






Post-diagnosis adiposity and colorectal cancer prognosis: A Global Cancer Update Programme (CUP Global) systematic literature review and meta-analysis

Nerea Becerra-Tomás¹ | Georgios Markozannes^{1,2}  | Margarita Cariolou¹ |
 Katia Balducci¹ | Rita Vieira¹ | Sonia Kiss¹ | Dagfinn Aune^{1,3,4}  |
 Darren C. Greenwood⁵ | Laure Dossus⁶ | Ellen Copson⁷ | Andrew G. Renehan⁸ |
 Martijn Bours⁹ | Wendy Demark-Wahnefried¹⁰  | Melissa M. Hudson¹¹ |
 Anne M. May¹² | Folakemi T. Odedina¹³ | Roderick Skinner¹⁴ |
 Karen Steindorf¹⁵ | Anne Tjønneland^{16,17} | Galina Velikova¹⁸ |
 Monica L. Baskin¹⁹ | Rajiv Chowdhury²⁰ | Lynette Hill²¹ | Sarah J. Lewis²² |
 Jaap Seidell²³ | Matty P. Weijenberg⁹ | John Krebs²⁴ | Amanda J. Cross¹ |
 Konstantinos K. Tsilidis^{1,2}  | Doris S. M. Chan¹ 

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

Funding information

American Institute for Cancer Research; World Cancer Research Fund; Wereld Kanker Onderzoek Fonds

Abstract

The adiposity influence on colorectal cancer prognosis remains poorly characterised. We performed a systematic review and meta-analysis on post-diagnosis adiposity measures (body mass index [BMI], waist circumference, waist-to-hip ratio, weight) or their changes and colorectal cancer outcomes. PubMed and Embase were searched through 28 February 2022. Random-effects meta-analyses were conducted when at least three studies had sufficient information. The quality of evidence was interpreted and graded by the Global Cancer Update Programme (CUP Global) independent Expert Committee on Cancer Survivorship and Expert Panel. We reviewed 124 observational studies (85 publications). Meta-analyses were possible for BMI and all-cause mortality, colorectal cancer-specific mortality, and cancer recurrence/disease-free survival. Non-linear meta-analysis indicated a reverse J-shaped association between BMI and colorectal cancer outcomes (nadir at BMI 28 kg/m²). The highest risk, relative to the nadir, was observed at both ends of the BMI distribution (18 and 38 kg/m²), namely 60% and 23% higher risk for all-cause mortality; 95% and 26% for colorectal cancer-specific mortality; and 37% and 24% for cancer recurrence/disease-free survival, respectively. The higher risk with low BMI was

Konstantinos K. Tsilidis and Doris S. M. Chan contributed equally and shared last authorship.

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.

For affiliations refer to page 414

This is an open access article under the terms of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2024 The Authors. *International Journal of Cancer* published by John Wiley & Sons Ltd on behalf of UICC.

attenuated in secondary analyses of RCTs (compared to cohort studies), among studies with longer follow-up, and in women suggesting potential methodological limitations and/or altered physiological state. Descriptively synthesised studies on other adiposity-outcome associations of interest were limited in number and methodological quality. All the associations were graded as limited (likelihood of causality: no conclusion) due to potential methodological limitations (reverse causation, confounding, selection bias). Additional well-designed observational studies and interventional trials are needed to provide further clarification.

KEYWORDS

adiposity, colorectal cancer, evidence grading, systematic review

What's new?

The influence of adiposity on colorectal cancer prognosis remains poorly characterised. Here, as part of CUP Global, the evidence on post-diagnosis adiposity and colorectal cancer outcomes was systematically synthesised using standardised criteria, and a non-linear dose-response meta-analysis was conducted for the first time. Reverse J-shaped associations were observed between post-diagnosis BMI and all-cause mortality, colorectal cancer-specific mortality, and recurrence. Synthesised studies on other adiposity-outcome associations were limited in number and methodological quality. All evidence was graded as 'limited-no conclusion' for the likelihood of causality due to potential methodological limitations, calling for additional well-designed observational studies and intervention trials.

1 | INTRODUCTION

In 2020, colorectal cancer was the third most diagnosed cancer with 1.9 million new cases, and the second most frequent cause of cancer mortality with 930,000 deaths globally.¹ Colorectal cancer incidence has declined or stabilised among adults aged 50 years and above in high-income countries, while it is increasing among younger adults and in low and middle-income countries.^{2,3} Colorectal cancer survival rates are gradually improving over time,⁴ likely due to improved early detection methods and advances in cancer treatments.⁵ The increasing number of colorectal cancer survivors (more than 5.25 million people are living with this disease worldwide³), however, highlights the need to better quantify the relationship between post-diagnosis modifiable lifestyle factors (such as diet, physical activity, and adiposity) and survival outcomes to guide the development of evidence-based recommendations for this specific population.⁶

The prevalence of overweight and obesity rapidly increased worldwide⁷ from 1975 to 2016. The Third Expert report from the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR)⁸ concluded that there was strong evidence (likelihood of causality: convincing) that greater adiposity (i.e., expressed by increased body mass index [BMI], waist circumference or waist-to-hip ratio) increases the risk of colorectal cancer. However, the potential impact of excess adiposity after diagnosis on colorectal cancer prognosis is not well understood. Previously published meta-analyses have analysed the association between post-diagnosis BMI and colorectal cancer outcomes (i.e., all-cause mortality, colorectal cancer-specific

mortality, and recurrence).⁹⁻¹³ The most comprehensive and recent one,¹³ which included 56 publications assessing BMI at any post-diagnosis period, showed that colorectal cancer survivors who were underweight (<18.5 kg/m²) had a higher risk of all-cause mortality, colorectal cancer-specific mortality, and recurrence than those with normal weight (18.5–25 kg/m²). No differences were observed between those with overweight (25–30 kg/m²) and normal weight. Colorectal cancer survivors with obesity (>30 kg/m²) had worse disease-free survival, while those with morbid obesity (>35 kg/m²) had a higher risk for all-cause mortality, colorectal cancer-specific mortality, and recurrence. However, this meta-analysis combined unadjusted and adjusted risk estimates, which can result in confounded associations between adiposity and colorectal cancer outcomes. In addition, questions remain about the shape of the dose-response relationship, as all previous meta-analyses were conducted on categorical data, assuming constant risks within the different BMI categories analysed. Thus, conducting a non-linear dose-response meta-analysis was highly desirable and useful for characterising thresholds, as previously examined in breast cancer survivors.¹⁴

Therefore, as part of the work for the Global Cancer Update Programme (CUP Global),¹⁵ we conducted a systematic literature review and meta-analysis to summarise the epidemiological evidence on the role of post-diagnosis adiposity in colorectal cancer outcomes.

The current article presents the evidence on adiposity and colorectal cancer outcomes, whereas evidence on diet, physical activity and the overall summary are presented in the accompanied papers.¹⁶⁻¹⁸

2 | METHODS

This systematic review is part of the ongoing CUP Global, formerly known as the WCRF/AICR Continuous Update Project.¹⁵ The detailed pre-published protocol can be found elsewhere.¹⁹ The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist is in Supplementary Table 1.

2.1 | Search strategy, selection criteria and data extraction

A comprehensive search was conducted in PubMed and Embase databases through 28 February 2022. The reference lists of relevant articles, reviews and meta-analyses were manually checked for potential additional publications.

Inclusion criteria were randomised controlled trials (RCTs), longitudinal observational studies, or pooled analyses of these designs, with at least 100 participants diagnosed with first primary colorectal cancer or its subtypes (for brevity the term 'colorectal' is used for any colorectal cancer regardless of the cancer site, colon or rectum) during adulthood; that investigated associations between post-diagnosis BMI, waist circumference, waist-to-hip ratio, weight, or changes in these exposures with all-cause mortality, colorectal cancer and subsite-specific mortality, colorectal cancer recurrence/disease-free survival (as defined in studies) (Supplementary Table 2), any second primary cancer, or cardiovascular disease mortality.

The article with the largest number of outcome events with sufficient information for analysis was selected when multiple articles from the same or similar populations reported the same exposure-outcome associations. Relevant data, including study and participants' characteristics and results of analyses, were extracted into the CUP Global database. A second reviewer independently checked the study selection and data extraction. Any disagreements were resolved by consensus with a third reviewer.

2.2 | Risk of bias assessment

A modified version of the Risk of Bias for Nutrition Observational Studies (RoB-NObs) tool²⁰ was utilised to assess the risk of bias of the studies included in the dose-response meta-analyses. The tool was originally developed by the U.S Department of Agriculture (USDA) Nutrition Evidence Systematic Review after modifications to the Cochrane's collaboration Risk of bias In Non-randomised Studies of Interventions (ROBINS-I).²¹ The Imperial College London (ICL) review team further refined and tested the tool to ensure its suitability for investigating exposure-outcome associations in cancer survivorship studies. This involved adapting the tool's prompting questions and providing additional guidance to encompass adiposity, physical activity, and dietary/nutritional exposures. The tool consists of seven domains, including confounding, participant selection, exposure classification, departures from intended exposures, missing data, outcome measurement, and selective reporting (the working document version dated 11/07/2023 can be found in Supplementary Table 3).

The studies not included in the dose-response meta-analyses, were assessed descriptively considering the most likely influential sources of bias (selection bias, information bias of exposure and outcome assessment, and residual confounding by cancer stage and treatment).

2.3 | Evidence synthesis

Publications were meta-analysed or descriptively synthesised when at least three studies were identified for a given exposure, except for exposures related to the WCRF/AICR Cancer Prevention Recommendations that were descriptively synthesised even when there were fewer than three included studies to identify any potential discrepancies compared to what has been currently recommended to cancer prevention.

2.4 | Statistical methods for meta-analysis

Linear and non-linear dose-response and categorical meta-analyses were conducted using the inverse variance weighted random-effects model²² to calculate summary relative risk (RR) estimates and 95% confidence intervals (CIs). A descriptive synthesis, which consisted of systematically gathering, tabulating, and descriptively summarising the findings of the individual studies, was performed when results could not be summarised in dose-response or categorical meta-analyses.

