 publications from 51 cohort studies, encompassing 281,560 incident cancer cases across 19 major cancer sites. Using harmonised exposure definitions and pre-specified analytic strategies, we quantified associations for SSBs, ASBs, and fruit and vegetable juices overall and by types. We found that higher intake of SSBs is associated with higher risks of pancreatic, colorectal, ovarian, endometrial, kidney, and breast cancer overall and by menopausal status. We also found a positive association between carbonated ASBs and leukaemia incidence. Orange juice and citrus and orange juices combined were associated with higher risks of melanoma and skin basal cell and squamous cell carcinomas. There was also evidence of a positive association between fruit and vegetable juice and prostate cancer incidence.

Implications of all the available evidence

Taken together, the evidence supports limiting consumption of SSBs as part of cancer prevention strategies, extending concerns beyond weight gain to site-specific cancer risk. The findings also highlight that not all beverage substitutes are necessarily risk-free, with emerging evidence for ASBs and citrus juices warranting caution. These results reinforce existing public health policies targeting sugary drink consumption and underscore the need for clearer dietary guidance that differentiates between beverage and juice types.

Text Box (Panel) 1. Mechanistic review

Evidence of biological plausibility in humans was also considered by the Expert Panel and assessed separately using a structured framework. This first involved expert input and use of an automated tool (https://www.temmpo.org.uk/) to identify intermediate phenotypes of potential interest. Insulin- and glucose-related biomarkers and, in the case of citrus fruit juices and skin cancer, furocoumarins were identified as intermediate phenotypes of interest. CUP Global collaborators at International Agency for Research on Cancer (IARC) then reviewed the evidence linking exposures, intermediate phenotypes, and outcomes. Finally, the CUP Global Expert Committee on Cancer Mechanisms (MEC) evaluated the review findings using a decision-support tool and agreed on biological plausibility statements.

Based on IARC's review findings, the MEC did not identify strong evidence of biological mechanisms linking soft drinks and cancer through insulin- and glucose-related intermediate phenotypes (Fontvieille et al., unpublished). This was due to several limitations in the current literature including a general lack of longitudinal study designs, standardised definitions and measurements of (subtypes of) exposures and intermediate phenotypes, and adequate control for key confounders. The MEC also acknowledged that furocoumarins may be implicated in biological mechanisms linking citrus fruit juices (including orange juice) to skin cancer; however, further research is required to fully characterise these mechanisms and potential interaction between furocoumarins and sun exposure. Of note, furocoumarin concentrations are higher in grapefruit than in oranges. The lack of association for grapefruit juice may reflect low consumption and a high proportion of non-consumers. Furocoumarins are concentrated in the citrus peel, and levels may therefore differ between homemade juices, which exclude the peel, and industrially processed juices, which may incorporate it. Further research is needed to characterise regional variation in intake, processing effects, the stability of furocoumarins during heat treatment, and the associations of other furocoumarin-containing foods such as parsnips and celery.

Text Box (Panel) 2: Grading the quality of evidence

The CUP Global Expert Panel interpreted and graded the quality of the evidence following pre-defined CUP Global evidence grading criteria designed to evaluate the likelihood of causality (**Supplementary Table 5)**. Evidence conclusions were made based on aspects related to the quantity, consistency, magnitude and precision of the summary estimates, presence of a dose-response relationship, study design and risk of bias, generalisability and mechanistic plausibility of the results from observational studies. Evidence grades were classified as convincing, probable, limited suggestive, limited no conclusion, or substantial effect on risk unlikely (indicating the likelihood of causality).

Based on evaluation by the CUP Global Expert Panel, there was evidence of a probable causal positive association between SSBs intake and pancreatic and colorectal cancers, and between citrus and orange juice and melanoma, as well as basal and squamous cell carcinomas of the skin, supported by consistent findings across studies, study size, risk of bias, and plausible biological mechanisms. Positive associations between SSBs and ovarian and endometrial cancers were observed but graded as limited suggestive owing to small numbers of studies and cases. For postmenopausal breast cancer, there was consistent evidence of a positive association from large cohort studies, but the CIs were wide and crossed the null value; thus, the expert panel concluded limited suggestive evidence. Evidence for other cancer sites was graded as limited no conclusion and/or substantial effects on risk unlikely, reflecting null findings, heterogeneity, small study numbers, risk of bias, and limited mechanistic support. Evidence based on a single study was classified as insufficient evidence to draw a conclusion

For ASBs, most associations were graded as limited no conclusion, reflecting small numbers of studies or cases, evidence of no association, imprecise estimates, between-study heterogeneity, and concerns about bias, particularly reverse causation related to diabetes, adiposity, prior SSBs intake, or recent weight gain. Evidence for the positive associations between carbonated ASBs and leukaemia was graded as limited suggestive, based on the relatively strong magnitude of associations observed in large cohort studies with repeated dietary assessments and low risk of bias, thereby reducing concerns about reverse causation.

For juices, a pooled analysis of 15 cohorts showed a positive association between fruit and vegetable juices and prostate cancer; however, the evidence was graded as limited suggestive due to potential detection bias and limited mechanistic support. Most other associations for juices were graded as limited no conclusion reflecting small numbers of studies or cases, imprecise estimates, between-study heterogeneity, and risk of bias. An online interactive tool to help explore the evidence can be found at: https://teacup.cc.ic.ac.uk/soft-drinks-cancer.html. Evidence presented in this systematic literature review will form part of the Fourth Expert Report which will be developed by WCRF International in the coming years.

Acknowledgments:
We thank Teresa Norat for leading the WCRF/AICR Continuous Update Project (CUP) as principal investigator from 2007 to 2020 and for developing the original review protocols. We thank the current and past WCRF International CUP/CUP Global Imperial team members for their contribution to the literature search, study selection, and/or data extraction; Lam Teng and past CUP/CUP Global Imperial database managers for implementing and updating the CUP Global database; and project manager: Eduardo Seleiro for organising the references, proofreading the manuscript and coordinating the work of CUP Global at Imperial College London. We also thank the CUP Global Expert Committee on Cancer Mechanisms (MEC) for evaluating and reviewing the findings of the mechanistic review.

IARC disclaimer:
Where authors are identified as personnel of the International Agency for Research on Cancer/World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy, or views of the International Agency for Research on Cancer/World Health Organization.

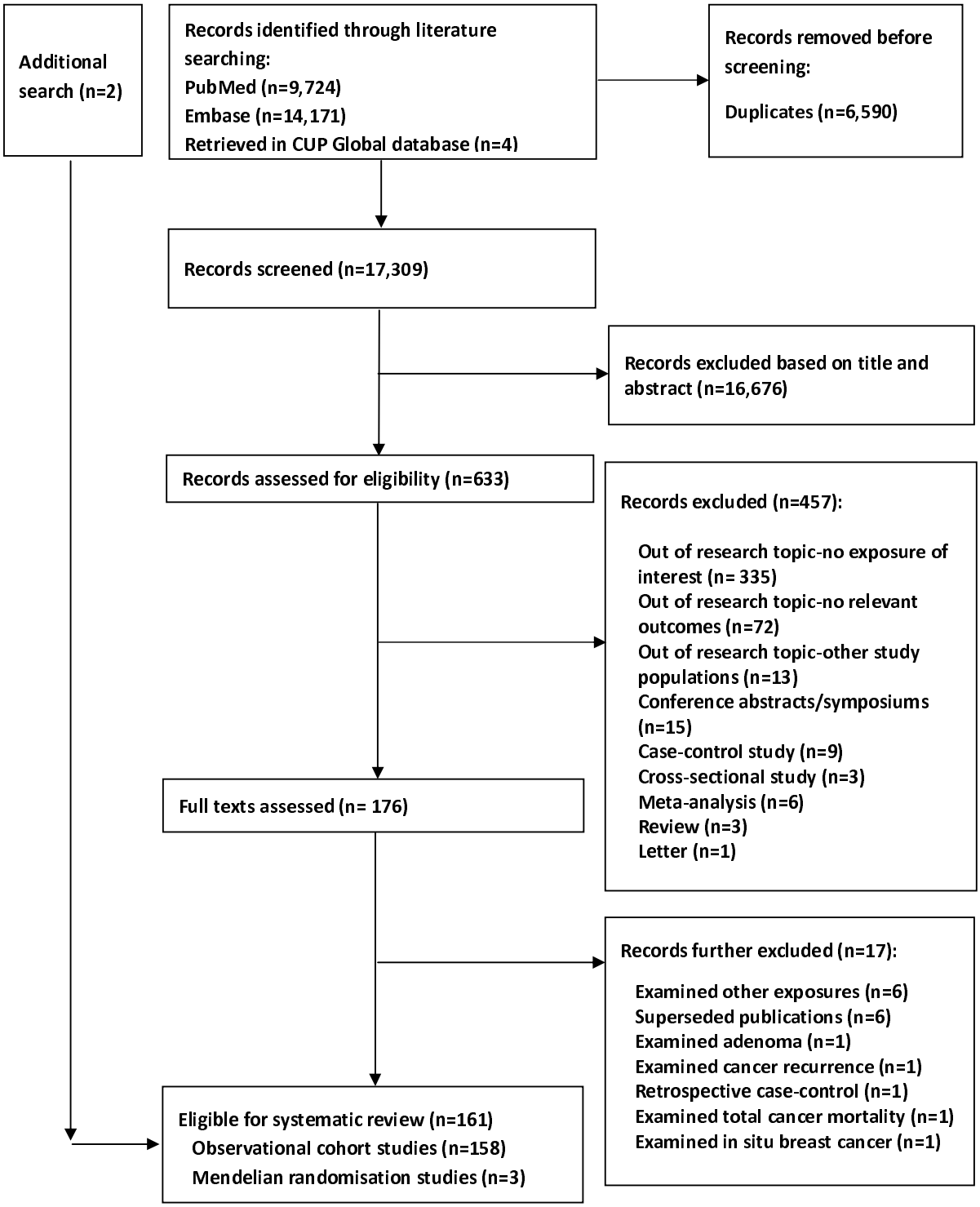
Funding information:
This work was funded by the World Cancer Research Fund network of charities (American Institute for Cancer Research [AICR]; World Cancer Research Fund [WCRF]; Wereld Kanker Onderzoek Fonds) (CUP Global Special Grant 2024).

