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SPECIAL REPORT

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Post-diagnosis adiposity, physical activity, sedentary behaviour, dietary factors, supplement use and colorectal cancer prognosis: Global Cancer Update Programme (CUP Global) summary of evidence grading

Konstantinos K. Tsilidis[1,2] | Georgios Markozannes[1,2] | Nerea Becerra-Tomás[1] | Margarita Cariolou[1] | Katia Balducci[1] | Rita Vieira[1] | Sonia Kiss[1] | Dagfinn Aune[1,3,4] | Darren C. Greenwood[5] | Laure Dossus[6] | Esther M. González-Gil[6] | Marc J. Gunter[1,6] | Kate Allen[7] | Nigel T. Brockton[8] | Helen Croker[7] | Vanessa L. Gordon-Dseagu[7] | Panagiota Mitrou[7] | Nicole Musuwo[7] | Martin J. Wiseman[7] | Ellen Copson[9] | Andrew G. Renehan[10] | Martijn Bours[11] | Wendy Demark-Wahnefried[12] | Melissa M. Hudson[13] | Anne M. May[14] | Folakemi T. Odedina[15] | Roderick Skinner[16] | Karen Steindorf[17] | Anne Tjønneland[18,19] | Galina Velikova[20] | Monica L. Baskin[21] | Rajiv Chowdhury[22] | Lynette Hill[7] | Sarah J. Lewis[23] | Jaap Seidell[24] | Matty P. Weijenberg[11] | John Krebs[25] | Amanda J. Cross[1] | Doris S. M. Chan[1]

Correspondence
Doris S. M. Chan, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, St. Mary's Campus, Norfolk Place, London W2 1PG, UK.
Email: d.chan@imperial.ac.uk

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Abstract

Based on the World Cancer Research Fund Global Cancer Update Programme, we performed systematic reviews and meta-analyses to investigate the association of post-diagnosis adiposity, physical activity, sedentary behaviour, and dietary factors with colorectal cancer prognosis. We searched PubMed and Embase until 28th February, 2022. An independent expert committee and expert panel graded the quality of evidence. A total of 167 unique publications were reviewed, and all but five were observational studies. The quality of the evidence was graded conservatively due to the high risk of several biases. There was evidence of non-linearity in the associations between body mass index and colorectal cancer prognosis. The associations appeared reverse J-shaped, and the quality of this evidence was graded as limited (likelihood of causality: limited-no conclusion). The evidence on recreational physical

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activity and lower risk of all-cause mortality (relative risk [RR] highest vs. lowest: 0.69, 95% confidence interval [CI]: 0.62–0.77) and recurrence/disease-free survival (RR: 0.80, 95% CI: 0.70–0.92) was graded as limited-suggestive. There was limited-suggestive evidence for the associations between healthy dietary and/or lifestyle patterns (including diets that comprised plant-based foods), intake of whole grains and coffee with lower risk of all-cause mortality, and between unhealthy dietary patterns and intake of sugary drinks with higher risk of all-cause mortality. The evidence for other exposures on colorectal cancer outcomes was sparse and graded as limited-no conclusion. Analyses were conducted excluding cancer patients with metastases without substantial changes in the findings. Well-designed intervention and cohort studies are needed to support the development of lifestyle recommendations for colorectal cancer patients.

KEYWORDS
adiposity, colorectal cancer, diet, evidence grading, physical activity, prognosis, sedentary behaviour, survival, systematic review

What's new?

A better understanding of the associations of post-diagnosis modifiable lifestyle factors with outcomes could inform tailored prevention strategies for colorectal cancer survivors. The Global Cancer Update Programme (CUP Global) conducted systematic reviews, meta-analyses, and independent quality of evidence grading on the associations of post-diagnosis adiposity, physical activity, sedentary behaviour, and dietary factors with colorectal cancer prognosis. Although "limited," the evidence suggested that a physically active lifestyle, a healthy diet, and avoidance of sugary drinks or sedentary behaviour may be associated with longer overall survival. Well-designed cohort and intervention studies are needed to further develop lifestyle recommendations for colorectal cancer survivors.

1 | INTRODUCTION

As colorectal cancer survival rates are improving over time,[1] there is an urgent need to understand the relationship between modifiable risk factors such as adiposity, physical activity, sedentary behaviour, and diet assessed after colorectal cancer diagnosis with subsequent outcomes to develop evidence-based lifestyle recommendations for colorectal cancer survivors. To date, although there is a breadth of knowledge on the relationship between modifiable lifestyle factors and colorectal cancer incidence,[2–5] less is known about how they might influence outcomes after colorectal cancer diagnosis.

Several meta-analyses of observational studies have investigated associations of post-diagnosis adiposity, physical activity, sedentary behaviour, and diet with colorectal cancer survival outcomes.[6–9] Most papers performed categorical meta-analyses and did not explore potential non-linearity. Formal evaluation of the quality of this evidence has not been systematically performed. In addition, several organisations have published physical activity guidelines for cancer survivors,[10–12] but only the Physical Activity Guidelines for Americans in 2018, which largely focused on published evidence syntheses, formally evaluated the evidence quality.[13]

As part of the World Cancer Research Fund (WCRF) Global Cancer Update Programme (CUP Global),[14] formerly known as the WCRF/American Institute for Cancer Research (AICR) Continuous Update Project, we conducted comprehensive systematic literature reviews and meta-analyses to evaluate the evidence on adiposity, physical activity, sedentary behaviour, and diet with prognostic outcomes after colorectal cancer diagnosis. Subsequently, the quality of the evidence was independently interpreted and graded by the CUP Global Expert Committee on Cancer Survivorship and Expert Panel. This paper presents the summary of the quality of evidence grading, and more details on the rationale, methods, and findings are provided in the accompanied systematic review papers.[15–17]

2 | METHODS

2.1 | Structure of evidence synthesis team

This work involved four teams:

- The CUP Global Secretariat was responsible for coordinating the project, drafting the research questions, facilitating the Committee and Panel meetings, and summarising its main outputs.
- The CUP Global research team at Imperial College London (ICL) drafted the systematic review protocols, completed the literature

search and review for eligibility, extracted data into the CUP Global database, conducted data analysis, assessed risk of bias, produced and presented narrative, tabular and graphical summaries of the results, and drafted manuscripts.

- The CUP Global Expert Committee on Cancer Survivorship comprised independent experts with expertise in medical and surgical oncology, patient-oriented outcomes, clinical and nutritional epidemiology, biostatistics, and behavioural science. The Committee reviewed the research questions and protocols, interpreted the systematic literature reviews, and provided preliminary grading of the quality of the evidence.
- The CUP Global Expert Panel comprised independent experts with expertise in nutrition, physical activity, adiposity, cancer biology, epidemiology, cellular and other mechanisms of cancer development and progression, genetic and epigenetic aspects of cancer susceptibility and of tumour behaviour, gene-nutrient interactions, public health, and cancer survivorship, as well as a public representative. The Panel reviewed the research questions and protocols, interpreted the systematic literature reviews, and provided the final grading of the quality of the evidence. The quality of evidence was graded during a three-day in-person Panel meeting in November–December 2022 in London, United Kingdom.