Potential non-linear relationships were investigated by performing a one-stage non-linear dose-response meta-analysis²³ using restricted cubic splines with three knots placed at fixed percentiles (10th, 50th, and 90th) of the exposure distribution when at least five or more studies with data for at least three exposure categories were available (Text S1). Studies providing only a dichotomous or linear effect estimate were not included in the non-linear meta-analysis. All categories of BMI (including underweight) were included. Standard imputations were used to estimate missing information required for the analysis.^{24,25} The nadir of the dose-response curve for each exposure-outcome association was selected as the referent point. RRs and 95% CIs were calculated relative to this point.

Linear dose-response meta-analysis was conducted when there were at least three studies with sufficient data to do the analysis (Text S1). The dose-response estimate given in the original publications was used directly when available, otherwise, we computed the estimates per exposure increment unit using the generalised weighted least-squares regression model.^{26,27} For studies reporting results using BMI categories other than normal weight (BMI 18.5–24.9 kg/m² or as defined by studies) as a reference, the RRs and 95% CIs were re-calculated using the Hamling method.²⁸ The underweight category (BMI <18.5 kg/m² or as defined by studies) was excluded where possible from the linear dose-response meta-analysis on BMI to avoid possible influences on the risk estimation. If the study reported results separately by cancer site or other subgroups, we generated an overall estimate for subgroups combined using a fixed-effect model before pooling with other studies.

Categorical meta-analysis was performed to assess colorectal cancer prognosis in patients with underweight (BMI <18.5 kg/m² or

as defined by studies), overweight (BMI 25–29.9 kg/m² or as defined by studies), and obesity (≥ 30 kg/m² or as defined by studies) compared to those with normal weight (BMI 18.5–24.9 kg/m² or as defined by studies). Studies were included regardless of the BMI classification used (World Health Organisation [WHO] International,²⁹ or other study-defined categories). A few studies reported risk estimates for multiple sub-categories of normal weight,³⁰ overweight^{30–33} or obesity,^{30,34–37} and the Hamling method²⁸ was used to obtain an overall RR and 95% CIs for the comparisons of overweight and obese versus normal weight categories. RRs were re-calculated when the reference category was not the normal weight. Studies reporting two open-ended BMI categories only (e.g., >25 vs. <25 kg/m²; >30 vs. <30 kg/m²) or including underweight and normal weight or overweight and obesity in the same category were excluded from the analyses. A sensitivity analysis restricted to studies using the WHO classification system²⁹ was performed.

Heterogeneity between studies was assessed using the estimate of between study variances (τ^2) and reflected by the range of the estimates (RRs) provided in the forest plots. Additionally, we provided the I^2 metric,³⁸ which measures the proportion of total variability in effect estimates that is due to between-study heterogeneity rather than sampling error. Unlike I^2 , the τ^2 does not depend on the precision of a study (does not systematically increase with the number or size of the studies in a meta-analysis).³⁹ The 95% prediction interval (PI) was also used to estimate the range of results likely to contain the value of a new study.⁴⁰ Sources of heterogeneity were explored with non-linear dose–response subgroup meta-analyses. These analyses were based on a priori defined disease (cancer subsite, stage), study characteristics (sex, geographical location, study type, exposure time relative to primary cancer diagnosis, and length of follow-up) and by risk of bias assessment domains. One of our aims was to perform a subgroup analysis according to the time of BMI (adiposity index) assessment with respect to the cancer diagnosis and/or treatment. However, most studies assessed the exposure at diagnosis or shortly after, and very few at later periods of the cancer course,^{10,30,41,42} so it was not possible to perform predefined subgroup meta-analysis by exposure time relative to cancer diagnosis.

To explore the potential impact of bias due to reverse causation, a sensitivity analysis excluding, where possible, metastatic survivors was conducted.⁴³ When more than 10 studies were available in the linear dose–response meta-analysis, small study effects, such as publication bias, was examined using Egger's test⁴⁴ and via visual inspection of the funnel plots for asymmetry.

Statistical analyses were conducted using Stata 16 (StataCorp, College Station, TX, USA).

2.5 | Evidence grading criteria

The CUP Global independent Expert Committee on Cancer Survivorship and Expert Panel, convened by WCRF International, interpreted the findings independently of the ICL team. The Expert Committee made the preliminary conclusions, and the Expert Panel made the final

conclusions. The quality of the evidence was graded into strong (subgrades evaluating likelihood of causality: convincing, probable, or substantial effect on risk unlikely), or limited (subgrades evaluating likelihood of causality: suggestive or no conclusion) level, using predefined evidence grading criteria (Supplementary Table 4). The grades of the quality of the evidence reflect the independent Expert Committee's and Expert Panel's confidence that the association estimates are correct.

Additional details on the methods can be found in Supplementary Material (Text S1).

3 | RESULTS

3.1 | Study selection process

Figure 1 shows the flow-chart of the study selection process. There were 278 potentially eligible publications on post-diagnosis adiposity and colorectal cancer outcomes. We excluded 193 publications^{45–237} due to specific reasons related to the synthesis (Supplementary Table 5). Finally, 85 publications^{10,30–37,41,42,238–311} of 124 studies were included in the present review. A total of 96 studies (53 publications) were on BMI and all-cause mortality,^{10,30–36,41,42,238–244,246,252,253,255,257,259,261,263,265–270,274,276–280,282–285,287,290,292,295,296,299,300,302,303,307,308,310} 20 studies (19 publications) on BMI and colorectal cancer-specific mortality,^{30,36,37,41,238,240–242,245,253,260,265,271,281,289,294,295,304,306} and 72 studies (30 publications) on BMI and colorectal cancer recurrence/disease-free survival.^{31–36,42,239,240,247,251,253,256,257,259,269,278,280,285,286,288,292,293,295,298–300,305,307,310} There were very few studies for BMI and second primary cancer³⁷ (two studies), non-colorectal cancer related mortality^{37,289} (three studies) and cardiovascular disease mortality⁴¹ (one study). There were 13 studies (12 publications) on weight change and all-cause mortality,^{41,242,248–250,254,272,273,275,280,297,301} four studies (four publications) on weight change and colorectal-cancer-specific mortality,^{41,242,248,250} 10 studies (nine publications) on weight change and cancer recurrence/disease-free survival,^{249,254,258,273,275,280,291,297,309} and one study on weight change and cardiovascular mortality.⁴¹ A total of six studies (six publications) were on BMI change and all-cause mortality,^{248,262,264,275,278,287} one study on BMI change and colorectal cancer-specific mortality²⁴⁸ and three studies on BMI change and cancer recurrence/disease-free survival.^{254,275,278} There was only one study on waist circumference and recurrence/disease-free survival.³¹¹ No studies were found on post-diagnosis waist-to-hip ratio.

Meta-analyses were possible for post-diagnosis BMI and all-cause mortality, colorectal cancer-specific mortality, and recurrence/disease-free survival. Results were descriptively synthesised for post-diagnosis BMI and cardiovascular disease mortality, second primary cancer and non-colorectal cancer-related mortality, and for body weight and BMI change and colorectal cancer prognosis outcomes.

A detailed list of included and excluded studies in each specific meta-analysis or descriptive synthesis (with reasons for exclusion) is provided and referenced in Supplementary Table 5. The corresponding study and participants' characteristics are summarised in Supplementary Tables 6–13.

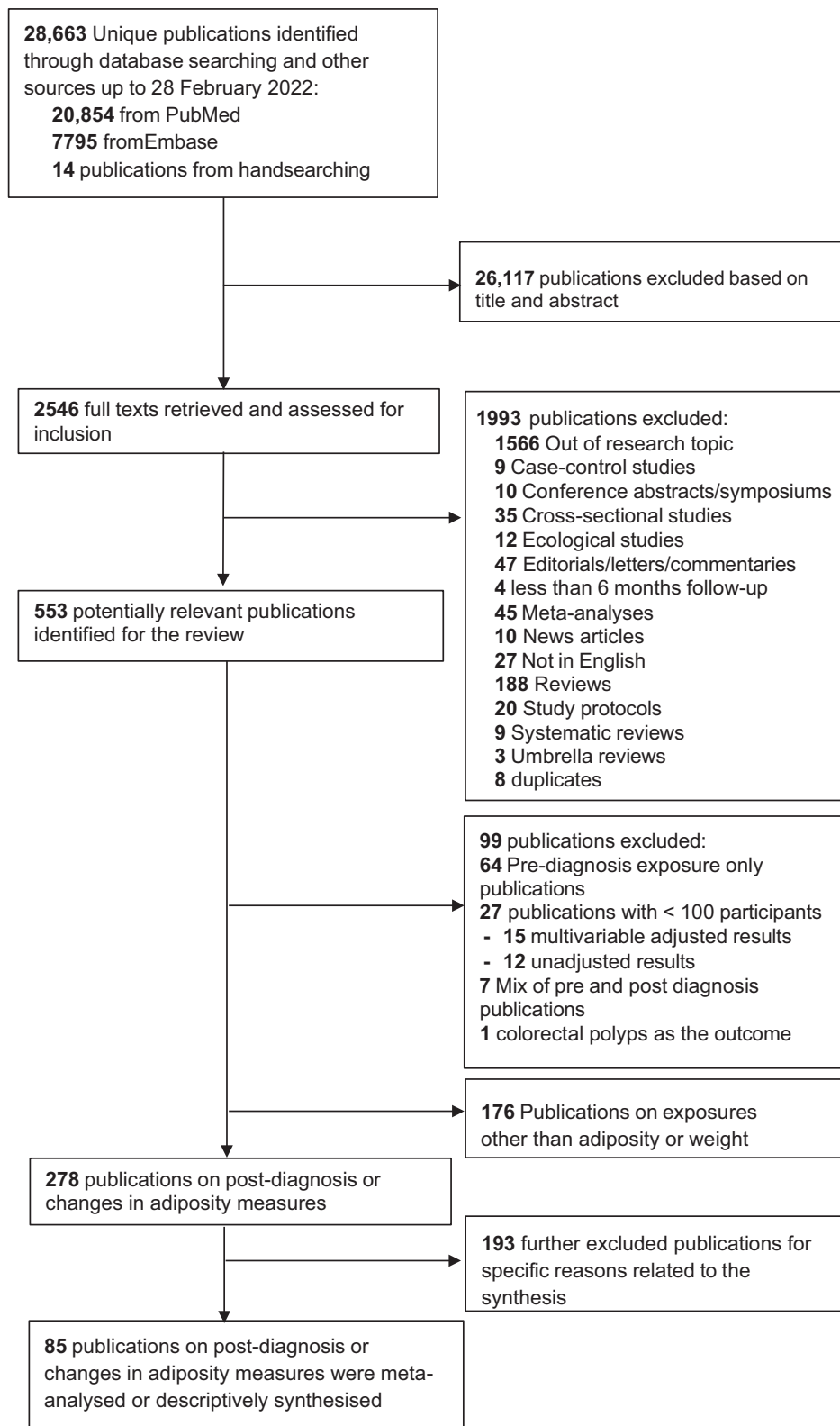


FIGURE 1 Flowchart of study selection process.