Conflict of interest:
None.

Data availability statement:
Only publicly available data were used in our study. Data sources and handling of these data are described in the materials and methods section. Data are extracted into the CUP Global database and further details are available from the corresponding author upon request.

Ethics statement:
Ethical approval was not required, since this work was based solely on the analysis of published data without collection of new data or participant involvement.

Figure 1. Flowchart of study selection process.



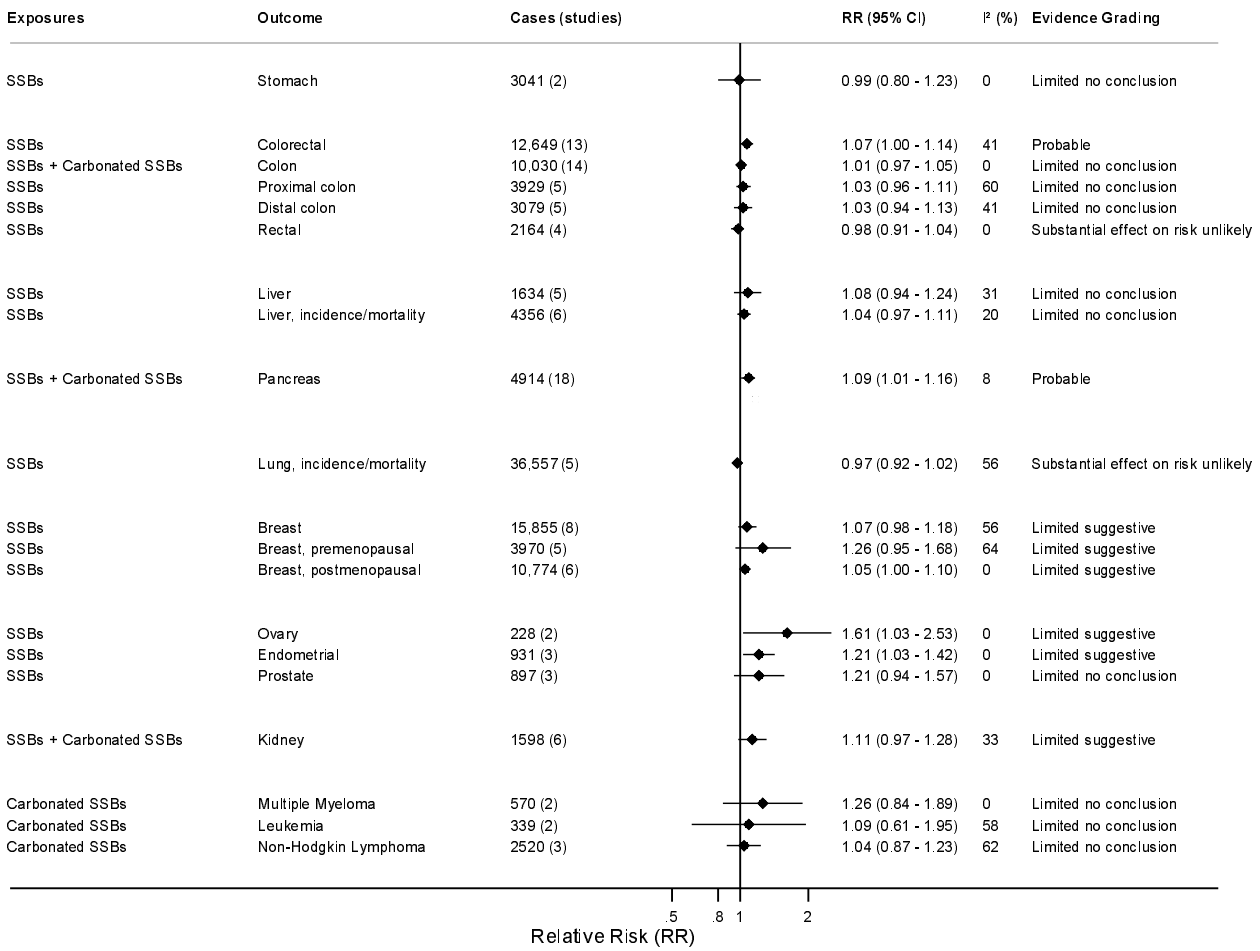


Figure 2. Summary forest plot showing the associations between sugar sweetened beverages (defined as liquids that are sweetened by adding free sugars, such as sucrose, high fructose corn syrup and sugars naturally present in honey, or syrups) (per 1 serving [355 mL]/day) and cancer risk (outcomes are incidence, unless otherwise stated). The forest plot shows the associations that received grading. Evidence grades were classified as convincing, probable, limited suggestive, limited no conclusion, or substantial effect on risk unlikely (indicating the likelihood of causality).

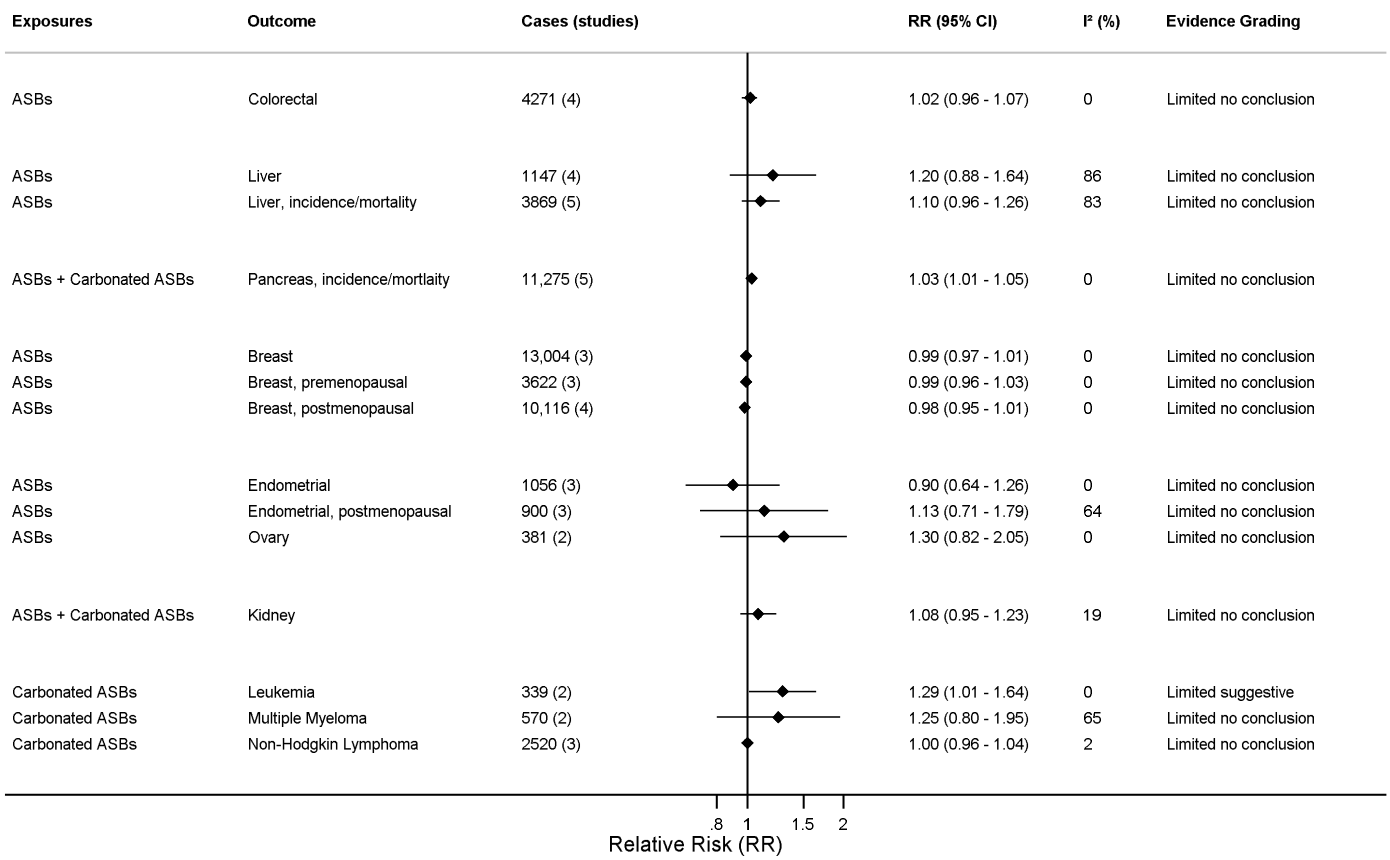


Figure 3. Summary forest plot showing the associations between artificially sweetened beverages (defined as low calorie or non-caloric beverages sweetened with artificial sweeteners, such as aspartame, acesulfame K, saccharin, sucralose, or neotame) (per 1 serving [355 mL]/day) and cancer risk (outcomes are incidence, unless otherwise stated). The forest plot shows the associations that received grading. Evidence grades were classified as convincing, probable, limited suggestive, limited no conclusion, or substantial effect on risk unlikely (indicating the likelihood of causality).