2.2 | Methods for systematic review

The systematic reviews were conducted following a pre-published protocol.[18] We searched in PubMed and Embase for relevant publications from inception of these databases to 28th February, 2022. The reference lists of identified articles and relevant reviews and meta-analyses were screened for additional publications. Eligible studies were randomised controlled trials (RCTs), longitudinal observational studies, and pooled analyses of such studies evaluating post-diagnosis adiposity (i.e., body mass index [BMI], waist circumference [WC], waist to hip circumference ratio [WHR], weight, or changes in these exposures), physical activity, sedentary behaviour, and dietary factors (i.e., dietary patterns, foods, beverages, macro- and micro-nutrients, and dietary supplements) in relation to colorectal cancer outcomes (i.e., all-cause mortality, cause-specific mortality, progression/recurrence/disease-free survival, and second primary cancers). Progression, recurrence and disease-free survival were studied as an aggregate outcome, as heterogeneous definitions were used in the primary studies. Studies were included if they had at least 100 participants, and RCTs also needed to have at least 6 months duration of follow-up. Study and participants' characteristics and results were extracted from each included publication into the CUP Global database. The quality of RCTs and observational studies was graded using version 2 of the Cochrane risk-of-bias tool for randomised trials (RoB 2)[19] and a modified version of the Risk of Bias for Nutrition Observational Studies (RoB-NObs) tool, respectively. The RoB-NObs tool was originally developed by the U.S. Department of Agriculture Nutrition Evidence Systematic Review[20] after modifications to the Cochrane's collaboration Risk Of Bias In Non-randomized Studies—of Interventions (ROBINS-I).[21] The RoB-NObs tool was further optimised and tested by the ICL review team.

2.3 | Methods for meta-analysis

We calculated summary relative risk (RR) estimates and their 95% confidence intervals (CIs) using the inverse variance weighted DerSimonian–Laird random-effects model.[22] Multivariable adjusted estimates were selected for the meta-analyses. Linear dose–response meta-analyses were conducted when there were at least three studies with sufficient data (effect size and measure of variability) using the generalised weighted least-squares regression model.[23] One-stage non-linear meta-analyses were conducted using restricted cubic splines with three knots placed at 10th, 50th and 90th percentiles of the exposure distribution when five or more studies, each with data for at least three exposure levels, were available.[24] Categorical meta-analyses were conducted in exceptional cases (i.e., for physical activity, where the format of information was often insufficient for estimating a dose–response slope; and for BMI categories to further evaluate the shape of the association by clinically defined subgroups). Studies were descriptively synthesised when meta-analysis was not possible. Heterogeneity was assessed using the estimate of between-study variance (tau^2).[25] The proportion of total variability in effect estimates due to between-study heterogeneity was assessed using the I^2 statistic.[26] Pre-defined subgroup meta-analyses stratified by selected study and participants' characteristics were conducted to explore potential sources of heterogeneity when at least three studies were available in one of the subgroups. Approximately 30% of the selected studies included colorectal cancer patients of mixed stage with a median percentage of stage IV patients lower than 20%.[15–17] Most of these studies did not conduct analyses by stage or after excluding stage IV patients. Our overall meta-analyses included patients of all stages, but we conducted subgroup analyses by stage. The Egger's regression asymmetry test and visual inspection of the funnel plots were conducted to examine small study effects, such as publication bias, when there were more than 10 studies.[27]

2.4 | Grading the quality of evidence

The CUP Global Expert Committee on Cancer Survivorship and Expert Panel graded the quality of the evidence as strong (subgrades evaluating likelihood of causality: convincing or probable or substantial effect on risk unlikely) or limited (subgrades evaluating likelihood of causality: limited-suggestive or limited-no conclusion) according to pre-defined criteria listed in Table 1, which evaluate the quantity, consistency, magnitude and precision of the summary estimates, existence of a dose–response relationship, study design and risk of bias, generalisability, and mechanistic plausibility of the results.

3 | RESULTS

Figure 1 shows the study selection process. Table 2 and Figure 2 show the summary findings and the judgement of the CUP Global Expert Panel. Box 1 presents a summary of the limitations of current research and suggestions for future research.

BOX 1 Overview of limitations of current research (mostly observational studies) and suggestions for future research

Limitations of current research	Suggestions for future research
Exposure assessment and misclassification	
• Measured exposures not fully representative of the intended exposure, e.g., BMI → adiposity; various physical activity types → total physical activity; Sitting/TV viewing time → total sedentary behaviour; food frequency questionnaires → consumed diet	• Alternative and/or more comprehensive exposure assessment ○ Central adiposity, body composition, fat/lean mass ○ Better tools to capture the complete breadth of the exposure (e.g., total physical activity and its dimensions—frequency, duration, intensity, volume; total sedentary behaviour) ○ Complementary dietary assessments (e.g., multiple 24-h recalls, food images & image recognition software)
• Exposure assessment was frequently based on non-validated tools for diet, physical activity, and sedentary behaviour	• Use of validated tools for exposure measurement (if possible, specifically on cancer survivors)
• Exposures are usually self-reported	• Exposure assessment enriched by objective measurements, e.g., dual-energy x-ray absorptiometry, computed tomography, magnetic resonance imaging, D3 creatine dilution, bioelectrical impedance analysis for measuring body composition/adiposity; wearables/activity trackers for measuring physical activity, sedentary behaviour; Identification of additional biomarkers for dietary intake using omics after validation in feeding studies
• Exposures usually captured at a single time point ○ Levels of exposure may differ across cancer continuum, e.g., exposure fluctuations during or close to treatment	• Repeated/longitudinal exposure measurements using time varying analyses or analyses stratified by timing of exposure assessment ○ Timing of exposure assessment should be accurately reported, e.g., before, during, after treatment, long-term
Confounders assessment/adjustment	
• Incomplete assessment of measured and unmeasured confounders	• Comprehensive assessment of confounders including cancer stage, cancer treatment and related characteristics (type, tolerance, completion), disease progression, comorbidities, socioeconomic status, adiposity (where relevant), smoking, using, if possible, objective or validated measures
• Confounders usually captured at a single time point	• Repeated/longitudinal confounders measurement using time-varying analyses
Outcome measurement	
• Definition and/or measurement of recurrence usually inconsistent across studies	• Comprehensive assessment and consistent definition of recurrence, progression-free survival, disease-free survival, time to progression • If possible, assess all different definitions separately
• Recurrence validation usually not clearly described	• If possible, use imaging, biochemistry or other objective measures
• Incomplete assessment of potential outcome-modifying variables, e.g., cancer stage/treatment modality	• Use stratified analyses or introduce interaction terms for cancer stage or treatment modality • Survivors with advanced and/or metastatic disease should not be mixed with earlier disease stages
• Many studies measure only main survival outcomes	• Complementary outcomes to support informed decisions, e.g., quality of life, fatigue, treatment tolerance/completion
Selection bias	
• Healthier cancer survivors likely to be selectively included in the study	• If possible, use of randomly sampled, or complete/consecutive cases from registries from diagnosis onwards • If possible, compare distribution of characteristics of included and excluded participants
Missing data	
• Differential rates of missing data (exposure/confounders/outcome) between the exposure groups	• If possible, compare the distributions and reasons of missing data across exposure groups • Perform multiple imputation/sensitivity analyses to assess the impact of missing data on observed association

Limitations of current research	Suggestions for future research
Reporting of the results	
• Studies sometimes lacked necessary data for inclusion in the meta-analyses	• Consistent and comprehensive reporting of all results to facilitate future evidence assessment, including sample sizes (numbers of events and non-events, overall and per exposure category for categorial analysis), measures of association and variation, clearly specified levels of exposure (for categorial analyses) or contrasts (for continuous analyses) • Adhere to reporting guidelines • Share study data to open access repositories to facilitate individual participant meta-analyses
Generalisability and applicability of findings	
• Generalisability of the findings is limited ○ Included studies mostly focused on specific populations, mainly affluent, western and white	• More studies in socio-demographically and ethnically diverse populations are warranted
• The applicability of lifestyle changes based on existing recommendations is not extensively evaluated	• Behavioural or other implementation research to inform on best prevention strategy tailored to the specific context
Alternative/complementary/modern study designs	
• "Traditional" observational studies have inherent limitations • Only few lifestyle modification randomised controlled trials (RCTs) on main cancer survival outcomes ○ Small samples and short follow-up ○ Blinding of participants often not possible ○ Suboptimal fidelity to the allocated interventions	• Carefully designed modern RCTs, e.g., pragmatic trials with focused personalised multi-component interventions • Use of objective surrogate measures (e.g., metabolomics, microbiomics) as outcomes in RCTs • Mechanistic and molecular epidemiology studies to infer mechanisms • Mendelian randomisation studies (adjusting for index event bias) • Target trial emulation observational studies

3.1 | Evidence summary for post-diagnosis adiposity and colorectal cancer prognosis

We included 124 longitudinal observational studies in the systematic review, which comprised more than 294,000 individuals with colorectal cancer, of whom more than 43,900 died of any cause, approximately 16,000 died of colorectal cancer, and approximately 24,600 experienced an additional colorectal cancer event (e.g., recurrence).[16] No relevant RCT was identified.