3.2 | Study characteristics

The 85 included publications were from 124 studies and comprised more than 294,000 colorectal cancer survivors, of whom more than 43,900 died of any causes, approximately 16,000 died of colorectal

cancer and approximately 24,600 experienced an additional colorectal cancer event. All included studies were observational, and no relevant RCTs were identified. Geographically, 24 publications were from Europe,^{10,33,35,42,243,253,266,268,272,276–279,282,284,291,293,296–298,303,308,310,311} 20 from North America,^{30–32,34,37,41,238,240,244,249,250,254,265,274,283,285,287,288,301,309}

19 from East or Southeast Asia,^{36,239,241,246,247,251,252,256,258,262,264,269,280,290,294,295,302,305,307} four from Australia/New Zealand,^{242,255,299,300} and 18 from mixed geographic locations^{248,257,259,273,275} or elsewhere.^{245,260,261,263,267,270,271,281,286,289,292,304,306} Most publications (n = 54) involved cancer survivors of any stage,^{10,30,33,35,36,41,42,238,239,241-245,247,248,250,252,253,256,260,261,263,266-268,270,271,274,277,279,281-284,286,288-290,292-294,296,298,300,302-308,310,311} 28 of which also included metastatic cancer survivors (median = 19.6%, range = 6%–58.9%; seven publications did not report % metastatic); 8 included stage II–III,^{31,32,37,240,258,259,275,280} 9 included stage III or locally advanced^{246,249,251,254,264,265,269,295,299} and 14 stage IV cancer survivors only.^{34,255,257,262,272,273,276,278,285,287,291,297,301,309}

3.3 | Post-diagnosis body mass index and colorectal cancer outcomes

Supplementary Table 14 shows a summary of the results of the meta-analyses. Overall, linear, non-linear dose–response and categorical meta-analyses were conducted, but evidence of non-linearity was detected, therefore we focussed on the non-linear analyses as the primary analyses. For the few studies^{245,257,269,271,277,282,289,303,304,306} that were not possible to include in any meta-analyses, we provided an overview of the findings (Supplementary Material—Text S2).

There was evidence of non-linearity between post-diagnosis BMI and all-cause mortality ($P_{\text{non-linearity}} < .001$, 46 studies, 37,310 deaths, 25 publications; BMI assessed from at-diagnosis to on average 4 years after diagnosis) (Figure 2A), colorectal cancer-specific mortality ($P_{\text{non-linearity}} < .001$, 13 studies, 15,366 deaths, 12 publications; BMI assessed from at-diagnosis to on average 18 months after diagnosis) (Figure 2B), and recurrence/disease-free survival ($P_{\text{non-linearity}} = .01$, 39 studies, 23,376 events, 18 publications; BMI assessed from at-diagnosis to on average 6 months after diagnosis or the end of the treatment) (Figure 2C). The shape of the association appeared reverse J-shaped with a common nadir at BMI of 28 kg/m². A high risk of colorectal cancer outcomes, relative to the nadir, was observed at the lowest and upper range of the BMI distribution. For BMI 18–24 kg/m², an 8%–60% higher risk of all-cause mortality, a 15%–95% higher risk of colorectal cancer-specific mortality, and a 5%–37% higher risk of recurrence/disease-free survival was observed. For BMI 32–38 kg/m², a 7%–23% higher risk of all-cause mortality, a 6%–26% higher risk of colorectal cancer-specific mortality, and a 7%–24% higher risk of recurrence/disease-free survival was observed.

Supplementary Figures 1–9 show the results of the categorical meta-analyses. Compared to colorectal cancer survivors of normal weight, underweight survivors had an increased risk of all-cause mortality (RR: 1.63; 95% CI: 1.43–1.84; $I^2 = 84%$, $\tau^2 = 0.07$, RR range = 0.58–10.20), colorectal cancer-specific mortality (RR: 1.60; 95% CI: 1.26–2.02; $I^2 = 71%$, $\tau^2 = 0.07$, RR range = 0.64–3.76) and recurrence/disease-free survival (RR: 1.41; 95% CI: 1.16–1.73; $I^2 = 90%$, $\tau^2 = 0.11$, RR range = 0.49–5.88). Colorectal cancer survivors who were overweight, had a lower risk of all-cause mortality (RR: 0.90; 95% CI: 0.85–0.95; $I^2 = 72%$, $\tau^2 = 0.01$, RR

range = 0.56–1.63), colorectal cancer-specific mortality (RR: 0.79; 95% CI: 0.68–0.90; $I^2 = 75%$, $\tau^2 = 0.03$, RR range = 0.35–1.12) and recurrence/disease-free survival (RR: 0.92; 95% CI: 0.85–1.00; $I^2 = 70%$, $\tau^2 = 0.01$, RR range = 0.42–1.58) compared to normal weight survivors. There was little evidence of an inverse association between obesity and all-cause (RR: 0.93; 95% CI: 0.86–1.00; $I^2 = 71%$, $\tau^2 = 0.02$, RR range = 0.69–1.80), and colorectal cancer-specific mortality (RR: 0.90; 95% CI: 0.79–1.03; $I^2 = 57%$, $\tau^2 = 0.02$, RR range = 0.62–1.15) as the CIs crossed the null value, and no association was observed with recurrence/disease-free survival (RR: 0.99; 95% CI: 0.92–1.07; $I^2 = 49%$, $\tau^2 = 0.008$, RR range = 0.58–2.29).

There was no evidence of publication bias with Egger's test (p -value = .93 for all-cause mortality, 0.67 for colorectal cancer-specific mortality and 0.72 for recurrence/disease-free survival) (Supplementary Figures 10–12).

For second primary cancer, non-colorectal cancer mortality and cardiovascular disease death, studies were limited in number, thus could not be summarised in any meta-analysis. An overview of the findings is provided in Supplementary Material—Text S2.

3.4 | Subgroup non-linear meta-analysis

The results from the subgroup non-linear dose–response meta-analyses resembled those of the main analysis, with few exceptions (Supplementary Figures 13–46).

For all-cause mortality, there were differences when the analysis was stratified by cancer stage, sex, and study design. In the non-linear dose–response meta-analysis by cancer stage, the reverse J-shaped curve remained among any stage (excluding metastatic) colorectal cancer survivors ($P_{\text{non-linearity}} < .001$; 41 studies, 20 publications). However, a non-linear inverse association was observed in metastatic colorectal cancer survivors. A gradual reduction in risk was observed from the lowest levels of BMI up to 28 kg/m², that reached a plateau above this point ($P_{\text{non-linearity}} = .004$; 6 studies, 6 publications) (Supplementary Figure 14). In the non-linear dose–response meta-analysis by sex, the shape of the curve appeared reversed J-shaped in men ($P_{\text{non-linearity}} < .001$; 5 studies, 5 publications) and U-shaped in women ($P_{\text{non-linearity}} < .001$; 6 studies, 6 publications), reflecting a stronger positive association with low BMI among studies that included only men compared to women, with very little overlap in CIs between the two strata (Supplementary Figure 15). In the non-linear dose–response meta-analysis by study design (retrospective cohort, prospective cohort, or secondary analysis of clinical trials [i.e., observational follow-up analyses of patients enrolled in clinical treatment RCTs not aiming to evaluate body composition or weight management interventions]), the shape of the curve across strata was similar to the main analysis, but the increased risk of all-cause mortality in the low BMI range was attenuated for the secondary analysis of clinical trials (Supplementary Figure 17).