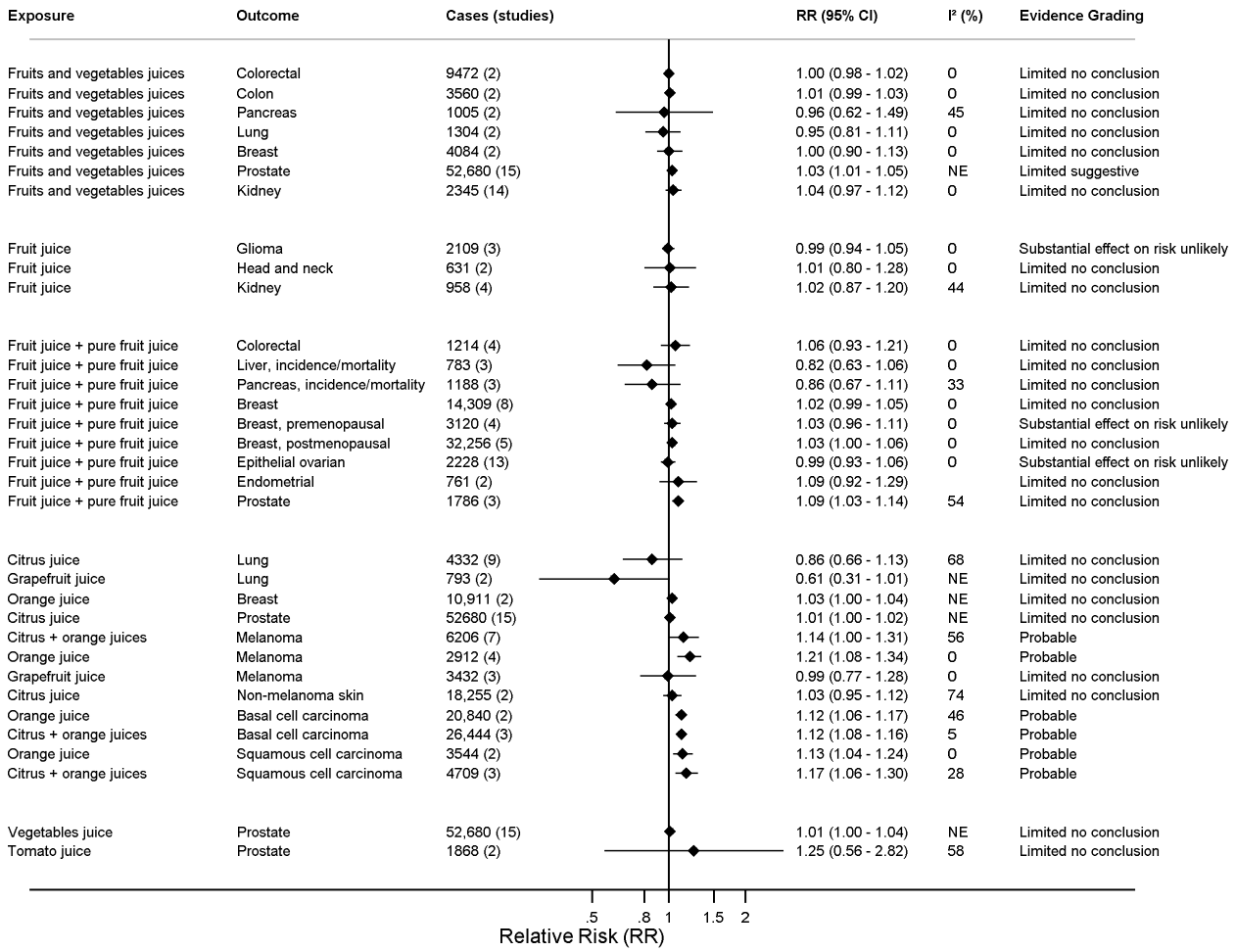


Figure 4. Summary forest plot showing the associations between juices (per 1 serving [177 mL]/day) and cancer risk (outcomes are incidence, unless otherwise stated). Juice exposures reflect definitions used in the individual studies and could include pure and commercially produced juices; where specific juice subtypes were reported separately (e.g., pure fruit juices), these were combined where appropriate for grading. The forest plot shows the associations that received grading. Evidence grades were classified as convincing, probable, limited suggestive, limited no conclusion, or substantial effect on risk unlikely (indicating the likelihood of causality).

References:

1. Malik VS, Willett WC, Hu FB. Global obesity: trends, risk factors and policy implications. *Nat Rev Endocrinol* 2013; **9**(1): 13-27.
2. Lara-Castor L, Micha R, Cudhea F, et al. Intake of sugar sweetened beverages among children and adolescents in 185 countries between 1990 and 2018: population based study. *Bmj* 2024; **386**: e079234.
3. Lara-Castor L, Micha R, Cudhea F, et al. Sugar-sweetened beverage intakes among adults between 1990 and 2018 in 185 countries. *Nat Commun* 2023; **14**(1): 5957.
4. Malik VS, Hu FB. Sugar-Sweetened Beverages and Cardiometabolic Health: An Update of the Evidence. *Nutrients* 2019; **11**(8).
5. Malik VS, Hu FB. The role of sugar-sweetened beverages in the global epidemics of obesity and chronic diseases. *Nat Rev Endocrinol* 2022; **18**(4): 205-18.
6. Greenwood DC, Threapleton DE, Evans CE, et al. Association between sugar-sweetened and artificially sweetened soft drinks and type 2 diabetes: systematic review and dose-response meta-analysis of prospective studies. *Br J Nutr* 2014; **112**(5): 725-34.
7. Lara-Castor L, O'Hearn M, Cudhea F, et al. Burdens of type 2 diabetes and cardiovascular disease attributable to sugar-sweetened beverages in 184 countries. *Nat Med* 2025.
8. Ertuglu LA, Afsar B, Yildiz AB, et al. Substitution of sugar-sweetened beverages for other beverages: can it be the next step towards healthy aging? *Current Nutrition Reports* 2021; **10**(4): 399-412.
9. Hu FB. Resolved: there is sufficient scientific evidence that decreasing sugar-sweetened beverage consumption will reduce the prevalence of obesity and obesity-related diseases. *Obes Rev* 2013; **14**(8): 606-19.
10. Escobar Gil T, Laverde Gil J. Artificially Sweetened Beverages Beyond the Metabolic Risks: A Systematic Review of the Literature. *Cureus* 2023; **15**(1): e33231.
11. Walker RW, Dumke KA, Goran MI. Fructose content in popular beverages made with and without high-fructose corn syrup. *Nutrition* 2014; **30**(7-8): 928-35.
12. Benton D, Young HA. Role of fruit juice in achieving the 5-a-day recommendation for fruit and vegetable intake. *Nutr Rev* 2019; **77**(11): 829-43.
13. Nguyen M, Jarvis SE, Chiavaroli L, et al. Consumption of 100% Fruit Juice and Body Weight in Children and Adults: A Systematic Review and Meta-Analysis. *JAMA Pediatr* 2024; **178**(3): 237-46.
14. Feng L, Gao J, Xia W, et al. Association of sugar-sweetened beverages with the risk of colorectal cancer: a systematic review and meta-analysis. *Eur J Clin Nutr* 2023; **77**(10): 941-52.
15. Li Y, Guo L, He K, Huang C, Tang S. Consumption of sugar-sweetened beverages and fruit juice and human cancer: a systematic review and dose-response meta-analysis of observational studies. *J Cancer* 2021; **12**(10): 3077-88.
16. Pan B, Lai H, Ma N, et al. Association of soft drinks and 100% fruit juice consumption with risk of cancer: a systematic review and dose-response meta-analysis of prospective cohort studies. *Int J Behav Nutr Phys Act* 2023; **20**(1): 58.
17. Diaz C, Rezende LFM, Sabag A, et al. Artificially Sweetened Beverages and Health Outcomes: An Umbrella Review. *Adv Nutr* 2023; **14**(4): 710-7.
18. WCRF/AICR. Diet, nutrition, physical activity and cancer: a global perspective: a summary of the Third Expert Report: World Cancer Research Fund International; 2018.
19. Markozannes G, Jayedi A, Cividini S, et al. A literature scanning and prioritization framework to guide future systematic reviews for World Cancer Research Fund International's Global Cancer Update Programme. *medRxiv* 2026: 2026.05.07.26352530.
20. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Bmj* 2021; **372**: n71.