The evidence on post-diagnosis BMI and risk of all-cause mortality, colorectal cancer-specific mortality, and recurrence/disease-free survival was substantial, but showed signs of non-linear associations and was limited in methodological quality (risk for reverse causation, selection bias, residual confounding, and exposure measurement error). The evidence was graded as limited (subgrade: limited-no conclusion). The shape of the associations appeared reverse J-shaped with a common nadir across all outcomes at BMI of 28 kg/m^2. A higher risk of poor colorectal cancer outcomes, relative to the nadir, was observed at the lowest and upper range of the BMI distribution. For BMI 18 to 24 kg/m^2, an 8% to 60% higher risk of all-cause mortality, a 15% to 95% higher risk of colorectal cancer-specific mortality, and a 5% to 37% higher risk of recurrence/disease-free survival was observed across the analyses. For BMI 32 to 38 kg/m^2, a 7% to 23% higher risk of all-cause mortality, a 6% to 26% higher risk of colorectal cancer-specific mortality, and a 7% to 24% higher risk of recurrence/disease-free survival was observed.

When the non-linear meta-analyses were performed in subgroups according to anatomical cancer subsite, cancer stage, sex, geographic location, study design (prospective vs. retrospective cohorts vs. secondary analyses of clinical trials), length of follow-up, and risk of bias in different RoB-NObs domains, the results were similar with few exceptions that all reflected potentially stronger methodological limitations or altered physiological state in certain subgroups.[16] A non-linear inverse association was observed for BMI and all-cause mortality in colorectal cancer survivors with metastases (higher risk for reverse causation and cancer-associated cachexia in this subgroup), which included a gradual reduction in risk from the lowest levels of BMI up to 28 kg/m^2 that reached a plateau above this point, compared to a reverse J-shaped association observed in all other cancer stages. The association of BMI with all-cause mortality was U-shaped in women and reverse J-shaped in men, reflecting a stronger positive association of low BMI in men (potentially due to stronger residual confounding by smoking) compared to women. Similarly, the association was U-shaped in secondary analyses of RCTs (potentially due to more standardised measurement of exposures, confounders and outcomes) compared to reverse J-shaped in all other study designs.

The evidence for post-diagnosis BMI with risk of second primary cancer (two studies), non-colorectal cancer-related mortality (three studies), and cardiovascular disease (CVD) mortality (one study) was sparse, and subjected to the same methodological issues mentioned previously, and therefore was graded as limited-no conclusion.

TABLE 1 Grading criteria for evidence on post-diagnosis adiposity, physical activity, sedentary behaviour, dietary factors, supplement use and colorectal cancer prognosis.

Evidence grades		Grading criteria for evidence on adiposity, physical activity, sedentary behaviour, diet and cancer survival	Het	PB	Mec
Strong evidence	Convincing	Evidence of an effect from at least two well-designed independent RCTs	No	No	Not required
	Probable	Evidence from at least two well-designed independent RCTs	Some	No	Not required
		OR Evidence from one well-designed RCT plus evidence from well-designed cohort studies	No	No	Required
		OR Evidence from at least one well-designed pooling study (of cohort studies)	No	No	Required
		OR Evidence from at least three independent well-designed cohort studies	No	No	Required
Limited evidence	Limited suggestive	Evidence from at least two well-designed RCTs but the confidence interval may include the null	Some	No	Not required
		OR Evidence from one well-designed RCT but the confidence interval may include the null	No	–	Required
		OR Evidence from a well-designed pooling study (of cohort studies)	Some	No	Not required
		OR Evidence from a well-designed pooling study (of cohort studies) but the confidence interval may include the null	Some	No	Required
		OR Evidence from at least two cohort studies	No	No	Not required
	Limited—no conclusion	Any of the following reasons: – Too few studies available – Inconsistency of direction of effect – Poor quality of studies	–	–	–
Strong evidence	Substantial effect on risk unlikely	Evidence pointing to absence of an effect (a summary estimate close to 1.0) from any of the following: (a) At least two well-designed independent RCTs (b) A well-designed pooling study (of cohort studies) (c) At least two well-designed cohort studies – Absence of a dose response relationship (in cohort studies)	No	–	Absence

Note: Het: Substantial unexplained heterogeneity or some unexplained heterogeneity. PB: Publication bias. Mec: Strong and plausible mechanistic evidence is required, not required (but desired), or absent. Special upgrading factors: (a) Presence of a plausible biological gradient ('dose–response') in the association. Such a gradient need not be linear or even in the same direction across the different levels of exposure, so long as this can be explained plausibly. (b) A particularly large summary effect size (a relative risk of 2.0 or more, or 0.5 or less, depending on the unit of exposure), after appropriate control for confounders. (c) Evidence from appropriately controlled experiments demonstrating one or more plausible and specific mechanisms. (d) All plausible known residual confounders or biases including reverse causation would reduce a demonstrated effect, or suggest a spurious effect when results show no effect. Special considerations important for evidence for colorectal cancer survivors including the following potential confounding variables—the type of tumour, type of treatment, amount of treatment received, and the dissemination of the disease.

There was only one study on WC and disease-free survival, and the evidence was graded as limited-no conclusion. No studies were identified for WHR. The evidence for body weight or BMI change and all outcomes was again scarce (one to six studies) and subject to the same methodological limitations, and no conclusions could be made. In general, (unexplained) weight or BMI loss were associated with a higher risk of all-cause and colorectal cancer-specific mortality. No associations were observed for weight/BMI gain.

3.2 | Evidence summary for post-diagnosis physical activity and colorectal cancer prognosis

We included 16 longitudinal observational studies in the systematic review, which comprised 82,220 individuals with colorectal cancer, of whom approximately 7800 died of any cause, approximately 1700 died of colorectal cancer, and approximately 2100 experienced an additional colorectal cancer event.[17] Most of these papers published data on any recreational physical activity, but associations were also reported by frequency, duration, intensity and volume, and few studies also included total physical activity of any type, change of physical activity, and sedentary behaviour. No relevant primary RCT was identified.