For colorectal cancer recurrence/disease-free survival, there were differences by the average length of follow-up, with little overlap of

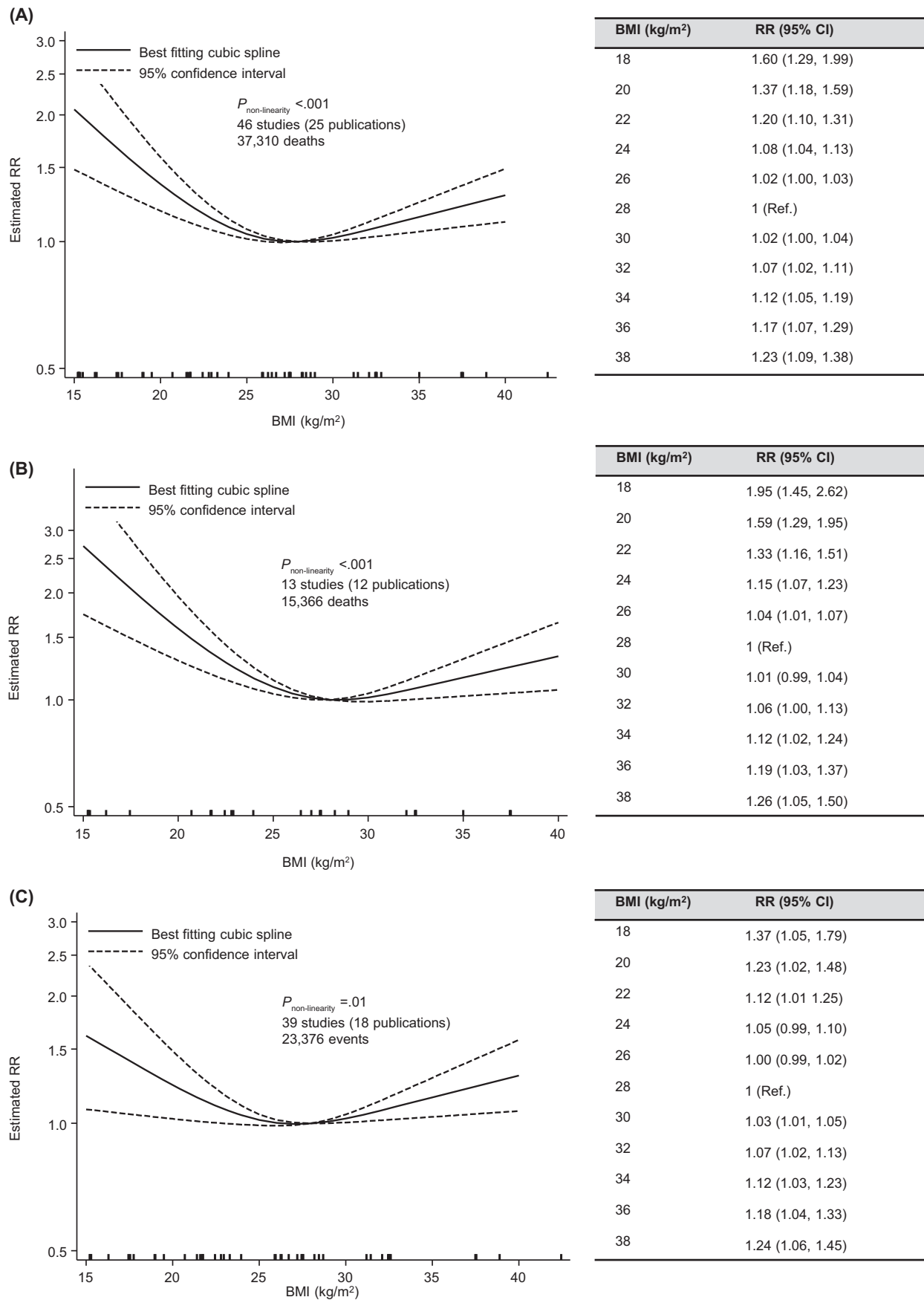


FIGURE 2 Legend on next page.

CI between the two strata (i.e., ≤ 5 years and >5 to ≤ 10 years) at low BMI levels. In studies with more than 5–10 years of follow-up, the shape of the curve was flat (nadir observed at BMI of 25 kg/m^2), with little evidence of a higher risk of recurrence/disease-free survival below and above the nadir ($P_{\text{non-linearity}} < .001$; 28 studies, 8 publications). However, among studies with an average length of follow-up of 5 or less years, the shape of the curve appeared J-shaped with the nadir at BMI of 25 kg/m^2 . The risk increased gradually from a BMI lower than 25 kg/m^2 , while above this point a sharply higher risk was observed but with very wide CIs ($P_{\text{non-linearity}} = .06$; 10 studies, 9 publications) (Supplementary Figure 40).

3.5 | Sensitivity analyses

In the non-linear analysis, the reverse J-shaped curve remained in the sensitivity analysis excluding (when possible) cancer survivors with metastatic stages (Supplementary Figures 47–49). Restricting the non-linear analysis to studies without including deaths in the recurrence definition, showed a suggestive J-shaped association between post-diagnosis BMI and cancer recurrence (nadir at a BMI around 25 kg/m^2). Compared to the nadir, a higher risk was observed from BMI below 25 kg/m^2 , and a higher risk of cancer recurrence was also observed above this point, but CIs were wide ($P_{\text{non-linearity}} = .06$; 34 studies, 13 publications) (Supplementary Figure 50). In categorical meta-analyses restricted to the studies that used the WHO classification system, results were similar (Supplementary Figures 51–59).

3.6 | Post-diagnosis body weight and BMI change and colorectal cancer outcomes

Post-diagnosis body weight and BMI change were evaluated for the timeframes (1) from before to 3 months or more after diagnosis (pre- to post-diagnosis; three and two publications, respectively); (2) from diagnosis or after diagnosis to any period post-diagnosis (post-diagnosis; two and one publications, respectively); and (3) specifically during/after cancer treatment (six and five publications, respectively). Meta-analyses were not possible because absolute or relative weight change categories across the studies were not homogeneous to pool them. These exposures were descriptively synthesised separately (Supplementary Tables 7–12).

Overall, pre- to post-diagnosis (Figure 3A) and post-diagnosis body weight loss (unknown causes) (Figure 3B) was associated with a higher risk of all-cause and colorectal cancer-specific mortality. There

was a suggestion that weight loss during/after cancer treatment (Figure 3C) was associated with a higher risk of all-cause mortality (only one out of nine comparisons showing a RR < 1) and recurrence/disease-free survival (only one out of eight comparisons showing a RR < 1). In general, there was no association between weight gain and colorectal cancer outcomes (Figure 3). Some studies ($n = 4$; three publications) were not directly comparable with the others and were excluded from the forest plot. The results of those studies are reported in Supplementary Material—Text S3.

The few studies investigating BMI change suggested a positive association between pre- to post-diagnosis and post-diagnosis BMI loss, but not gain, and all-cause and colorectal cancer-specific mortality (Supplementary Tables 10 and 11). There was a suggestion that BMI change (loss and gain) during/after cancer treatment was associated with a higher risk of all-cause mortality and disease-free survival/disease progression but, in general, wide CIs were observed across the different associations investigated (Supplementary Table 12).

3.7 | Post-diagnosis waist circumference and colorectal cancer outcomes

Only one retrospective study was identified, showing a lower risk of disease-free survival (hazard ratio, HR = 0.39; 95% CI = 0.21–0.75) in Dukes A–D colon cancer survivors with high waist circumference (≥ 94 cm in men and ≥ 80 cm in women) compared to those with a low waist circumference (< 94 cm in men and < 80 cm in women).³¹¹

3.8 | Risk of bias assessment

About 52%, 43%, and 60% of the studies on all-cause mortality, colorectal cancer-specific mortality and recurrence/disease-free survival, respectively, were rated as having a moderate risk of bias due to confounding (which is the best judgement they can reach in this domain), and 40%, 43% and 36%, respectively, as having critical risk of bias due to the lack of adjustment for the critically important confounding factors (i.e., age, stage and cancer treatment). Most studies ($\sim 80\%$) had serious risk of bias in participant selection related to the need for survival and a health status well enough to participate in a study. None of the included studies employed adjustment techniques to counteract the potential for selection bias. The percentage of studies with low/moderate risk of bias in classification of exposures was 54% in all-cause mortality, 72% in colorectal cancer-specific mortality, and 64% in recurrence/disease-free

FIGURE 2 Non-linear dose–response meta-analysis of post-diagnosis BMI and (A) all-cause mortality, (B) colorectal cancer-specific mortality, and (C) recurrence/disease-free survival in colorectal cancer survivors regardless of the stage. The solid line represents the estimated summary dose–response relationship and the short-dashed line the 95% confidence intervals. The tick marks inside the x-axis indicate the BMI values for which relative risk estimate(s) were available. Non-linear curve was estimated using restricted cubic spline regressions with three knots placed at fixed percentiles (10%, 50%, and 90%) of the body mass index distribution, which were pooled by fitting one-stage random-effects mixed models. The nadir of the dose–response curve (body mass index = 28 kg/m^2) was chosen as reference. The table shows selected body mass index values and their corresponding relative risk (95% confidence intervals) estimated in the non-linear dose–response meta-analysis.