21. USDA. Nutrition Evidence Systematic Review. Risk of Bias for Nutrition Observational Studies (RoB-NObs) Tool. 2022. https://nesr.usda.gov/sites/default/files/2019-07/RiskOfBiasForNutritionObservationalStudies-RoB-NObs.pdf (accessed April 2025).
22. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *Bmj* 2016; **355**: i4919.
23. Hamling J, Lee P, Weitkunat R, Ambühl M. Facilitating meta-analyses by deriving relative effect and precision estimates for alternative comparisons from a set of estimates presented by exposure level or disease category. *Stat Med* 2008; **27**(7): 954-70.
24. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; **7**(3): 177-88.
25. Deierlein AL, Raynor HA, Andres A, et al. Sugar-Sweetened Beverages and Growth, Body Composition, and Risk of Obesity: A Systematic Review with Meta-Analysis [Internet]. Alexandria (VA): USDA Nutrition Evidence Systematic Review; 2024 Nov. Methods. Available from: https://www.ncbi.nlm.nih.gov/books/NBK611226/. 2024.
26. Lee JE, Hunter DJ, Spiegelman D, et al. Intakes of coffee, tea, milk, soda and juice and renal cell cancer in a pooled analysis of 13 prospective studies. *Int J Cancer* 2007; **121**(10): 2246-53.
27. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002; **21**(11): 1539-58.
28. Viechtbauer W, Cheung MW. Outlier and influence diagnostics for meta-analysis. *Res Synth Methods* 2010; **1**(2): 112-25.
29. Orsini N. Weighted mixed-effects dose–response models for tables of correlated contrasts. *The Stata Journal* 2021; **21**(2): 320-47.
30. Royston P. A strategy for modelling the effect of a continuous covariate in medicine and epidemiology. *Stat Med* 2000; **19**(14): 1831-47.
31. Harrell FE. Regression modeling strategies: with applications to linear models, logistic regression, and survival analysis: Springer; 2001.
32. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *Bmj* 1997; **315**(7109): 629-34.
33. Burgess S, Woolf B, Mason AM, Ala-Korpela M, Gill D. Addressing the credibility crisis in Mendelian randomization. *BMC Med* 2024; **22**(1): 374.
34. Acuna N, Park SY, Le Marchand L, et al. Diet quality and risk of gastric adenocarcinoma: The Multiethnic Cohort. *Am J Clin Nutr* 2023; **117**(1): 46-54.
35. Agnoli C, Grioni S, Sieri S, et al. Italian Mediterranean Index and risk of colorectal cancer in the Italian section of the EPIC cohort. *Int J Cancer* 2013; **132**(6): 1404-11.
36. Allen NE, Balkwill A, Beral V, Green J, Reeves G. Fluid intake and incidence of renal cell carcinoma in UK women. *Br J Cancer* 2011; **104**(9): 1487-92.
37. Anic GM, Park Y, Subar AF, Schap TE, Reedy J. Index-based dietary patterns and risk of lung cancer in the NIH-AARP diet and health study. *Eur J Clin Nutr* 2016; **70**(1): 123-9.
38. Arthur RS, Kirsh VA, Mossavar-Rahmani Y, Xue X, Rohan TE. Sugar-containing beverages and their association with risk of breast, endometrial, ovarian and colorectal cancers among Canadian women. *Cancer Epidemiol* 2021; **70**: 101855.
39. Bao Y, Stolzenberg-Solomon R, Jiao L, et al. Added sugar and sugar-sweetened foods and beverages and the risk of pancreatic cancer in the National Institutes of Health-AARP Diet and Health Study. *Am J Clin Nutr* 2008; **88**(2): 431-40.
40. Barrubés L, Babio N, Hernández-Alonso P, et al. Association between the 2018 WCRF/AICR and the Low-Risk Lifestyle Scores with Colorectal Cancer Risk in the Predimed Study. *J Clin Med* 2020; **9**(4).

41. Bobe G, Weinstein SJ, Albanes D, et al. Flavonoid intake and risk of pancreatic cancer in male smokers (Finland). *Cancer Epidemiol Biomarkers Prev* 2008; **17**(3): 553-62.
42. Bosire C, Stampfer MJ, Subar AF, et al. Index-based dietary patterns and the risk of prostate cancer in the NIH-AARP diet and health study. *Am J Epidemiol* 2013; **177**(6): 504-13.
43. Botterweck AA, van den Brandt PA, Goldbohm RA. A prospective cohort study on vegetable and fruit consumption and stomach cancer risk in The Netherlands. *Am J Epidemiol* 1998; **148**(9): 842-53.
44. Chazelas E, Srour B, Desmetz E, et al. Sugary drink consumption and risk of cancer: results from NutriNet-Santé prospective cohort. *Bmj* 2019; **366**: l2408.
45. Chen CH, Tsai MK, Lee JH, et al. "Sugar-Sweetened Beverages" Is an Independent Risk From Pancreatic Cancer: Based on Half a Million Asian Cohort Followed for 25 Years. *Front Oncol* 2022; **12**: 835901.
46. Chen Y, Zeng S, Jiao B, et al. Adherence to the Diabetes Risk Reduction Diet and Bladder Cancer Risk in the Prostate, Lung, Colorectal, Ovarian (PLCO) Cohort. *Cancer Epidemiol Biomarkers Prev* 2023; **32**(12): 1726-33.
47. Drake I, Sonestedt E, Gullberg B, et al. Dietary intakes of carbohydrates in relation to prostate cancer risk: a prospective study in the Malmö Diet and Cancer cohort. *Am J Clin Nutr* 2012; **96**(6): 1409-18.
48. Dubrow R, Darefsky AS, Freedman ND, Hollenbeck AR, Sinha R. Coffee, tea, soda, and caffeine intake in relation to risk of adult glioma in the NIH-AARP Diet and Health Study. *Cancer Causes Control* 2012; **23**(5): 757-68.
49. Dunneram Y, Greenwood DC, Cade JE. Diet and risk of breast, endometrial and ovarian cancer: UK Women's Cohort Study. *Br J Nutr* 2019; **122**(5): 564-74.
50. Ellison LF. Tea and other beverage consumption and prostate cancer risk: a Canadian retrospective cohort study. *Eur J Cancer Prev* 2000; **9**(2): 125-30.
51. Farvid MS, Chen WY, Michels KB, Cho E, Willett WC, Eliassen AH. Fruit and vegetable consumption in adolescence and early adulthood and risk of breast cancer: population based cohort study. *Bmj* 2016; **353**: i2343.
52. Farvid MS, Chen WY, Rosner BA, Tamimi RM, Willett WC, Eliassen AH. Fruit and vegetable consumption and breast cancer incidence: Repeated measures over 30 years of follow-up. *Int J Cancer* 2019; **144**(7): 1496-510.
53. Feng X, Wang F, Yang W, et al. Association Between Genetic Risk, Adherence to Healthy Lifestyle Behavior, and Thyroid Cancer Risk. *JAMA Netw Open* 2022; **5**(12): e2246311.
54. Feskanich D, Willett WC, Hunter DJ, Colditz GA. Dietary intakes of vitamins A, C, and E and risk of melanoma in two cohorts of women. *Br J Cancer* 2003; **88**(9): 1381-7.
55. Feskanich D, Ziegler RG, Michaud DS, et al. Prospective study of fruit and vegetable consumption and risk of lung cancer among men and women. *J Natl Cancer Inst* 2000; **92**(22): 1812-23.
56. Fraser GE, Jacobsen BK, Knutsen SF, Mashchak A, Lloren JI. Tomato consumption and intake of lycopene as predictors of the incidence of prostate cancer: the Adventist Health Study-2. *Cancer Causes Control* 2020; **31**(4): 341-51.
57. Frazier AL, Ryan CT, Rockett H, Willett WC, Colditz GA. Adolescent diet and risk of breast cancer. *Breast Cancer Res* 2003; **5**(3): R59-64.
58. Freedman ND, Park Y, Subar AF, et al. Fruit and vegetable intake and esophageal cancer in a large prospective cohort study. *Int J Cancer* 2007; **121**(12): 2753-60.
59. Freedman ND, Park Y, Subar AF, et al. Fruit and vegetable intake and head and neck cancer risk in a large United States prospective cohort study. *Int J Cancer* 2008; **122**(10): 2330-6.