Post-diagnosis recreational physical activity was associated with a lower risk of all-cause mortality (11 studies, summary RR highest vs. lowest category: 0.69, 95% CI: 0.62–0.77, tau^2: 0.01, I^2: 50%) and cancer recurrence (3 studies, RR: 0.80, 95% CI: 0.70–0.92, tau^2: 0.002, I^2: 14%), but the evidence was graded as limited (subgrade: limited-suggestive) due to limitations in the methodological quality of the included studies (risk for reverse causation, selection bias, residual

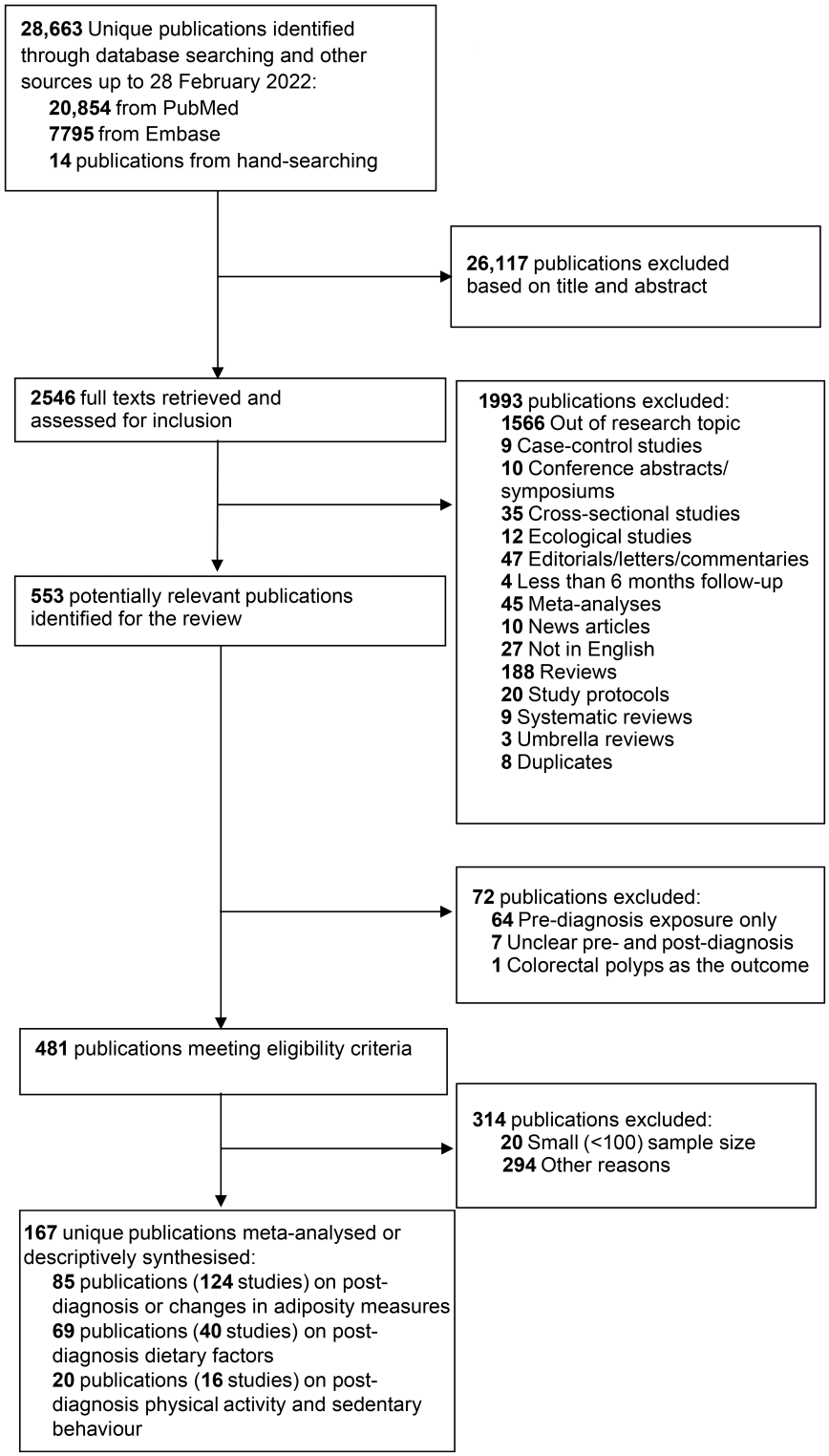


FIGURE 1 Study selection process from the systematic literature reviews on post-diagnosis adiposity, physical activity, sedentary behaviour, dietary factors, supplement use and colorectal cancer prognosis.

confounding, and exposure measurement error). A limited-no conclusion grading was given to recreational physical activity in relation to colorectal cancer- and CVD-specific mortality, and to recreational physical activity frequency, duration, intensity and volume, total physical activity and change of physical activity for all outcomes. This was primarily due to high risk of biases and substantial between-study heterogeneity. Across analyses, physical activity consistently showed evidence of inverse associations with all examined outcomes. Linear and non-linear meta-analyses were only possible for volume of recreational physical activity. Potential non-linearity was suggested, namely a linear lower risk of all-cause mortality with higher physical activity volume from little activity up to 20 metabolic equivalents of task [MET]-h/week (6 studies, RR at 20 MET-h/week: 0.56, 95% CI: 0.41–0.76), but with little data and no further reduction in risk at higher

TABLE 2 Evidence grades and main findings from the systematic literature reviews on post-diagnosis adiposity, physical activity, sedentary behaviour, dietary factors, supplement use and colorectal cancer prognosis.

	All-cause mortality	CRC mortality	CRC recurrence	Second primary cancer	Non-CRC mortality	CVD mortality
Exposure	**RR (95% CI) studies tau^2, I^2**	**RR (95% CI) studies tau^2, I^2**	**RR (95% CI) studies tau^2, I^2**	**RR (95% CI) studies tau^2, I^2**	**RR (95% CI) studies tau^2, I^2**	**RR (95% CI) studies tau^2, I^2**
Strong evidence (convincing)	–	–	–	–	–	–
Strong evidence (probable)	–	–	–	–	–	–
Limited evidence (limited—suggestive)						
Any recreational physical activity (highest vs. lowest category)	0.69 (0.62–0.77) 11 studies tau^2 = 0.01, I^2 = 50%	–	0.80 (0.70–0.92) 3 studies tau^2 = 0.002, I^2 = 14%	–	–	–
Healthy dietary and lifestyle patterns (highest vs. lowest score)	No MA,[a] but trend of inverse associations	–	–	–	–	–
Healthy dietary patterns (highest vs. lowest score)	No MA,[a] but trend of inverse associations	–	–	–	–	–
Unhealthy dietary patterns (highest vs. lowest score)	No MA,[a] but trend of positive associations	–	–	–	–	–
Whole grains (per 1 serving/day)	0.90 (0.83–0.97) 4 studies tau^2 = 0.00, I^2 = 0%	–	–	–	–	–
Total coffee (per 1 cup/day)	0.92 (0.89–0.95) 4 studies tau^2 = 0.00, I^2 = 0%	–	–	–	–	–
Caffeinated coffee (per 1 cup/day)	0.91 (0.86–0.97) 4 studies tau^2 = 0.002, I^2 = 45%	–	–	–	–	–
Decaffeinated coffee (per 1 cup/day)	0.86 (0.80–0.92) 4 studies tau^2 = 0.00, I^2 = 0%	–	–	–	–	–
Sugary drinks (per 1 serving/day)	1.20 (1.08–1.33) 4 studies tau^2 = 0.00, I^2 = 0%	–	–	–	–	–

TABLE 2 (Continued)