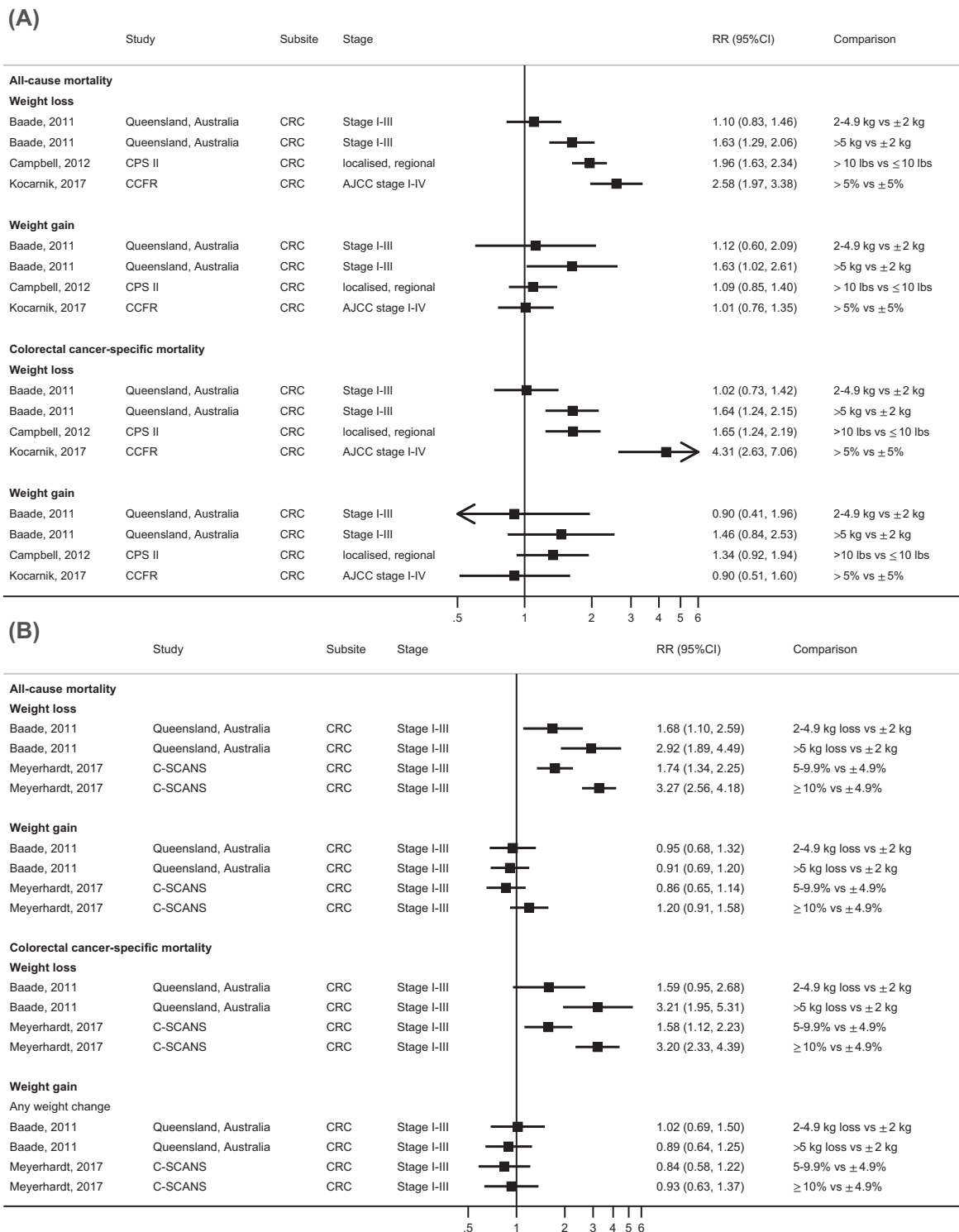


FIGURE 3 Forest plot showing the relative risk with 95% confidence interval for colorectal cancer outcomes by categorical comparison of (A) pre- to post-diagnosis weight change, (B) post-diagnosis (any period) weight change, and (C) during/right after treatment weight change. Individual studies reporting results for any weight change (% , kg, or lbs) categories are presented in the upper (weight loss) and lower (weight gain) panels of the graph by colorectal cancer outcomes. The same study may be represented more than once if different weight change categories were investigated. The squares represent the relative risk estimate (RR) for the different weight change categories and the horizontal line across each square represents the 95% confidence interval (CI) of the RR estimate. This figure does not represent a quantitative summation of results. Best, 2021³⁰¹ reported results at 3, 6 and 12 months. The forest plot only show results for at 12 months. Lee, 2020²⁷⁵ reported results for absolute and relative weight change. Only results for relative change were plotted. AJCC, American Joint Committee on Cancer; CALGB, BC, British Columbia; Cancer and Leukemia Group B; CCFR, Colon Cancer Family Registry; COL, colon; CPS-II, Cancer Prevention Study II Nutrition Cohort; CRC, colorectal cancer; C-SCANS, Colorectal Cancer-Sarcopenia And Near-term Survival study; MGH, Massachusetts General Hospital; UICC, Union for International Cancer Control.

(C)

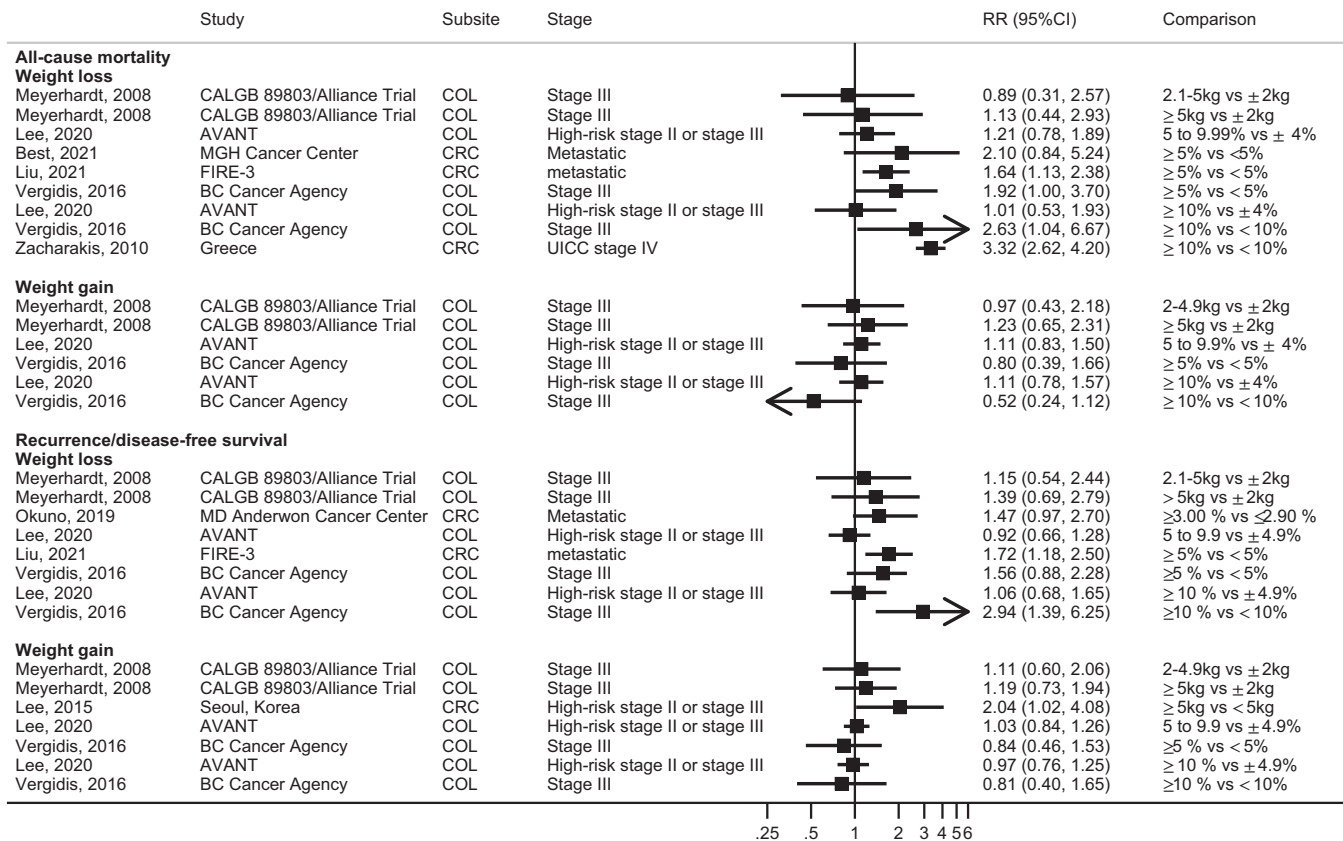


FIGURE 3 (Continued)

survival meta-analyses, with 44%, 29%, and 36%, respectively, rated with serious risk of bias, often due to the inclusion of a mixture of metastatic and non-metastatic colorectal cancer survivors (exposure may be influenced by undetected disease progression or recurrence). All the studies were rated as having a critical risk of bias due to departures from intended exposures, as time-varying exposure analysis was not performed. Approximately half of the studies (40%–56%) did not provide sufficient information to judge the risk of bias due to missing data. Most of the studies had low/moderate risk of bias in the measurement of the outcomes and selection of reported results (Supplementary Figures 60–65).

3.9 | Evidence grading

Table 1 presents the evidence grading. The evidence on post-diagnosis BMI and all-cause mortality, colorectal cancer-specific mortality, and colorectal cancer recurrence/disease-free survival was substantial, showing a reverse J-shaped relationship. However, due to high concerns of reverse causation, selection bias, confounding and errors in measuring and classifying the exposure, pertaining to studies of cancer survival, the evidence was graded as limited (subgrade for likelihood of causality: no conclusion).

The evidence on post-diagnosis BMI and second primary cancer, non-related colorectal cancer mortality and cardiovascular disease death was graded as limited-no conclusion due to the sparsity of studies and the same methodological issues mentioned previously.

The evidence on post-diagnosis waist circumference, body weight and BMI change was scarce and subject to the same aforementioned biases, and no conclusions could be made.

4 | DISCUSSION

This systematic review and meta-analysis showed evidence of non-linearity between post-diagnosis BMI and colorectal cancer outcomes (all-cause mortality, colorectal cancer-specific mortality, and cancer recurrence/disease-free survival). The associations appeared reverse J-shaped with a common nadir at BMI of 28 kg/m². A higher risk of poor colorectal cancer outcomes, relative to the nadir, was observed at the extremes of the BMI distributions. In most subgroups, the non-linear association was consistent. However, there was an indication that all-cause mortality differed according to study design. We observed weaker positive associations for low BMI (up to ~28 kg/m²) in secondary analysis of clinical trials compared with prospective cohorts and retrospective cohorts of cancer survivors. Similar

TABLE 1 Evidence grading and main findings from the meta-analyses and descriptive synthesis on post-diagnosis adiposity measures and colorectal cancer outcomes.