60. Freedman ND, Subar AF, Hollenbeck AR, Leitzmann MF, Schatzkin A, Abnet CC. Fruit and vegetable intake and gastric cancer risk in a large United States prospective cohort study. *Cancer Causes Control* 2008; **19**(5): 459-67.
61. Friberg E, Wallin A, Wolk A. Sucrose, high-sugar foods, and risk of endometrial cancer--a population-based cohort study. *Cancer Epidemiol Biomarkers Prev* 2011; **20**(9): 1831-7.
62. Fung TT, Chiuve SE, Willett WC, Hankinson SE, Hu FB, Holmes MD. Intake of specific fruits and vegetables in relation to risk of estrogen receptor-negative breast cancer among postmenopausal women. *Breast Cancer Res Treat* 2013; **138**(3): 925-30.
63. Fung TT, Hu FB, Hankinson SE, Willett WC, Holmes MD. Low-carbohydrate diets, dietary approaches to stop hypertension-style diets, and the risk of postmenopausal breast cancer. *Am J Epidemiol* 2011; **174**(6): 652-60.
64. Genkinger JM, Li R, Spiegelman D, et al. Coffee, tea, and sugar-sweetened carbonated soft drink intake and pancreatic cancer risk: a pooled analysis of 14 cohort studies. *Cancer Epidemiol Biomarkers Prev* 2012; **21**(2): 305-18.
65. Gnagnarella P, Maisonneuve P, Bellomi M, et al. Red meat, Mediterranean diet and lung cancer risk among heavy smokers in the COSMOS screening study. *Ann Oncol* 2013; **24**(10): 2606-11.
66. Heath AK, Clasen JL, Jayanth NP, et al. Soft Drink and Juice Consumption and Renal Cell Carcinoma Incidence and Mortality in the European Prospective Investigation into Cancer and Nutrition. *Cancer Epidemiol Biomarkers Prev* 2021; **30**(6): 1270-4.
67. Heath AK, Muller DC, van den Brandt PA, et al. Diet-wide association study of 92 foods and nutrients and lung cancer risk in the European Prospective Investigation into Cancer and Nutrition study and the Netherlands Cohort Study. *Int J Cancer* 2022; **151**(11): 1935-46.
68. Heath AK, Muller DC, van den Brandt PA, et al. Nutrient-wide association study of 92 foods and nutrients and breast cancer risk. *Breast Cancer Res* 2020; **22**(1): 5.
69. Hirvonen T, Mennen LI, de Bree A, et al. Consumption of antioxidant-rich beverages and risk for breast cancer in French women. *Ann Epidemiol* 2006; **16**(7): 503-8.
70. Hodge AM, Bassett JK, Milne RL, English DR, Giles GG. Consumption of sugar-sweetened and artificially sweetened soft drinks and risk of obesity-related cancers. *Public Health Nutr* 2018; **21**(9): 1618-26.
71. Holick CN, Smith SG, Giovannucci E, Michaud DS. Coffee, tea, caffeine intake, and risk of adult glioma in three prospective cohort studies. *Cancer Epidemiol Biomarkers Prev* 2010; **19**(1): 39-47.
72. Hur J, Otegbeye E, Joh HK, et al. Sugar-sweetened beverage intake in adulthood and adolescence and risk of early-onset colorectal cancer among women. *Gut* 2021; **70**(12): 2330-6.
73. Ibiebele TI, van der Pols JC, Hughes MC, Marks GC, Williams GM, Green AC. Dietary pattern in association with squamous cell carcinoma of the skin: a prospective study. *Am J Clin Nutr* 2007; **85**(5): 1401-8.
74. Inoue-Choi M, Robien K, Mariani A, Cerhan JR, Anderson KE. Sugar-sweetened beverage intake and the risk of type I and type II endometrial cancer among postmenopausal women. *Cancer Epidemiol Biomarkers Prev* 2013; **22**(12): 2384-94.
75. Ishitani K, Lin J, Manson JE, Buring JE, Zhang SM. Caffeine consumption and the risk of breast cancer in a large prospective cohort of women. *Arch Intern Med* 2008; **168**(18): 2022-31.
76. Iso H, Kubota Y. Nutrition and disease in the Japan Collaborative Cohort Study for Evaluation of Cancer (JACC). *Asian Pac J Cancer Prev* 2007; **8 Suppl**: 35-80.
77. Jiang Z, Chen H, Li M, Wang W, Long F, Fan C. Associations between colorectal cancer risk and dietary intake of tomato, tomato products, and lycopene: evidence from a prospective study of 101,680 US adults. *Front Oncol* 2023; **13**: 1220270.

78. Jin D, Lu Y, Wu W, et al. Diet-Wide Association, Genetic Susceptibility and Colorectal Cancer Risk: A Prospective Cohort Study. *Nutrients* 2023; **15**(22).
79. Jones GS, Graubard BI, Ramirez Y, et al. Sweetened beverage consumption and risk of liver cancer by diabetes status: A pooled analysis. *Cancer Epidemiol* 2022; **79**: 102201.
80. Julián-Serrano S, Reedy J, Robien K, Stolzenberg-Solomon R. Adherence to 5 Diet Quality Indices and Pancreatic Cancer Risk in a Large US Prospective Cohort. *Am J Epidemiol* 2022; **191**(9): 1584-600.
81. Kanehara R, Park SY, Okada Y, et al. Intake of Sugar and Food Sources of Sugar and Colorectal Cancer Risk in the Multiethnic Cohort Study. *J Nutr* 2024; **154**(8): 2481-92.
82. Kang M, Wilkens LR, Wirth MD, et al. Diet Quality and Risk of Bladder Cancer in the Multiethnic Cohort Study. *Nutrients* 2024; **16**(12).
83. Key TJ, Balkwill A, Bradbury KE, et al. Foods, macronutrients and breast cancer risk in postmenopausal women: a large UK cohort. *Int J Epidemiol* 2019; **48**(2): 489-500.
84. Khairan P, Sobue T, Eshak ES, et al. Sugary drink consumption and the subsequent risk of gastric cancer: The Japan Public Health Center-based Prospective Study. *Eur J Clin Nutr* 2023; **77**(2): 218-25.
85. Khan MM, Goto R, Kobayashi K, et al. Dietary habits and cancer mortality among middle aged and older Japanese living in hokkaido, Japan by cancer site and sex. *Asian Pac J Cancer Prev* 2004; **5**(1): 58-65.
86. Kim EH, Hankinson SE, Eliassen AH, Willett WC. A prospective study of grapefruit and grapefruit juice intake and breast cancer risk. *Br J Cancer* 2008; **98**(1): 240-1.
87. Kim J, Boushey CJ, Wilkens LR, Haiman CA, Le Marchand L, Park SY. Plant-based dietary patterns defined by a priori indices and colorectal cancer risk by sex and race/ethnicity: the Multiethnic Cohort Study. *BMC Med* 2022; **20**(1): 430.
88. Kim J, Setiawan VW, Wilkens LR, Le Marchand L, Park SY. Healthful Plant-Based Dietary Pattern and Risk of Hepatocellular Carcinoma in a Multiethnic Population: A Cohort Study. *Am J Clin Nutr* 2023; **118**(1): 194-200.
89. 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): 1200-9.
90. Kjaerheim K, Gaard M, Andersen A. The role of alcohol, tobacco, and dietary factors in upper aerogastric tract cancers: a prospective study of 10,900 Norwegian men. *Cancer Causes Control* 1998; **9**(1): 99-108.
91. Koushik A, Hunter DJ, Spiegelman D, et al. Fruits and vegetables and ovarian cancer risk in a pooled analysis of 12 cohort studies. *Cancer Epidemiol Biomarkers Prev* 2005; **14**(9): 2160-7.
92. Kuan AS, Green J, Kitahara CM, et al. Diet and risk of glioma: combined analysis of 3 large prospective studies in the UK and USA. *Neuro Oncol* 2019; **21**(7): 944-52.
93. Kunzmann AT, Coleman HG, Huang WY, Cantwell MM, Kitahara CM, Berndt SI. Fruit and vegetable intakes and risk of colorectal cancer and incident and recurrent adenomas in the PLCO cancer screening trial. *Int J Cancer* 2016; **138**(8): 1851-61.
94. Lan T, Park Y, Colditz GA, et al. Adolescent Plant Product Intake in Relation to Later Prostate Cancer Risk and Mortality in the NIH-AARP Diet and Health Study. *J Nutr* 2021; **151**(10): 3223-31.
95. Larsson SC, Bergkvist L, Wolk A. Consumption of sugar and sugar-sweetened foods and the risk of pancreatic cancer in a prospective study. *Am J Clin Nutr* 2006; **84**(5): 1171-6.
96. Larsson SC, Giovannucci EL, Wolk A. Sweetened Beverage Consumption and Risk of Biliary Tract and Gallbladder Cancer in a Prospective Study. *J Natl Cancer Inst* 2016; **108**(10).
97. Lee J, Shin A, Shin WK, Choi JY, Kang D, Lee JK. Adherence to the World Cancer Research Fund/American Institute for Cancer Research and Korean Cancer Prevention