Exposure	All-cause mortality RR (95% CI) studies tau^2, I^2	CRC mortality RR (95% CI) studies tau^2, I^2	CRC recurrence RR (95% CI) studies tau^2, I^2	Second primary cancer RR (95% CI) studies tau^2, I^2	Non-CRC mortality RR (95% CI) studies tau^2, I^2	CVD mortality RR (95% CI) studies tau^2, I^2
Limited evidence (limited—no conclusion)						
BMI	Reverse J-shaped 46 studies	Reverse J-shaped 13 studies	Reverse J-shaped 39 studies	No MA[a]	No MA[a]	No MA[a]
Waist circumference	–	–	No MA[a]	–	–	
Weight/BMI change	No MA[a]	No MA[a]	No MA[a]	–	–	No MA[a]
Any total physical activity (highest vs. lowest category)	0.74 (0.59–0.94) 5 studies tau^2 = 0.02, I^2 = 39%	–	0.87 (0.63–1.20) 3 studies tau^2 = NA, I^2 = 0%	–	–	–
Any recreational physical activity (highest vs. lowest category)	–	0.63 (0.47–0.84) 6 studies tau^2 = 0.06, I^2 = 58%	–	–	–	–
Frequency of recreational physical activity (highest vs. lowest category)	0.77 (0.72–0.83) 3 studies tau^2 = 0.00, I^2 = 0%	–	–	–	–	–
Duration of recreational physical activity (highest vs. lowest category)	0.74 (0.63–0.87) 3 studies tau^2 = 0.00, I^2 = 0%	–	–	–	–	–
Intensity (any) of recreational physical activity (highest vs. lowest category)	0.65 (0.53–0.80) 6 studies tau^2 = 0.03, I^2 = 60%	0.40 (0.25–0.62) 3 studies tau^2 = 0.00, I^2 = 0%	0.83 (0.73–0.94) 2 studies tau^2 = 0.00, I^2 = 0%	–	–	
Intensity (moderate-to-vigorous) of recreational physical activity (highest vs. lowest category)	0.68 (0.57–0.81) 4 studies tau^2 = 0.02, I^2 = 60%	0.82 (0.74–0.89) 3 studies tau^2 = 0.00, I^2 = 0%	–	–	–	0.63 (0.33–1.22) 3 studies tau^2 = 0.26, I^2 = 79%
Volume of recreational physical activity (per 10 MET-h/week)	0.76 (0.66–0.88) 6 studies tau^2 = 0.02, I^2 = 86%	0.73 (0.63–0.84) 4 studies tau^2 = 0.00, I^2 = 0%	–	–	–	–
Volume of recreational physical activity (highest vs. lowest category)	0.60 (0.48–0.75) 6 studies tau^2 = 0.04, I^2 = 65%	0.52 (0.30–0.87) 4 studies tau^2 = 0.17, I^2 = 62%	0.73 (0.50–1.06) 2 studies tau^2 = NA, I^2 = 55%	–	–	–

(Continues)

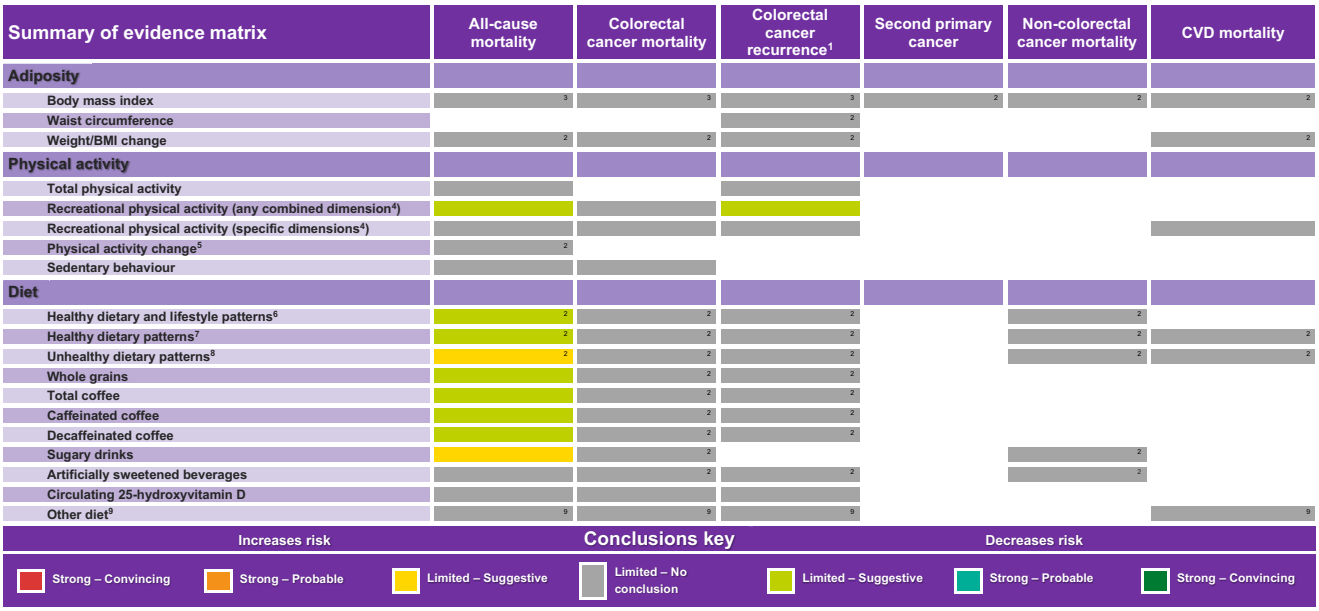
TABLE 2 (Continued)

Exposure	All-cause mortality RR (95% CI) studies tau^2, I^2	CRC mortality RR (95% CI) studies tau^2, I^2	CRC recurrence RR (95% CI) studies tau^2, I^2	Second primary cancer RR (95% CI) studies tau^2, I^2	Non-CRC mortality RR (95% CI) studies tau^2, I^2	CVD mortality RR (95% CI) studies tau^2, I^2
Physical activity change	No MA[a]	–	–	–	–	–
Sedentary behaviour (sitting time while watching TV, per 120 min/week)	1.13 (1.02–1.26) 3 studies tau^2 = 0.00, I^2 = 0%	–	–	–	–	–
Sedentary behaviour (sitting time while watching TV, highest vs. lowest category)	1.28 (1.06–1.55) 3 studies tau^2 = 0.00, I^2 = 0%	1.45 (0.95–2.21) 2 studies tau^2 = NA, I^2 = 0%	–	–	–	–
Artificially sweetened beverages (per 1 serving/day)	0.71 (0.60–0.84) 3 studies tau^2 = 0.00, I^2 = 0%	–	–	–	–	–
Circulating 25-hydroxyvitamin D (per 10 nmol/L)	0.95 (0.92–0.98) 10 studies tau^2 = 0.002, I^2 = 84%	0.96 (0.92–0.99) 4 studies tau^2 = 0.00, I^2 = 0%	–	–	–	–
Other diet[b]	With or without MA[a]					

Abbreviations: BMI, body mass index; CCSM, colorectal cancer-specific mortality; CI, confidence interval; CRC, colorectal cancer; CVD, cardiovascular disease; CVDM, cardiovascular disease mortality; DFS, disease-free survival; MA, meta-analysis; MET, metabolic equivalent of task; NA, not applicable; RR, summary relative risk.

[a]Studies were descriptively synthesised, as the data was not sufficient for conducting meta-analysis.

[b]Healthy dietary and lifestyle patterns (CCSM, recurrence/DFS, CVDM), healthy dietary patterns (CCSM, recurrence/DFS), unhealthy dietary patterns (CCSM, recurrence/DFS), fruits and vegetables, nuts and peanuts, whole grains (CCSM, recurrence/DFS), red meat and processed meat, fish, shellfish, and other seafoods, dairy products, milk, dietary carbohydrate, dietary fibre, dietary glycaemic load and index, dietary insulin load and index, dietary protein, dietary fats, marine omega-3 polyunsaturated fatty acids, sugary drinks (CCSM, recurrence/DFS, non-CCSM), fruit juices, total, caffeinated, and decaffeinated coffee (CCSM, recurrence/DFS), alcohol, dietary supplementations, dietary and supplemental folate, circulating folate, dietary and supplemental vitamin D, circulating 25-hydroxyvitamin D (recurrence/DFS), dietary and supplemental calcium, dietary calcium.



Note: Empty cells included few or no studies and were not assigned an evidence grade.