	Exposure	Outcome	Summary of findings	Conclusions
Strong evidence	Convincing	-	-	-
	Probable	-	-	-
Limited evidence	Suggestive	-	-	-
	No conclusion	Post-diagnosis BMI	<p>46 studies (25 publications), 37,310 deaths. Reverse J-shaped association with nadir at BMI of 28 kg/m² and higher risk at both ends of the BMI distributions (8%–60% for 18–24 kg/m² and 7%–23% for 32–38 kg/m², compared with 28 kg/m²)</p> <p>13 studies (12 publications), 15,366 deaths. Reverse J-shaped curve with nadir at BMI of 28 kg/m² and higher risk at both ends of the BMI distributions (15%–95% for 18–24 kg/m² and 6%–26% for 32–38 kg/m², compared with 28 kg/m²)</p> <p>39 studies (18 publications), 23,376 events. Reverse J-shaped curve with nadir at BMI of 28 kg/m² and higher risk at both ends of the BMI distributions (5%–37% for 18–24 kg/m² and 7%–24% for 32–38 kg/m², compared with 28 kg/m²)</p> <p>3 studies (2 publications). No meta-analysis.</p>	<p>Substantial amount of observational data, showing evidence of a non-linear relationship, limited in methodological quality (confounding, selection bias, reverse causation, measurement error and classification of exposures).</p> <p>The evidence is sparse and subject to potential methodological issues.</p>
Pre- to post-diagnosis weight change (gain or loss)	Pre- to post-diagnosis weight change (gain or loss)	Non-colorectal cancer related mortality	2 studies (1 publication). No meta-analysis.	The evidence is sparse and subject to potential methodological issues.
		Second primary cancer	1 study (1 publication). No meta-analysis.	
All-cause mortality	All-cause mortality	CVD mortality	3 studies (3 publications). No meta-analysis. Consistent pattern of positive associations with weight loss. RRs ranging from 1.10 to 2.58. In 3/4 categorical comparisons the 95% CIs did not include the null.	The evidence is sparse and subject to potential methodological issues.
		Colorectal cancer-specific mortality	3 studies (3 publications). No meta-analysis. Consistent pattern of positive associations with weight loss. RRs ranging from 1.02 to 4.31. In 3/4 categorical comparisons the 95% CIs did not include the null.	
CVD mortality	All-cause mortality	Colorectal cancer-specific mortality	No association with weight gain.	
		All-cause mortality	1 study (1 publication). No meta-analysis. 2 studies. No meta-analysis.	

TABLE 1 (Continued)

Exposure	Outcome	Summary of findings	Conclusions
Post-diagnosis (any period) weight change (gain or loss)		Consistent pattern of positive associations with weight loss. RRs ranging from 1.74 to 3.27 (none of the 95% CIs included the null). No association with weight gain.	
	Colorectal cancer-specific mortality	2 studies. No meta-analysis. Consistent pattern of positive associations with weight loss. RRs ranging from 1.58 to 3.21. In 3/4 categorical comparisons the 95% CIs did not include the null.	
	All-cause mortality	No association with weight gain. 6 studies (6 publications). No meta-analysis. Consistent pattern of positive associations with weight loss (only one categorical comparison with RR <1). In the 8 categorical comparisons showing positive associations, the RRs ranged from 1.01 to 3.32, in 4 of which the 95% CIs did not include the null.	
During/after cancer treatment weight change (gain or loss)		No association with weight gain.	
	Recurrence/disease-free survival	5 studies (5 publications). No meta-analysis. Consistent pattern of positive associations with weight loss (only one categorical comparison with RR <1). In the 7 categorical comparisons showing positive associations, the RRs ranged from 1.06 to 2.94, in 2 of which the 95% CIs did not include the null.	
	All-cause mortality	No association with weight gain.	The evidence is sparse and subject to potential methodological issues
Pre- to post-diagnosis BMI change (gain or loss)		2 studies (2 publications). No meta-analysis. In general, positive associations with BMI loss but not gain.	
	Colorectal cancer-specific mortality	1 study (1 publication). 13% higher risk per each 1 kg/m ² BMI loss (RR: 1.13; 95% CI: 1.06–1.20)	
	All-cause mortality	1 study (1 publication). RR and 95% CI of 1.50 (1.10–2.10) and 1.90 (1.30–2.80) for BMI loss 5%–10% and >10% vs. <5%, respectively.	
During/after cancer treatment weight change (gain or loss)		4 studies (4 publications). No meta-analysis. Suggestive pattern of positive associations with BMI loss and gain but, in general, wide CIs across the different associations investigated.	

(Continues)

TABLE 1 (Continued)

Exposure	Outcome	Summary of findings	Conclusions
Post-diagnosis waist circumference	Recurrence/disease-free survival	3 studies (3 publications). No meta-analysis. Suggestive pattern of positive associations with BMI loss and gain but, in general, wide CIs across the different associations investigated.	The evidence is sparse and subject to potential methodological issues
Post-diagnosis waist circumference	Recurrence/disease-free survival	1 study (1 publication). RR and 95% CI of 0.39 (0.21–0.75) for those with high waist circumference compared to those with a low waist circumference.	

Abbreviations: BMI, body mass index; CIs, confidence intervals; CVD, cardiovascular disease; RR, relative risk.

associations were also observed for recurrence/disease-free survival but the CIs were wide. The association between BMI and all-cause mortality appeared U-shaped in women and reverse J-shaped in men, showing a stronger positive association with low BMI in men than in women. Moreover, an inverse non-linear association between BMI and all-cause mortality was observed in metastatic colorectal cancer survivors, with a reduction in risk observed from the lowest BMI levels up to a BMI of 28 kg/m², but a flat line above this point. Besides, the higher risk of all-cause mortality and recurrence/disease-free survival with low BMI, relative to the nadir, was attenuated among studies with longer duration of follow-up. This observation was more evident for recurrence/disease-free survival, where there was little overlap of CIs between the strata at low BMI levels, while wide CIs were observed for all-cause mortality.

In the present non-linear meta-analysis on post-diagnosis BMI, colorectal cancer survivors with obesity had a higher risk of mortality and recurrence. The underlying biological mechanisms for these observations are poorly defined and might be related to factors that are also associated with colorectal cancer incidence, including obesity-related insulin resistance³¹² and inflammation.³¹³ High insulin levels and consequent alterations in the insulin-like growth factor axis,³¹⁴ leading to activation of several oncogenic pathways that favour tumour growth,³¹⁵ have been proposed as one putative explanation. However, while there is substantial evidence to support this hypothesis in colorectal cancer incidence, the evidence on this potential mechanism is limited and inconsistent in relation to survival and recurrence.^{316–318} The effects of systemic inflammation on colorectal cancer progression are extensive, including the promotion of proliferation, angiogenesis and metastasis, and the suppression of anti-tumour immunity.³¹⁹ In fact, inflammatory parameters such as high neutrophil-lymphocyte ratio^{320,321} and platelet-lymphocyte ratio³²² have been associated with poor clinical outcomes in colorectal cancer survivors. In addition, patients with obesity may also be more likely to have poorer outcomes due to possible suboptimal chemotherapy dosing³²³ or increased frequency of complications.^{64,324}

Non-linear meta-analysis also showed higher mortality and recurrence rates on the left side of the curve (up to BMI 24 kg/m²), especially at the lower end of the BMI range (18 kg/m²). This increased risk could be the result of other comorbidities, such as chronic respiratory conditions,³²⁵ or disease severity rather than BMI itself. Colorectal cancer survivors with more aggressive cancer or advanced stage may experience illness-related weight loss that results in low/normal BMI categories at diagnosis.³²⁶ In addition, cancer treatment may contribute to changes in body composition through its adverse effects on lean muscle mass.³²⁷ Therefore, the higher risk of mortality and recurrence observed in underweight or normal-weight colorectal cancer survivors could be due to the cachexia present in these patients. The depletion of skeletal muscle and elevated coagulation state caused by cancer-associated cachexia may contribute to a worse prognosis and death rate.^{328,329}

To explore the potential impact of reverse causality, we performed a sensitivity analysis excluding (where possible) studies of metastatic survivors. The results remained similar possibly because

most studies included colorectal cancer survivors of any stage and most, with few exceptions, did not provide results by stage. Nonetheless, a gradual reduction in all-cause mortality risk was observed from the lowest levels of BMI up to 28 kg/m², that reached a plateau above this point in the subgroup of only metastatic colorectal cancer survivors. These data suggest that unfavourable disease characteristics, such as tumour biology and poor response to treatment, and cancer-related cachexia resulting in low BMI may have a more negative impact on survival than the potential adverse effects related to high BMI.³³⁰ Moreover, in the recurrence/disease-free survival and all-cause mortality meta-analyses, there was a suggestion of heterogeneity by average length of follow-up. Increasing follow-up duration results in an increase in the number of deaths and a decrease in the proportion of deaths occurring early in follow-up (when sicker cachectic survivors would most likely have died). The higher risk of mortality and recurrence for low BMI, relative to the nadir, was attenuated among studies with more than 5–10 years of follow-up, compared to the studies with 5 or less years. These results suggest that the worse survival and cancer outcomes observed in the low/normal BMI categories is at least partially due to reverse causation.

The association between low BMI and mortality and recurrence might also be confounded by smoking,^{331,332} which increases mortality risk and is typically inversely associated with BMI.³³³ Moreover, our results showed a stronger association for low BMI in men than in women, which may be due to greater residual confounding by smoking in men. However, we could not explore the potential influence of smoking in our dose–response meta-analyses, since a limited number of included studies adjusted for smoking. The only study that reported results stratified by smoking status¹⁰ demonstrated an inverse association between overweight, compared to normal weight, and all-cause mortality for ever smokers, but not in never smokers.

We observed the lowest risk of mortality and recurrence among overweight colorectal cancer survivors (BMI 28 kg/m²). Some plausible biological mechanisms have been proposed. For example, higher BMI has been associated with better tolerance to some anticancer therapies and with higher energy reserves to support the body during the stress of cancer treatment.⁴³ However, the observed associations in the overall analyses are likely to be due to methodological issues in observational studies of BMI and cancer survival and are not necessarily causal. These include collider bias (a type of selection bias), confounding and reverse causality,^{43,326,334} which could explain not only the increased risk of poor outcomes at low/normal BMI levels but also why being overweight appears to be protective. Moreover, BMI is not a perfect measure of adiposity since it does not differentiate between muscle and fat mass.³³⁵ Despite having the same BMI, individuals can have different adipose tissue distributions and metabolic profiles. In fact, an analysis of the Colorectal Cancer-Sarcopenia And Near-term Survival study (C-SCANS) study showed that a large percentage of survivors with a BMI 18–25 kg/m² were at higher risk of mortality due to low muscle mass. However, those with a BMI between 25 and 30 kg/m² had the lowest risk of mortality and presented adequate muscle mass and low or modest adiposity mass.³³⁶ To better

understand the association of adiposity and prognosis in colorectal cancer survivors, more precise and direct measures of body composition, including fat free mass, are needed.