Guidelines and cancer risk: a prospective cohort study from the Health Examinees-Gem study. *Epidemiol Health* 2023; **45**: e2023070.
98. Lee JE, Giovannucci E, Smith-Warner SA, Spiegelman D, Willett WC, Curhan GC. Total fluid intake and use of individual beverages and risk of renal cell cancer in two large cohorts. *Cancer Epidemiol Biomarkers Prev* 2006; **15**(6): 1204-11.
99. Leone A, Martínez-González M, Martin-Gorgojo A, et al. Mediterranean diet, Dietary Approaches to Stop Hypertension, and Pro-vegetarian dietary pattern in relation to the risk of basal cell carcinoma: a nested case-control study within the Seguimiento Universidad de Navarra (SUN) cohort. *Am J Clin Nutr* 2020; **112**(2): 364-72.
100. Leung CY, Abe SK, Sawada N, et al. Sugary drink consumption and risk of kidney and bladder cancer in Japanese adults. *Sci Rep* 2021; **11**(1): 21701.
101. Leung CY, Abe SK, Sawada N, et al. Sugary Drink Consumption and Subsequent Colorectal Cancer Risk: The Japan Public Health Center-Based Prospective Cohort Study. *Cancer Epidemiol Biomarkers Prev* 2021; **30**(4): 782-8.
102. Li YD, Fu YX, Gong LL, et al. Ultra-processed food consumption and renal cell carcinoma incidence and mortality: results from a large prospective cohort. *BMC Med* 2024; **22**(1): 459.
103. Lin Y, Kikuchi S, Tamakoshi A, et al. Dietary habits and pancreatic cancer risk in a cohort of middle-aged and elderly Japanese. *Nutr Cancer* 2006; **56**(1): 40-9.
104. Linseisen J, Rohrmann S, Miller AB, et al. Fruit and vegetable consumption and lung cancer risk: updated information from the European Prospective Investigation into Cancer and Nutrition (EPIC). *Int J Cancer* 2007; **121**(5): 1103-14.
105. Luo X, Sui J, Yang W, et al. Type 2 Diabetes Prevention Diet and Hepatocellular Carcinoma Risk in US Men and Women. *Am J Gastroenterol* 2019; **114**(12): 1870-7.
106. Luu HN, Neelakantan N, Geng TT, et al. Quality diet indexes and risk of hepatocellular carcinoma: Findings from the Singapore Chinese Health Study. *Int J Cancer* 2021; **148**(9): 2102-14.
107. Mahamat-Saleh Y, Cervenka I, Al-Rahmoun M, et al. Citrus intake and risk of skin cancer in the European Prospective Investigation into Cancer and Nutrition cohort (EPIC). *Eur J Epidemiol* 2020; **35**(11): 1057-67.
108. Makarem N, Bandera EV, Lin Y, Jacques PF, Hayes RB, Parekh N. Consumption of Sugars, Sugary Foods, and Sugary Beverages in Relation to Adiposity-Related Cancer Risk in the Framingham Offspring Cohort (1991-2013). *Cancer Prev Res (Phila)* 2018; **11**(6): 347-58.
109. Malik VS, Li Y, Pan A, et al. Long-Term Consumption of Sugar-Sweetened and Artificially Sweetened Beverages and Risk of Mortality in US Adults. *Circulation* 2019; **139**(18): 2113-25.
110. Marley AR, Li M, Champion VL, Song Y, Han J, Li X. The association between citrus consumption and melanoma risk in the UK Biobank. *Br J Dermatol* 2021; **185**(2): 353-62.
111. Marley AR, Li M, Champion VL, Song Y, Han J, Li X. Citrus Consumption and Risk of Non-Melanoma Skin Cancer in the UK Biobank. *Nutr Cancer* 2022; **74**(3): 810-5.
112. Masala G, Assedi M, Bendinelli B, et al. Fruit and vegetables consumption and breast cancer risk: the EPIC Italy study. *Breast Cancer Res Treat* 2012; **132**(3): 1127-36.
113. McCullough ML, Hodge RA, Campbell PT, Guinter MA, Patel AV. Sugar- and Artificially-Sweetened Beverages and Cancer Mortality in a Large U.S. Prospective Cohort. *Cancer Epidemiol Biomarkers Prev* 2022; **31**(10): 1907-18.
114. McCullough ML, Teras LR, Shah R, Diver WR, Gaudet MM, Gapstur SM. Artificially and sugar-sweetened carbonated beverage consumption is not associated with risk of lymphoid neoplasms in older men and women. *J Nutr* 2014; **144**(12): 2041-9.
115. Melough MM, Sakaki J, Liao LM, Sinha R, Cho E, Chun OK. Association between Citrus Consumption and Melanoma Risk in the NIH-AARP Diet and Health Study. *Nutr Cancer* 2021; **73**(9): 1613-20.

116. Melough MM, Wu S, Li WQ, et al. Citrus Consumption and Risk of Cutaneous Malignant Melanoma in the Women's Health Initiative. *Nutr Cancer* 2020; **72**(4): 568-75.
117. Merritt MA, Tzoulaki I, Tworoger SS, et al. Investigation of dietary factors and endometrial cancer risk using a nutrient-wide association study approach in the EPIC and Nurses' Health Study (NHS) and NHSII. *Cancer Epidemiol Biomarkers Prev* 2015; **24**(2): 466-71.
118. Merritt MA, Tzoulaki I, van den Brandt PA, et al. Nutrient-wide association study of 57 foods/nutrients and epithelial ovarian cancer in the European Prospective Investigation into Cancer and Nutrition study and the Netherlands Cohort Study. *Am J Clin Nutr* 2016; **103**(1): 161-7.
119. Michaud DS, Spiegelman D, Clinton SK, et al. Fluid intake and the risk of bladder cancer in men. *N Engl J Med* 1999; **340**(18): 1390-7.
120. Michaud DS, Spiegelman D, Clinton SK, Rimm EB, Willett WC, Giovannucci EL. Fruit and vegetable intake and incidence of bladder cancer in a male prospective cohort. *J Natl Cancer Inst* 1999; **91**(7): 605-13.
121. Michels KB, Rosner BA, Chumlea WC, Colditz GA, Willett WC. Preschool diet and adult risk of breast cancer. *Int J Cancer* 2006; **118**(3): 749-54.
122. Miller PE, Cross AJ, Subar AF, et al. Comparison of 4 established DASH diet indexes: examining associations of index scores and colorectal cancer. *Am J Clin Nutr* 2013; **98**(3): 794-803.
123. Mills PK, Beeson WL, Phillips RL, Fraser GE. Bladder cancer in a low risk population: results from the Adventist Health Study. *Am J Epidemiol* 1991; **133**(3): 230-9.
124. Mommers M, Schouten LJ, Goldbohm RA, van den Brandt PA. Consumption of vegetables and fruits and risk of ovarian carcinoma. *Cancer* 2005; **104**(7): 1512-9.
125. Mueller NT, Odegaard A, Anderson K, et al. Soft drink and juice consumption and risk of pancreatic cancer: the Singapore Chinese Health Study. *Cancer Epidemiol Biomarkers Prev* 2010; **19**(2): 447-55.
126. Mullee A, Romaguera D, Pearson-Stuttard J, et al. Association Between Soft Drink Consumption and Mortality in 10 European Countries. *JAMA Intern Med* 2019; **179**(11): 1479-90.
127. Navarrete-Muñoz EM, Wark PA, Romaguera D, et al. Sweet-beverage consumption and risk of pancreatic cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Am J Clin Nutr* 2016; **104**(3): 760-8.
128. Nomura SJ, Dash C, Rosenberg L, Yu J, Palmer JR, Adams-Campbell LL. Adherence to diet, physical activity and body weight recommendations and breast cancer incidence in the Black Women's Health Study. *Int J Cancer* 2016; **139**(12): 2738-52.
129. Nomura SJ, Dash C, Rosenberg L, Yu J, Palmer JR, Adams-Campbell LL. Is adherence to diet, physical activity, and body weight cancer prevention recommendations associated with colorectal cancer incidence in African American women? *Cancer Causes Control* 2016; **27**(7): 869-79.
130. Nomura SJ, Inoue-Choi M, Lazovich D, Robien K. WCRF/AICR recommendation adherence and breast cancer incidence among postmenopausal women with and without non-modifiable risk factors. *Int J Cancer* 2016; **138**(11): 2602-15.
131. Nöthlings U, Murphy SP, Wilkens LR, Henderson BE, Kolonel LN. Dietary glycemic load, added sugars, and carbohydrates as risk factors for pancreatic cancer: the Multiethnic Cohort Study. *Am J Clin Nutr* 2007; **86**(5): 1495-501.
132. Oh CC, Jin A, Yuan JM, Koh WP. Coffee, tea, caffeine, and risk of nonmelanoma skin cancer in a Chinese population: The Singapore Chinese Health Study. *J Am Acad Dermatol* 2019; **81**(2): 395-402.
133. Olsen A, Tjønneland A, Thomsen BL, et al. Fruits and vegetables intake differentially affects estrogen receptor negative and positive breast cancer incidence rates. *J Nutr* 2003; **133**(7): 2342-7.