[1] The definition of "recurrence" is heterogeneous, comprising a mixture of local, regional, or distant recurrence (metastasis), second primary cancer, any primary cancers, colorectal cancer-related deaths, and/or any causes of death.
[2] No meta-analysis.
[3] Non-linear association (reverse J-shaped).
[4] Frequency, duration, intensity, volume.
[5] Pre-to-post-diagnosis and post-diagnosis.
[6] Defined based on recommendations for cancer prevention or a healthy lifestyle including diet, physical activity, and adiposity as components.
[7] Dietary guidelines or recommendations, namely (modified) Mediterranean diets, (healthy) plant-based diet, prudent dietary patterns.
[8] Unhealthy plant-based diet, pro-hyperinsulinemia diet, western dietary patterns, pro-inflammatory diet
[9] Other dietary exposures with or without meta-analysis:
Nuts and peanuts, fruits and vegetables, (unprocessed) red meat, processed meat, fish and seafoods, specific dairy products and milk, fruit juices, beer, wine, liquor, glycaemic load/index, insulin load/index, carbohydrate, dietary fibre, total dietary fat and specific fat types, dietary protein, dietary supplements, dietary and/or supplemental folate, supplemental calcium, and circulating concentrations of folate or folic acid.

FIGURE 2 Summary quality of evidence matrix from the systematic literature reviews on post-diagnosis adiposity, physical activity, sedentary behaviour, dietary factors, supplement use and colorectal cancer prognosis.

volumes. In a limited number of sensitivity and subgroup meta-analyses that were possible based on the available study-specific data, the results were not different after excluding patients with locally advanced or metastatic tumours, and according to anatomical cancer subsite and sex.

Sedentary behaviour measured as time sitting while watching TV was positively associated with risk of all-cause (3 studies, RR highest vs. lowest category: 1.28, 95% CI: 1.06–1.55, tau^2: 0.00, I^2: 0%) and colorectal cancer-specific (2 studies, RR: 1.45, 95% CI: 0.95–2.21, I^2: 0%) mortality, but the evidence was judged as limited due to small number of studies and/or methodological limitations, and no conclusion could be drawn.

3.3 | Evidence summary for post-diagnosis dietary factors and colorectal cancer prognosis

We included five RCTs and 35 longitudinal observational studies in the systematic review,[15] which comprised 30,242 individuals with colorectal cancer, of whom over 8700 died of any cause, 2100 died of colorectal cancer, and 3700 experienced an additional colorectal cancer event. Meta-analyses were possible for intake of whole grains, nuts and peanuts, red and processed meat, dairy products, sugary drinks, artificially sweetened beverages, coffee, alcohol, dietary glycaemic load/index, insulin load/index, marine omega-3 polyunsaturated fatty acids, supplemental calcium, and circulating 25-hydroxyvitamin D (25(OH)D) concentrations. RCTs were identified only for supplementation of protein, omega-3 fatty acids, vitamin C (1 study each), and vitamin D3 (2 studies), which were descriptively synthesised.[15]

The evidence was graded as limited-suggestive for healthy dietary and lifestyle patterns, which included diet, physical activity, and adiposity as components (e.g., WCRF/AICR, American Cancer Society scores), and lower risk of all-cause mortality. Six observational studies investigated four patterns, and results were generally consistent in the direction of an inverse association (RRs for highest vs. lowest scores ranged from 0.58 to 0.80; 3 out of 5 CIs crossing the null), apart from one study that indicated a positive association with CIs crossing the null. The evidence was also graded as limited-suggestive for healthy dietary patterns (e.g., Mediterranean, Dietary Approaches to Stop Hypertension [DASH], plant-based diets) and lower risk of all-cause mortality. Of 20 association estimates, 18 showed inverse associations (RRs ranged from 0.46 to 0.98; 12 CIs crossing the null), and two positive associations with CIs crossing the null. Similarly, 8 association estimates of unhealthy dietary patterns (e.g., Western diet) showed generally consistent positive associations (6 of 8 RRs were positive, 4 CIs of which crossed the null) with all-cause mortality, which was graded as limited-suggestive evidence.

The evidence was graded as limited-suggestive for intake of whole grains and total, caffeinated, and decaffeinated coffee with lower risk of all-cause mortality. A one serving/day higher whole grain intake yielded a 10% lower all-cause mortality risk (4 studies, RR: 0.90, 95% CI: 0.83–0.97, tau^2: 0.00; I^2: 0%). A one cup/day higher total (4 studies, RR: 0.92, 95% CI: 0.89–0.95, tau^2: 0.00; I^2: 0%),

caffeinated (RR: 0.91, 95% CI: 0.86–0.97, tau^2: 0.002; I^2: 45%), and decaffeinated (RR: 0.86, 95% CI: 0.80–0.92, t^2: 0.00; I^2: 0%) coffee was inversely associated with risk of all-cause mortality. Intake of sugary drinks was positively associated with risk of all-cause mortality (4 studies, RR per 1 serving/day: 1.20, 95% CI: 1.08–1.33, tau^2: 0.00; I^2: 0%), which was also graded as limited-suggestive evidence.

Intake of artificially sweetened beverages and circulating 25(OH)D concentrations were inversely associated with all-cause and colorectal cancer-specific mortality, but the evidence was graded as limited-no conclusion because of the high risk of potential biases (e.g., reverse causation, residual confounding).

The evidence on other dietary factors and colorectal cancer outcomes showed on average no association and/or was limited in methodological quality (Table 2, Figure 2), thus it was graded as limited and no conclusion could be made.

4 | DISCUSSION

As part of CUP Global, we conducted systematic reviews and meta-analyses and graded the quality of the evidence for the association of adiposity, physical activity, sedentary behaviour, and dietary factors with colorectal cancer prognostic outcomes. A better understanding of the association of modifiable lifestyle factors with outcomes after colorectal cancer diagnosis can inform the development of tailored prevention strategies for colorectal cancer survivors.

There was evidence of non-linearity in the associations between post-diagnosis BMI and risk of all-cause mortality, colorectal cancer-specific mortality, and recurrence/disease-free survival. The associations appeared reverse J-shaped with a common nadir at BMI of 28 kg/m^2. A higher risk of these outcomes, relative to the point of lowest risk on the curve, was observed at both ends of the BMI distribution (<24 and >32 kg/m^2). The quality of this evidence was graded as limited-no conclusion due to the high risk of several biases. The results were similar in several subgroups. The evidence of other adiposity indices (i.e., WC and weight/BMI change) on colorectal cancer outcomes was sparse, and also graded as limited-no conclusion.

The evidence for the association of post-diagnosis recreational physical activity and lower risk of all-cause mortality and recurrence/disease-free survival was rated as limited-suggestive. The association with all-cause mortality appeared to decrease linearly with increasing recreational physical activity levels from little activity up to around 20 MET-h/week (roughly equivalent to 5 h of moderate-intensity physical activity/week) without further risk reduction after that, suggesting that even low physical activity might provide survival benefits. Sedentary behaviour was positively associated with all-cause and colorectal cancer-specific mortality, but only three studies were available,[28–30] and the evidence was rated as limited-no conclusion.

There was limited-suggestive evidence for the associations between healthy dietary and/or lifestyle patterns (including diets that comprised plant-based foods), intake of whole grain and coffee (total, caffeinated, decaffeinated) with lower risk of all-cause mortality, and for the associations between unhealthy dietary patterns and intake of sugary drinks with higher risk of all-cause mortality. The evidence for other diet-outcome associations was graded as limited-no conclusion.