Despite the substantial body of evidence, considering all the aforementioned potential methodological limitations of the observational studies included in the present work, the CUP Global independent Expert Panel agreed to cautiously grade the evidence as limited (sub-grade for likelihood of causality: no conclusion) for post-diagnosis BMI and colorectal cancer outcomes. The CUP Global Expert Panel recognised that the limitations of the evidence represent an opportunity for further research to clarify the nature of the consistent associations between measures of adiposity and cancer related outcomes. Furthermore, the panel recognised a need to better inform cancer patients about the links between adiposity and cancer survivorship, beyond making firm recommendations based on high quality evidence.

Meta-analysis was not possible for body weight and BMI change. The descriptive synthesis showed a suggestion of a positive pattern between weight loss, but not weight gain, and colorectal cancer outcomes. One of the main limitations of the included studies is the lack of information on the intentionality of weight loss, which could be secondary to cancer treatment or progressive disease. In non-cancer studies, unintentional weight loss has been associated with higher mortality, while intentional weight loss has not.^{337,338} Interventional clinical trials could offer better insights into the potential consequences of intentional weight loss. Unfortunately, to date no trials on colorectal cancer survivors have directly looked at the impact of weight loss on mortality and recurrence. Additionally, with regards to weight gain, studies did not specify whether it was after unintentional weight loss (recovery), due to side effects of cancer treatment, or other reasons.

Several limitations in relation to the evidence should be considered when interpreting the results of the present systematic review and meta-analysis. All included studies were observational in nature, thus susceptible to different biases, such as survival bias, measurement error, residual confounding, and reverse causation. In general, in the included studies, BMI was only assessed at one point in time; few examined the associations together with pre-diagnosis weight status, and time-varying analysis, which might better reflect the cumulative effect of adiposity on cancer survival, was not performed. Similarly, confounding factors (e.g., treatment dose and duration, disease severity, smoking behaviour) most likely also change over time and this was not considered. We could not perform subgroup analysis by BMI assessment timeframe relative to cancer diagnosis because most studies assessed BMI at diagnosis or shortly after, and very few included assessments later in the cancer course.^{10,30,41,42} Colorectal cancer survivors are likely to experience weight fluctuations during and/or after cancer treatment because of the disease and/or its treatment. Hence, BMI could have a different influence on survival and recurrence depending on the timing of the assessment. The limited number of studies included in certain subgroups resulted in very wide confidence intervals, which may have limited the power to detect differences between strata. It was also not possible to evaluate the potential variability in the strength and direction of the associations

by race or ethnicity and molecular cancer subtypes because the included studies did not provide sufficient data. Furthermore, despite the worse long-term outcomes being reported for emergency compared with elective presentations of colorectal cancer,³³⁹ the included studies lacked data on the impact of presentation mode on adiposity measurements and oncological outcomes. In addition, although BMI is widely used as a measure of obesity, it does not distinguish between body fat and lean body mass and does not capture adiposity distribution.³³⁵ Unfortunately, we identified only one study on post-diagnosis waist circumference³¹¹ and none on post-diagnosis waist-to-hip ratio. Moreover, our search strategy was not specific enough for identifying other body composition measures that might be more accurate in assessing adiposity than BMI, weight, waist circumference, waist-to-hip ratio or their changes. Finally, the literature search ended on 28 February 2022. Thereby, any relevant studies published after this date were not included. However, given that RCTs are considered the most influential studies in our evidence grading criteria, we conducted a literature search focusing on RCTs that were published after this date until 31 August 2023, but we did not identify any related to body composition or weight management among colorectal cancer survivors. In addition, because of the already large number of studies included in the meta-analysis, any further observational studies would most likely have little or modest influence on the results of the main analyses. As such, we anticipate that the conclusions on the present evidence would remain unchanged.

Despite limitations, this is the most comprehensive systematic review and dose–response meta-analysis on post-diagnosis adiposity and colorectal cancer outcomes conducted to date. Using standardised criteria and a rigorous approach, the substantial body of evidence (124 studies and over 294,000 colorectal cancer survivors) was systematically synthesised and interpreted and graded by the CUP Global independent Expert Committee on Cancer Survivorship and Expert Panel following pre-defined standardised grading criteria.

5 | CONCLUSION

In conclusion, the present work suggests a reverse J-shaped association between post-diagnosis BMI and all-cause mortality, colorectal cancer-specific mortality, and recurrence, with higher risks for these outcomes at both ends of the BMI distribution (18–24 and 32–38 kg/m²). However, despite the substantial body of evidence, the associations were graded as ‘limited-no conclusion’ for the likelihood of causality owing to methodological limitations of individual studies in this field. For changes in post-diagnosis weight and BMI, the evidence was also ‘limited-no conclusion’ due to the limited number of studies and same methodological issues. Well-designed observational studies with more accurate measures of adiposity, longer follow-up, repeated measures, detailed information on participant’s medical and lifestyle factors, and stratified analysis (e.g., by cancer stage, smoking status [including amount and duration], ethnicity and molecular subtypes), as well as high-quality trials are needed to strengthen the evidence that contributes towards the development of specific lifestyle

recommendations for colorectal cancer survivors. Nevertheless, even in the absence of such trials, there is a need to better inform cancer patients about the links between obesity and cancer-related, and other, outcomes.

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. Nerea Becerra-Tomás did the study selections, data extraction, and checked, analysed, and interpreted the data. 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 ICL. Laure Dossus was a CUP Global collaborator on biological processes and provided input into the biological mechanism citations in the manuscript. 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 on Cancer Survivorship. John Krebs, Matty P. Weijenberg, Monica 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 M. 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 (LH) did not contribute to the final decisions made by the Panel. Nerea Becerra-Tomás drafted the original manuscript. 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

¹Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK

²Department of Hygiene and Epidemiology, University of Ioannina Medical School, Ioannina, Greece

³Department of Nutrition, Oslo New University College, Oslo, Norway

⁴Department of Research, The Cancer Registry of Norway, Oslo, Norway

⁵Leeds Institute for Data Analytics, Faculty of Medicine and Health, University of Leeds, Leeds, UK

⁶Nutrition and Metabolism Branch, International Agency for Research on Cancer, World Health Organization, Lyon, France

⁷Cancer Sciences Academic Unit, Faculty of Medicine, University of Southampton, Southampton, UK

⁸The 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

⁹Department of Epidemiology, GROW School for Oncology and Reproduction, Maastricht University, Maastricht, The Netherlands

¹⁰O'Neal Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, Alabama, USA

¹¹Department of Oncology, St Jude Children's Research Hospital, Memphis, Tennessee, USA

¹²Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

¹³Mayo Clinic Comprehensive Cancer Center, Jacksonville, Florida, USA

¹⁴Department 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

¹⁵Division of Physical Activity, Prevention and Cancer, German Cancer Research Center (DKFZ) and National Center for Tumor Diseases (NCT), Heidelberg, Germany

¹⁶Danish Cancer Society Research Center, Diet, Cancer and Health, Copenhagen, Denmark

¹⁷Department of Public Health, University of Copenhagen, Copenhagen, Denmark

¹⁸School of Medicine, Faculty of Medicine and Health, University of Leeds, Leeds, UK

¹⁹UPMC Hillman Cancer Center, Pittsburgh, Pennsylvania, USA

²⁰Department of Global Health, Robert Stempel College of Public Health and Social Work, Florida International University, Miami, Florida, USA

²¹World Cancer Research Fund International, London, UK

²²Department of Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK

²³Department of Health Sciences, Faculty of Science, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

²⁴Department of Biology, University of Oxford, Oxford, UK

ACKNOWLEDGEMENTS

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 protocol. We thank the WCRF International CUP Global ICL team members: Leila Abar, Neesha Nanu, Jakub Sobiecki, Britta Talumaa, and Victoria White, for their contribution to the literature search, study selection, and/or data extraction; and database managers: Rui Vieira, Christophe Stevens, Yusuf O. Anifowoshe, and Lam Teng for implementing and updating

the CUP Global database. We also acknowledge the input from the CUP Global Secretariat members: Helen Croker, Panagiota Mitrou, Martin Wiseman, Kate Allen, Nigel T Brockton, Vanessa Gordon-Dseagu (and previous CUP Global Secretariat member Nicole Musuwo), for providing overall coordination for the work and for convening and facilitating discussions with the CUP Global Expert Committee and Expert Panel. We acknowledge the contribution of the Protocol Expert Group (PEG) (Annie Anderson, Steven Clinton, John Mathers, Anne McTiernan, Lesley Turner, and Fränzel van Duijnhoven) and the Outcomes After a Cancer Diagnosis (OACD) CUP Transition workstream (Anne McTiernan, Steven Clinton, Viv Lund) to the development of the original protocol for this work.

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 [WKOF]) (CUP Global Special Grant 2018). The funders of this study had no role in the decisions about the design and conduct of the study; collection, management, analysis, or interpretation of the data; or the preparation, review, or approval of the manuscript. The process used was based on the method developed by WCRF International's Methodology Task Force for the WCRF/AICR Second Expert Report. The views expressed in this review are the opinions of the authors. They may differ from those in future updates of the evidence related to food, nutrition, physical activity, and cancer incidence and survival.

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. Further details are available from the corresponding author upon request.