134. Ozasa K, Watanabe Y, Ito Y, et al. Dietary habits and risk of lung cancer death in a large-scale cohort study (JACC Study) in Japan by sex and smoking habit. *Jpn J Cancer Res* 2001; **92**(12): 1259-69.
135. Pacheco LS, Anderson CAM, Lacey JV, Jr., et al. Sugar-sweetened beverages and colorectal cancer risk in the California Teachers Study. *PLoS One* 2019; **14**(10): e0223638.
136. Papadimitriou N, Bouras E, van den Brandt PA, et al. A Prospective Diet-Wide Association Study for Risk of Colorectal Cancer in EPIC. *Clin Gastroenterol Hepatol* 2022; **20**(4): 864-73.e13.
137. Papadimitriou N, Muller D, van den Brandt PA, et al. A nutrient-wide association study for risk of prostate cancer in the European Prospective Investigation into Cancer and Nutrition and the Netherlands Cohort Study. *Eur J Nutr* 2020; **59**(7): 2929-37.
138. Park SY, Ollberding NJ, Woolcott CG, Wilkens LR, Henderson BE, Kolonel LN. Fruit and vegetable intakes are associated with lower risk of bladder cancer among women in the Multiethnic Cohort Study. *J Nutr* 2013; **143**(8): 1283-92.
139. Petimar J, Wilson KM, Wu K, et al. A Pooled Analysis of 15 Prospective Cohort Studies on the Association between Fruit, Vegetable, and Mature Bean Consumption and Risk of Prostate Cancer. *Cancer Epidemiol Biomarkers Prev* 2017; **26**(8): 1276-87.
140. Podoltsev NA, Wang X, Wang R, et al. Lifestyle factors and risk of myeloproliferative neoplasms in the NIH-AARP diet and health study. *Int J Cancer* 2020; **147**(4): 948-57.
141. Podoltsev NA, Wang X, Wang R, et al. Diet and Risk of Myeloproliferative Neoplasms in Older Individuals from the NIH-AARP Cohort. *Cancer Epidemiol Biomarkers Prev* 2020; **29**(11): 2343-50.
142. Rashidkhani B, Lindblad P, Wolk A. Fruits, vegetables and risk of renal cell carcinoma: a prospective study of Swedish women. *Int J Cancer* 2005; **113**(3): 451-5.
143. Ren JS, Freedman ND, Kamangar F, et al. Tea, coffee, carbonated soft drinks and upper gastrointestinal tract cancer risk in a large United States prospective cohort study. *Eur J Cancer* 2010; **46**(10): 1873-81.
144. Ringel NE, Hovey KM, Andrews CA, et al. Association of Artificially Sweetened Beverage Consumption and Urinary Tract Cancers in the Women's Health Initiative Observational Study. *Eur Urol Open Sci* 2023; **47**: 80-6.
145. Romanos-Nanclares A, Collins LC, Hu FB, et al. Sugar-Sweetened Beverages, Artificially Sweetened Beverages, and Breast Cancer Risk: Results From 2 Prospective US Cohorts. *J Nutr* 2021; **151**(9): 2768-79.
146. Romanos-Nanclares A, Toledo E, Gardeazabal I, Jiménez-Moleón JJ, Martínez-González MA, Gea A. Sugar-sweetened beverage consumption and incidence of breast cancer: the Seguimiento Universidad de Navarra (SUN) Project. *Eur J Nutr* 2019; **58**(7): 2875-86.
147. Ros MM, Bas Bueno-de-Mesquita HB, Büchner FL, et al. Fluid intake and the risk of urothelial cell carcinomas in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Int J Cancer* 2011; **128**(11): 2695-708.
148. Sakaki JR, Melough MM, Roberts MB, et al. Citrus Consumption and the Risk of Non-Melanoma Skin Cancer in the Women's Health Initiative. *Cancers (Basel)* 2021; **13**(9).
149. Sakauchi F, Khan MM, Mori M, et al. Dietary habits and risk of ovarian cancer death in a large-scale cohort study (JACC study) in Japan. *Nutr Cancer* 2007; **57**(2): 138-45.
150. Schernhammer ES, Bertrand KA, Birmann BM, Sampson L, Willett WC, Feskanich D. Consumption of artificial sweetener- and sugar-containing soda and risk of lymphoma and leukemia in men and women. *Am J Clin Nutr* 2012; **96**(6): 1419-28.
151. Schernhammer ES, Hu FB, Giovannucci E, et al. Sugar-sweetened soft drink consumption and risk of pancreatic cancer in two prospective cohorts. *Cancer Epidemiol Biomarkers Prev* 2005; **14**(9): 2098-105.

152. Schuurman AG, Goldbohm RA, Dorant E, van den Brandt PA. Vegetable and fruit consumption and prostate cancer risk: a cohort study in The Netherlands. *Cancer Epidemiol Biomarkers Prev* 1998; **7**(8): 673-80.
153. Sesso HD, Buring JE, Zhang SM, Norkus EP, Gaziano JM. Dietary and plasma lycopene and the risk of breast cancer. *Cancer Epidemiol Biomarkers Prev* 2005; **14**(5): 1074-81.
154. Shigihara M, Obara T, Nagai M, et al. Consumption of fruits, vegetables, and seaweeds (sea vegetables) and pancreatic cancer risk: the Ohsaki Cohort Study. *Cancer Epidemiol* 2014; **38**(2): 129-36.
155. Smith-Warner SA, Spiegelman D, Yaun SS, et al. Fruits, vegetables and lung cancer: a pooled analysis of cohort studies. *Int J Cancer* 2003; **107**(6): 1001-11.
156. Sonestedt E, Borgquist S, Ericson U, et al. Plant foods and oestrogen receptor alpha- and beta-defined breast cancer: observations from the Malmo Diet and Cancer cohort. *Carcinogenesis* 2008; **29**(11): 2203-9.
157. Steel H, Park SY, Lim T, et al. Diet Quality and Pancreatic Cancer Incidence in the Multiethnic Cohort. *Cancer Epidemiol Biomarkers Prev* 2023; **32**(1): 123-31.
158. Steinmetz KA, Kushi LH, Bostick RM, Folsom AR, Potter JD. Vegetables, fruit, and colon cancer in the Iowa Women's Health Study. *Am J Epidemiol* 1994; **139**(1): 1-15.
159. Stepien M, Duarte-Salles T, Fedirko V, et al. Consumption of soft drinks and juices and risk of liver and biliary tract cancers in a European cohort. *Eur J Nutr* 2016; **55**(1): 7-20.
160. Stolzenberg-Solomon RZ, Chang SC, Leitzmann MF, et al. Folate intake, alcohol use, and postmenopausal breast cancer risk in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. *Am J Clin Nutr* 2006; **83**(4): 895-904.
161. 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): 1193-207.
162. Thompson CA, Habermann TM, Wang AH, et al. Antioxidant intake from fruits, vegetables and other sources and risk of non-Hodgkin's lymphoma: the Iowa Women's Health Study. *Int J Cancer* 2010; **126**(4): 992-1003.
163. Tworoger SS, Gertig DM, Gates MA, Hecht JL, Hankinson SE. Caffeine, alcohol, smoking, and the risk of incident epithelial ovarian cancer. *Cancer* 2008; **112**(5): 1169-77.
164. van Gils CH, Peeters PH, Bueno-de-Mesquita HB, et al. Consumption of vegetables and fruits and risk of breast cancer. *Jama* 2005; **293**(2): 183-93.
165. Voorrips LE, Goldbohm RA, van Poppel G, Sturmans F, Hermus RJ, van den Brandt PA. Vegetable and fruit consumption and risks of colon and rectal cancer in a prospective cohort study: The Netherlands Cohort Study on Diet and Cancer. *Am J Epidemiol* 2000; **152**(11): 1081-92.
166. Voorrips LE, Goldbohm RA, Verhoeven DT, et al. Vegetable and fruit consumption and lung cancer risk in the Netherlands Cohort Study on diet and cancer. *Cancer Causes Control* 2000; **11**(2): 101-15.
167. Vrieling A, Verhage BA, van Duijnhoven FJ, et al. Fruit and vegetable consumption and pancreatic cancer risk in the European Prospective Investigation into Cancer and Nutrition. *Int J Cancer* 2009; **124**(8): 1926-34.
168. Wang L, Du M, Wang K, et al. Association of ultra-processed food consumption with colorectal cancer risk among men and women: results from three prospective US cohort studies. *Bmj* 2022; **378**: e068921.
169. Wang YC, Lin CH, Huang SP, Chen M, Lee TS. Risk Factors for Female Breast Cancer: A Population Cohort Study. *Cancers (Basel)* 2022; **14**(3).
170. Wu S, Cho E, Feskanich D, et al. Citrus consumption and risk of basal cell carcinoma and squamous cell carcinoma of the skin. *Carcinogenesis* 2015; **36**(10): 1162-8.