This evidence base has important limitations. The vast majority of included studies were observational, and the findings are susceptible to different biases (Box 1).[31] All studies measured physical activity levels, sedentary behaviour and dietary exposures using self-reported data, introducing potential measurement error. TV viewing time was used as a surrogate measure of sedentary behaviour, which does not capture other aspects such as occupational sedentary time. Most studies used BMI as a measure of adiposity, but BMI does not distinguish between body fat and lean body mass and does not capture adiposity distribution.[32] In addition, most studies assessed all lifestyle exposures at one point in time, and this assessment ranged from immediately after diagnosis to many years post-diagnosis, introducing heterogeneity and inability to capture changes that are very likely to occur in the cancer survival continuum. Many studies were not able to adequately adjust for cancer treatment, disease progression, comorbidities, and pre-cancer exposures that may confound the observed associations. Another important limitation is the possibility of selection bias, because inclusion of participants in the studies depends on survival time after disease diagnosis. Several studies only reported analyses from a mixture of patients with early and metastatic tumours. The potential risk of bias and clinical context is very different in these patient groups.[33] However, when meta-analyses were conducted excluding patients with metastases, substantial changes in the findings were not observed. Other limitations of this work include the limited representation from populations of non-white origin, not evaluating associations of lifestyle factors with other oncological outcomes, such as cancer treatment tolerance and completion, and the potential missed studies published after February 28, 2022. We conducted a literature search focusing on RCTs published after this date until 31 August, 2023, but we did not identify any related to our exposures of interest. Therefore, we anticipate that the conclusions on the present evidence would remain unchanged given that RCTs are considered the most influential studies in our evidence grading criteria. Considering the potential methodological limitations, the independent Expert Panel graded the quality of the evidence conservatively.

Despite the limitations of the evidence base, this programme of work has several strengths. We conducted the most comprehensive systematic literature search for adiposity, physical activity (overall and by frequency, duration, intensity, and volume), sedentary behaviour, and dietary factors in relation to prognostic outcomes after a colorectal cancer diagnosis, which has enhanced the evidence base. We performed both linear and non-linear dose–response meta-analyses to avoid the limitations of categorical meta-analyses and to enable more precise inference and potential recommendations regarding the effective dose of the modifiable lifestyle exposures. In addition, an independent Expert Committee on Cancer Survivorship and Expert Panel systematically graded the quality and uncertainty of the evidence according to the pre-defined WCRF/AICR evidence grading criteria.

In conclusion, our systematic reviews and meta-analyses provide limited but suggestive evidence for associations between post-colorectal cancer diagnosis recreational physical activity, healthy dietary

and/or lifestyle patterns, intake of whole grain and coffee with lower risk of all-cause mortality, and for the associations between unhealthy dietary patterns and intake of sugary drinks with higher risk of all-cause mortality. To strengthen the evidence that contributes towards the development of tailored lifestyle recommendations for colorectal cancer survivors (Box 1), there is a need for RCTs evaluating the effects of lifestyle modifications that have shown survival benefits in the present review, and large well-designed observational studies with more accurate and repeated exposure and confounder information. Nevertheless, even in the absence of stronger evidence, there is potential to use this evidence as guidance for colorectal cancer patients and their health professionals that a physically active lifestyle and consumption of a healthy diet, including dietary patterns emphasising plant-based foods, and avoidance of sugary drinks and sedentary behaviour may be associated with longer overall survival after a colorectal cancer diagnosis.

AUTHOR CONTRIBUTIONS

Konstantinos K. Tsilidis and Doris S. M. Chan are co-principal investigators of CUP Global at Imperial College London (ICL). Doris S. M. Chan and Konstantinos K. Tsilidis implemented the study according to the protocol reviewed by the CUP Global Protocol Expert Group (PEG). Katia Balducci and Sonia Kiss did the literature search. Katia Balducci, Sonia Kiss, Margarita Cariolou and Rita Vieira did the study selection. Katia Balducci, Sonia Kiss, Margarita Cariolou, Rita Vieira, Georgios Markozannes and Nerea Becerra-Tomás did the data extraction and checking. Georgios Markozannes, Margarita Cariolou and Nerea Becerra-Tomás did the risk of bias assessment. Doris S. M. Chan, Georgios Markozannes, Margarita Cariolou, Nerea Becerra-Tomás, Katia Balducci, Sonia Kiss and Rita Vieira analysed and interpreted the data. Konstantinos K. Tsilidis interpreted the data and drafted the original manuscript. Dagfinn Aune was a WCRF International CUP Global ICL team member who revised the manuscript. Darren C. Greenwood was a statistical adviser. Amanda J. Cross was a CUP Global advisor at Imperial College London. Laure Dossus, Esther M. González-Gil, and Marc J. Gunter were CUP Global collaborators on biological processes and provided input into the biological mechanism citations in the manuscript. Kate Allen, Panagiota Mitrou, Martin J. Wiseman, Helen Croker, Vanessa L. Gordon-Dseagu, Nicole Musuwo and Nigel T. Brockton were CUP Global Secretariat members. Ellen Copson was a PEG member, Chair of CUP Global Expert Committee on Cancer Survivorship, and Expert Panel member. Wendy Demark-Wahnefried and Galina Velikova were PEG, OACD, and CUP Global Expert Committee members. Andrew G. Renehan was PEG member and Deputy Chair of CUP Global Expert Committee. John Krebs, Matty P. Weijenberg, Monica L. Baskin, Sarah J. Lewis, Jaap Seidell, Rajiv Chowdhury, and Lynette Hill were CUP Global Expert Panel members. Anne M. May, Anne Tjonneland, Karen Steindorf, Martijn Bours, Melissa Hudson, Roderick Skinner, and Folakemi T. Odedina were CUP Global Expert Committee members. All members of the CUP Global Expert Committee and Expert Panel provided input into the judgements on the evidence and advised on the interpretation of the review, the public representative (Lynette Hill) did not contribute to the final decisions made by the Panel. All authors reviewed and provided comments on the manuscript. Doris S. M. Chan is the guarantor and has full access to all the data and takes responsibility for the integrity of the data and the accuracy of the data analysis. The work reported in the paper has been performed by the authors, unless clearly specified in the text.

AFFILIATIONS

[1]Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK
[2]Department of Hygiene and Epidemiology, University of Ioannina Medical School, Ioannina, Greece
[3]Department of Nutrition, Oslo New University College, Oslo, Norway
[4]Department of Research, The Cancer Registry of Norway, Oslo, Norway
[5]Leeds Institute for Data Analytics, Faculty of Medicine and Health, University of Leeds, Leeds, UK
[6]Nutrition and Metabolism Branch, International Agency for Research on Cancer, World Health Organization, Lyon, France
[7]World Cancer Research Fund International, London, UK
[8]American Institute for Cancer Research, Washington, DC, USA
[9]Cancer Sciences Academic Unit, Faculty of Medicine, University of Southampton, Southampton, UK
[10]The Christie NHS Foundation Trust, Manchester Cancer Research Centre, NIHR Manchester Biomedical Research Centre, Division of Cancer Sciences, School of Medical Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK
[11]Department of Epidemiology, GROW School for Oncology and Reproduction, Maastricht University, Maastricht, The Netherlands
[12]O'Neal Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, Alabama, USA
[13]Department of Oncology, St Jude Children's Research Hospital, Memphis, Tennessee, USA
[14]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands
[15]Mayo Clinic Comprehensive Cancer Center, Jacksonville, Florida, USA
[16]Department of Paediatric and Adolescent Haematology/Oncology, Great North Children's Hospital and Translational and Clinical Research Institute, and Centre for Cancer, Newcastle University, Newcastle upon Tyne, UK
[17]Division of Physical Activity, Prevention and Cancer, German Cancer Research Center (DKFZ) and National Center for Tumor Diseases (NCT), Heidelberg, Germany
[18]Danish Cancer Society Research Center, Diet, Cancer and Health, Copenhagen, Denmark
[19]Department of Public Health, University of Copenhagen, Copenhagen, Denmark
[20]School of Medicine, Faculty of Medicine and Health, University of Leeds, Leeds, UK
[21]UPMC Hillman Cancer Center, Pittsburgh, Pennsylvania, USA
[22]Department of Global Health, Robert Stempel College of Public Health and Social Work, Florida International University, Miami, Florida, USA

[23]Department of Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK
[24]Department of Health Sciences, Faculty of Science, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands
[25]Department of Biology, University of Oxford, Oxford, UK

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CONFLICT OF INTEREST STATEMENT

Ellen Copson declared research support from Seca. Galina Velikova declared honoraria from Pfizer, Novartis, and Eisai, an institutional grant from Pfizer, and advisory board and consultancy fees from AstraZeneca, Roche, Novartis, Pfizer, Seagene, Eisai, and Sanofi. All other authors have no conflict of interest related to this work.