171. Wu S, Han J, Feskanich D, et al. Citrus Consumption and Risk of Cutaneous Malignant Melanoma. *J Clin Oncol* 2015; **33**(23): 2500-8.
172. Wu X, Peng L, Luo H, et al. Adherence to diabetes risk reduction diet and the risk of head and neck cancer: a prospective study of 101,755 American adults. *Front Nutr* 2023; **10**: 1218632.
173. Xiang L, Xiao Y, Xu Z, et al. Association of diabetes risk reduction diet with renal cancer risk in 101,755 participants: a prospective study. *J Transl Med* 2023; **21**(1): 684.
174. Xiao Q, Park Y, Hollenbeck AR, Kitahara CM. Dietary flavonoid intake and thyroid cancer risk in the NIH-AARP diet and health study. *Cancer Epidemiol Biomarkers Prev* 2014; **23**(6): 1102-8.
175. Xu X, Xie B, Li S, Wang S, Xia D, Meng H. Association of dietary tomato intake with bladder cancer risk in a prospective cohort of 101,683 individuals with 12.5 years of follow-up. *Aging (Albany NY)* 2021; **13**(13): 17629-37.
176. Yamagiwa Y, Sawada N, Shimazu T, et al. Fruit and vegetable intake and pancreatic cancer risk in a population-based cohort study in Japan. *Int J Cancer* 2019; **144**(8): 1858-66.
177. You D, Xu H, Chen X, et al. Association between soft drink consumption types and risk of lung cancer and all-cancer: A prospective study of PLCO data. *J Biomed Res* 2022; **36**(6): 390-400.
178. Yuan C, Joh HK, Wang QL, et al. Sugar-sweetened beverage and sugar consumption and colorectal cancer incidence and mortality according to anatomic subsite. *Am J Clin Nutr* 2022; **115**(6): 1481-9.
179. Zamora-Ros R, Béraud V, Franceschi S, et al. Consumption of fruits, vegetables and fruit juices and differentiated thyroid carcinoma risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. *Int J Cancer* 2018; **142**(3): 449-59.
180. Zamora-Ros R, Cayssials V, Clèries R, et al. Sweetened beverages are associated with a higher risk of differentiated thyroid cancer in the EPIC cohort: a dietary pattern approach. *Eur J Nutr* 2023; **62**(1): 105-14.
181. Zeegers MP, Goldbohm RA, van den Brandt PA. Consumption of vegetables and fruits and urothelial cancer incidence: a prospective study. *Cancer Epidemiol Biomarkers Prev* 2001; **10**(11): 1121-8.
182. Zhang X, Albanes D, Beeson WL, et al. Risk of colon cancer and coffee, tea, and sugar-sweetened soft drink intake: pooled analysis of prospective cohort studies. *J Natl Cancer Inst* 2010; **102**(11): 771-83.
183. Zhang X, Zhao L, Christopher CN, et al. Association of dietary insulinemic and inflammatory potential with risk of liver cancer and chronic liver disease mortality in postmenopausal women: a prospective cohort study. *Am J Clin Nutr* 2023; **118**(3): 530-7.
184. Zhang ZQ, Li QJ, Hao FB, Wu YQ, Liu S, Zhong GC. Adherence to the 2018 World Cancer Research Fund/American Institute for Cancer Research cancer prevention recommendations and pancreatic cancer incidence and mortality: A prospective cohort study. *Cancer Med* 2020; **9**(18): 6843-53.
185. Zhao L, Jin L, Petrick JL, et al. Specific botanical groups of fruit and vegetable consumption and liver cancer and chronic liver disease mortality: a prospective cohort study. *Am J Clin Nutr* 2023; **117**(2): 278-85.
186. Zhao L, Zhang X, Coday M, et al. Sugar-Sweetened and Artificially Sweetened Beverages and Risk of Liver Cancer and Chronic Liver Disease Mortality. *Jama* 2023; **330**(6): 537-46.
187. Zhao L, Zhang X, Yu D, et al. Ultra-processed products and risk of liver cancer: A prospective cohort study. *Clin Nutr* 2024; **43**(10): 2298-304.
188. Zhong GC, Li Z, You AJ, Zhu Q, Wang CR, Yang PF. Plant-based diets and the risk of pancreatic cancer: a large prospective multicenter study. *Am J Clin Nutr* 2023; **117**(2): 235-42.

189. Zhong GC, Zhu Q, Cai D, et al. Ultra-processed food consumption and the risk of pancreatic cancer in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. *Int J Cancer* 2023; **152**(5): 835-44.
190. Zhu Z, Peng L, Gu H, et al. Association between dietary approaches to stop hypertension eating pattern and lung cancer risk in 98,459 participants: results from a large prospective study. *Front Nutr* 2023; **10**: 1142067.
191. Jin X, Wu M, Dong S, Liu H, Ma H. Artificially sweetened beverages consumption and risk of obesity-related cancers: a wide-angled Mendelian randomization study. *Front Nutr* 2024; **11**: 1347724.
192. Liu C, Zheng S, Gao H, et al. Causal relationship of sugar-sweetened and sweet beverages with colorectal cancer: a Mendelian randomization study. *Eur J Nutr* 2023; **62**(1): 379-83.
193. Pan H, Feng C, Zhou Z, et al. The causal association between artificial sweeteners and the risk of cancer: a Mendelian randomization study. *Food Funct* 2024; **15**(8): 4527-37.
194. Hasan N, Yazdanpanah O, Khaleghi B, Benjamin DJ, Kalebasty AR. The role of dietary sugars in cancer risk: A comprehensive review of current evidence. *Cancer Treat Res Commun* 2025; **43**: 100876.
195. Lauby-Secretan B, Scoccianti C, Loomis D, Grosse Y, Bianchini F, Straif K. Body Fatness and Cancer--Viewpoint of the IARC Working Group. *N Engl J Med* 2016; **375**(8): 794-8.
196. Karikas GA, Schulpis KH, Reclos G, Kokotos G. Measurement of molecular interaction of aspartame and its metabolites with DNA. *Clin Biochem* 1998; **31**(5): 405-7.
197. Shephard SE, Wakabayashi K, Nagao M. Mutagenic activity of peptides and the artificial sweetener aspartame after nitrosation. *Food Chem Toxicol* 1993; **31**(5): 323-9.
198. FDA. US Food and Drug Administration. Aspartame: Commissioner's final decision. *Federal Register* 1981; **46**(142): 38285–308.
199. Butchko HH, Stargel WW, Comer CP, et al. Aspartame: review of safety. *Regul Toxicol Pharmacol* 2002; **35**(2 Pt 2): S1-93.
200. FAO/WHO. Joint, FAO WHO Expert Committee on Food Additives: Summary of findings of the evaluation of aspartame at the International Agency for Research on Cancer (IARC) Monographs Programme's 134th Meeting, 6–13 June 2023. *WHO Expert Committee on Food Additives (JECFA) 96th meeting*, 2023. (accessed.
201. Ahmad M, Bajahlan AS. Leaching of styrene and other aromatic compounds in drinking water from PS bottles. *J Environ Sci (China)* 2007; **19**(4): 421-6.
202. Sielken RL, Jr., Valdez-Flores C. Butadiene cancer exposure-response modeling: based on workers in the styrene-butadiene-rubber industry: total leukemia, acute myelogenous leukemia, chronic lymphocytic leukemia, and chronic myelogenous leukemia. *Regul Toxicol Pharmacol* 2011; **60**(3): 332-41.
203. Walter JF, Gange RW, Mendelson IR. Psoralen-containing sunscreen induces phototoxicity and epidermal ornithine decarboxylase activity. *J Am Acad Dermatol* 1982; **6**(6): 1022-7.
204. Kornhauser A, Wamer WG, Giles AL, Jr. Psoralen phototoxicity: correlation with serum and epidermal 8-methoxypsoralen and 5-methoxypsoralen in the guinea pig. *Science* 1982; **217**(4561): 733-5.
205. Scott BR, Pathak MA, Mohn GR. Molecular and genetic basis of furocoumarin reactions. *Mutat Res* 1976; **39**(1): 29-74.
206. Ortega N, Tennant PW, Greenwood DC, et al. Meta-analyses of dietary exposures must consider energy adjustment: recommendations from a meta-scientific review. *arXiv preprint arXiv:251207531* 2025.
207. Ibsen DB, Laursen ASD, Würtz AML, et al. Food substitution models for nutritional epidemiology. *The American journal of clinical nutrition* 2021; **113**(2): 294-303.

208. Nguyen M, Jarvis SE, Tinajero MG, et al. Sugar-sweetened beverage consumption and weight gain in children and adults: a systematic review and meta-analysis of prospective cohort studies and randomized controlled trials. *Am J Clin Nutr* 2023; **117**(1): 160-74.