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, and in the separate systematic reviews. Further details are available from the corresponding author upon request.

ORCID

Konstantinos K. Tsilidis https://orcid.org/0000-0002-8452-8472
Dagfinn Aune https://orcid.org/0000-0002-4533-1722
Wendy Demark-Wahnefried https://orcid.org/0000-0001-5241-932X
Doris S. M. Chan https://orcid.org/0000-0002-0198-1897

REFERENCES

1. Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet (London, England)*. 2018;391:1023-1075.
2. World Cancer Research Fund International/American Institute for Cancer Research. *Diet, Nutrition, Physical Activity and Cancer: A Global Perspective*. Continuous Update Project Report. 2018. Accessed December 2022. https://www.wcrf.org/dietandcancer
3. Kyrgiou M, Kalliala I, Markozannes G, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. *BMJ*. 2017;356:j477.
4. Papadimitriou N, Markozannes G, Kanellopoulou A, et al. An umbrella review of the evidence associating diet and cancer risk at 11 anatomical sites. *Nat Commun*. 2021;12:4579.
5. Rezende LFM, Sa TH, Markozannes G, et al. Physical activity and cancer: an umbrella review of the literature including 22 major anatomical sites and 770 000 cancer cases. *Br J Sports Med*. 2018;52:826-833.
6. Qiu S, Jiang C, Zhou L. Physical activity and mortality in patients with colorectal cancer: a meta-analysis of prospective cohort studies. *Eur J Cancer Prev*. 2020;29:15-26.
7. Hoang T, Kim H, Kim J. Dietary intake in association with all-cause mortality and colorectal cancer mortality among colorectal cancer survivors: a systematic review and meta-analysis of prospective studies. *Cancers (Basel)*. 2020;12:12.
8. Simillis C, Taylor B, Ahmad A, et al. A systematic review and meta-analysis assessing the impact of body mass index on long-term survival outcomes after surgery for colorectal cancer. *Eur J Cancer*. 2022;172:237-251.
9. Swain CTV, Nguyen NH, Eagles T, et al. Postdiagnosis sedentary behavior and health outcomes in cancer survivors: a systematic review and meta-analysis. *Cancer*. 2020;126:861-869.
10. Rock CL, Thomson CA, Sullivan KR, et al. American Cancer Society nutrition and physical activity guideline for cancer survivors. *CA Cancer J Clin*. 2022;72:230-262.
11. WHO Guidelines on Physical Activity and Sedentary Behaviour. Accessed March 2023. https://www.who.int/publications/i/item/9789240015128
12. Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise guidelines for cancer survivors: consensus statement from international multidisciplinary roundtable. *Med Sci Sports Exerc*. 2019;51:2375-2390.
13. U.S. Department of Health and Human Services. *Physical Activity Guidelines for Americans*. 2nd ed. U.S. Department of Health and Human Services; 2018.
14. Global Cancer Update Programme (CUP Global). Accessed March 2023. https://www.wcrf.org/diet-activity-and-cancer/global-cancer-update-programme/about-the-global-cancer-update-programme/
15. Chan DSM, Cariolou M, Markozannes G, et al. Post-diagnosis dietary factors, supplement use and colorectal cancer prognosis: a Global Cancer Update Programme (CUP Global) systematic literature review and meta-analysis. *Int J Cancer*. 2024;155(3):445-470. doi:10.1002/ijc.34906
16. Becerra-Tomás N, Markozannes G, Cariolou M, et al. Post-diagnosis adiposity and colorectal cancer prognosis: a Global Cancer Update

Programme (CUP Global) systematic literature review and meta-analysis. *Int J Cancer*. 2024;155(3):400-425. doi:10.1002/ijc.34905
17. Markozannes G, Becerra-Tomás N, Cariolou M, et al. Post-diagnosis physical activity and sedentary behaviour and colorectal cancer prognosis: a Global Cancer Update Programme (CUP Global) systematic literature review and meta-analysis. *Int J Cancer*. 2024;155(3):426-444. doi:10.1002/ijc.34903
18. Chan DSM, Tsilidis K, Becerra-Tomas N, et al. Global Cancer Update Programme Protocol for the data collection and systematic literature review on the role of diet, body fatness and physical activity on survival after colorectal cancer. 2022. Accessed March 2023. https://osf.io/r5ud2/registrations
19. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ (Clinical Research Ed)*. 2019;366:l4898.
20. USDA. *Nutrition Evidence Systematic Review*. Risk of Bias for Nutrition Observational Studies (RoB-NObs) Tool.
21. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ (Clinical Research Ed)*. 2016;355:i4919.
22. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7:177-188.
23. Greenland S, Longnecker MP. Methods for trend estimation from summarized dose–response data, with applications to meta-analysis. *Am J Epidemiol*. 1992;135:1301-1309.
24. Orsini N, Li R, Wolk A, Khudyakov P, Spiegelman D. Meta-analysis for linear and nonlinear dose–response relations: examples, an evaluation of approximations, and software. *Am J Epidemiol*. 2012;175:66-73.
25. Rucker G, Schwarzer G, Carpenter JR, Schumacher M. Undue reliance on I(2) in assessing heterogeneity may mislead. *BMC Med Res Methodol*. 2008;8:79.
26. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med*. 2002;21:1539-1558.
27. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315:629-634.
28. Arem H, Pfeiffer RM, Engels EA, et al. Pre- and postdiagnosis physical activity, television viewing, and mortality among patients with colorectal cancer in the National Institutes of Health-AARP Diet and Health Study. *J Clin Oncol*. 2015;33:180-188.
29. Cao Y, Meyerhardt JA, Chan AT, Wu K, Fuchs CS, Giovannucci EL. Television watching and colorectal cancer survival in men. *Cancer Causes Control*. 2015;26:1467-1476.
30. Ratjen I, Schafmayer C, di Giuseppe R, et al. Postdiagnostic physical activity, sleep duration, and TV watching and all-cause mortality among long-term colorectal cancer survivors: a prospective cohort study. *BMC Cancer*. 2017;17:701.
31. Chubak J, Boudreau DM, Wirtz HS, McKnight B, Weiss NS. Threats to validity of nonrandomized studies of postdiagnosis exposures on cancer recurrence and survival. *J Natl Cancer Inst*. 2013;105:1456-1462.
32. Christakoudi S, Tsilidis KK, Evangelou E, Riboli E. Association of body-shape phenotypes with imaging measures of body composition in the UK Biobank cohort: relevance to colon cancer risk. *BMC Cancer*. 2021;21:1106.
33. Parkin E, O'Reilly DA, Sherlock DJ, Manoharan P, Renehan AG. Excess adiposity and survival in patients with colorectal cancer: a systematic review. *Obes Rev*. 2014;15:434-451.

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