ORCID

Georgios Markozannes  <https://orcid.org/0000-0001-8481-579X>

Dagfinn Aune  <https://orcid.org/0000-0002-4533-1722>

Wendy Demark-Wahnefried  <https://orcid.org/0000-0001-5241-932X>

Konstantinos K. Tsilidis  <https://orcid.org/0000-0002-8452-8472>

Doris S. M. Chan  <https://orcid.org/0000-0002-0198-1897>

REFERENCES

1. Morgan E, Arnold M, Gini A, et al. Global burden of colorectal cancer in 2020 and 2040: incidence and mortality estimates from GLOBOCAN. *Gut*. 2023;72:338-344.
2. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *Ca-Cancer J Clin*. 2021;71: 209-249.

3. Xi Y, Xu PF. Global colorectal cancer burden in 2020 and projections to 2040. *Transl Oncol.* 2021;14:101174.
4. Jiang YF, Yuan HY, Li ZY, et al. Global pattern and trends of colorectal cancer survival: a systematic review of population-based registration data. *Cancer Biol Med.* 2022;19:175-186.
5. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin.* 2015;65:87-108.
6. Vijayvergia N, Denlinger CS. Lifestyle factors in cancer survivorship: where we are and where we are headed. *J Pers Med.* 2015;5:243-263.
7. Ezzati M, Bentham J, Di Cesare M, et al. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet.* 2017;390:2627-2642.
8. World Cancer Research Fund/American Institute for Cancer Research. *Diet, Nutrition, Physical Activity and Cancer: A Global Perspective.* Continuous Update Project Expert Report; 2018. Accessed December 2022. <http://dietandcancerreport.org>
9. Wu SJ, Liu J, Wang XH, Li MJ, Gan Y, Tang YF. Association of obesity and overweight with overall survival in colorectal cancer patients: a meta-analysis of 29 studies. *Cancer Cause Control.* 2014;25:1489-1502.
10. Schlesinger S, Siegert S, Koch M, et al. Postdiagnosis body mass index and risk of mortality in colorectal cancer survivors: a prospective study and meta-analysis. *Cancer Causes Control.* 2014;25:1407-1418.
11. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. *PLoS One.* 2015;10(3):e0120706.
12. Li YD, Li CH, Wu GL, et al. The obesity paradox in patients with colorectal cancer: a systematic review and meta-analysis. *Nutr Rev.* 2022;80:1755-1768.
13. 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.
14. Chan DSM, Vieira R, Abar L, et al. Postdiagnosis body fatness, weight change and breast cancer prognosis: Global Cancer Update Programme (CUP global) systematic literature review and meta-analysis. *Int J Cancer.* 2023;152:572-599.
15. Global Cancer Update Programme (CUP Global). Accessed November 2022. <https://www.wcrf.org/diet-activity-and-cancer/global-cancer-update-programme/about-the-global-cancer-update-programme/>
16. Chan DSM, Cariolou M, Markozannes G, et al. Post-diagnosis dietary factors, supplement use and colorectal cancer prognosis: Global Cancer Update Programme (CUP Global) systematic literature review and meta-analysis. *Int J Cancer.* 2024;155(3):445-470.
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.
18. Tsilidis KK, Markozannes G, Becerra-Tomás N, et al. Post-diagnosis adiposity, physical activity, sedentary behaviour, dietary factors and colorectal cancer prognosis: Global Cancer Update Programme (CUP Global) summary of evidence grading. *Int J Cancer.* 2024;155(3):400-425.
19. 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.* Accessed November 17, 2022. <https://osf.io/r5ud2/registrations>
20. USDA Nutrition Evidence Systematic Review. Risk of Bias for Nutrition Observational Studies (RoB-NObs) Tool. Accessed November 2022. <https://nesr.usda.gov/sites/default/files/2019-07/RiskOfBiasForNutritionObservationalStudies-RoB-NObs.pdf>
21. Sterne JA, Hernan MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ.* 2016;355:i4919.
22. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials.* 1986;7:177-188.
23. Orsini N. Weighted mixed-effects dose-response models for tables of correlated contrasts. *Stata J.* 2021;21:320-347.
24. Bekkering GE, Harris RJ, Thomas S, et al. How much of the data published in observational studies of the association between diet and prostate or bladder cancer is usable for meta-analysis? *Am J Epidemiol.* 2008;167:1017-1026.
25. Aune D, Greenwood DC, Chan DS, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. *Ann Oncol.* 2012;23:843-852.
26. 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.
27. Orsini N, Bellocco R, Greenland S. Generalized least squares for trend estimation of summarized dose-response data. *Stata J.* 2006;6:40-57.
28. 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;27:954-970.
29. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser.* 2000;894:i-xii, 1-253.
30. Kroenke CH, Neugebauer R, Meyerhardt J, et al. Analysis of body mass index and mortality in patients with colorectal cancer using causal diagrams. *JAMA Oncol.* 2016;2:1137-1145.
31. Meyerhardt JA, Catalano PJ, Haller DG, et al. Influence of body mass index on outcomes and treatment-related toxicity in patients with colon carcinoma. *Cancer.* 2003;98:484-495.
32. Meyerhardt JA, Tepper JE, Niedzwiecki D, et al. Impact of body mass index on outcomes and treatment-related toxicity in patients with stage II and III rectal cancer: findings from intergroup trial 0114. *J Clin Oncol.* 2004;22:648-657.
33. Diefenhardt M, Ludmir EB, Hofheinz RD, et al. Impact of body-mass index on treatment and outcome in locally advanced rectal cancer: a secondary, post-hoc analysis of the CAO/ARO/AIO-04 randomized phase III trial. *Radiother Oncol.* 2021;164:223-231.
34. Guercio BJ, Zhang S, Venook AP, et al. *Body Mass Index and Weight Loss in Metastatic Colorectal Cancer in CALGB (Alliance)/SWOG 80405.* Vol 4. JNCI Cancer Spectr; 2020:pkaa024.
35. Kalb M, Langheinrich MC, Merkel S, et al. Influence of body mass index on long-term outcome in patients with rectal cancer—a single centre experience. *Cancers (Basel).* 2019;11:609.
36. Chiu CC, Ho CH, Hung CM, et al. Correlation of body mass index with oncologic outcomes in colorectal cancer patients: a large population-based study. *Cancers (Basel).* 2021;13:3592.
37. Dignam JJ, Polite BN, Yothers G, et al. Body mass index and outcomes in patients who receive adjuvant chemotherapy for colon cancer. *J Natl Cancer Inst.* 2006;98:1647-1654.
38. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med.* 2002;21:1539-1558.
39. 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.
40. Borenstein M, Higgins JP, Hedges LV, Rothstein HR. Basics of meta-analysis: I(2) is not an absolute measure of heterogeneity. *Res Synth Methods.* 2017;8:5-18.
41. Campbell PT, Newton CC, Dehal AN, Jacobs EJ, Patel AV, Gapstur SM. Impact of body mass index on survival after colorectal

- cancer diagnosis: the Cancer Prevention Study-II Nutrition Cohort. *J Clin Oncol*. 2012;30:42-52.
42. van Zutphen M, Boshuizen HC, Kenkhuis MF, et al. Lifestyle after colorectal cancer diagnosis in relation to recurrence and all-cause mortality. *Am J Clin Nutr*. 2021;113:1447-1457.
 43. Anderson AS, Martin RM, Renehan AG, et al. Cancer survivorship, excess body fatness and weight-loss intervention—where are we in 2020? *Br J Cancer*. 2021;124:1057-1065.
 44. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315:629-634.
 45. Abbass T, Tsz Ho YT, Horgan PG, Dolan RD, McMillan DC. The relationship between computed tomography derived skeletal muscle index, psoas muscle index and clinical outcomes in patients with operable colorectal cancer. *Clin Nutr ESPEN*. 2020;39:104-113.
 46. Abe S, Kawai K, Nozawa H, et al. Preoperative sarcopenia is a poor prognostic factor in lower rectal cancer patients undergoing neoadjuvant chemoradiotherapy: a retrospective study. *Int J Clin Oncol*. 2022;27:141-153.
 47. Abe S, Nozawa H, Kawai K, et al. Poor nutrition and sarcopenia are related to systemic inflammatory response in patients with rectal cancer undergoing preoperative chemoradiotherapy. *Int J Colorectal Dis*. 2022;37:189-200.
 48. Alexander D, Allardice GM, Moug SJ, Morrison DS. A retrospective cohort study of the influence of lifestyle factors on the survival of patients undergoing surgery for colorectal cancer. *Colorectal Dis*. 2017;19:544-550.
 49. Almasaudi AS, Dolan RD, Edwards CA, McMillan DC. Hypoalbuminemia reflects nutritional risk, body composition and systemic inflammation and is independently associated with survival in patients with colorectal cancer. *Cancers (Basel)*. 2020;12:1986.
 50. Almasaudi AS, McSorley ST, Dolan RD, Edwards CA, McMillan DC. The relation between Malnutrition Universal Screening Tool (MUST), computed tomography-derived body composition, systemic inflammation, and clinical outcomes in patients undergoing surgery for colorectal cancer. *Am J Clin Nutr*. 2019;110:1327-1334.
 51. Amptoulach S, Gross G, Kalaitzakis E. Differential impact of obesity and diabetes mellitus on survival after liver resection for colorectal cancer metastases. *J Surg Res*. 2015;199:378-385.
 52. Aparicio T, Ducreux M, Faroux R, et al. Overweight is associated to a better prognosis in metastatic colorectal cancer: a pooled analysis of FFCD trials. *Eur J Cancer*. 2018;98:1-9.
 53. Artac M, Korkmaz L, Coskun HS, et al. Bevacuzimab may be less effective in obese metastatic colorectal cancer patients. *J Gastrointest Cancer*. 2019;50:214-220.
 54. Asghari-Jafarabadi M, Hajizadeh E, Kazemnejad A, Fatemi SR. Site-specific evaluation of prognostic factors on survival in Iranian colorectal cancer patients: a competing risks survival analysis. *Asian Pac J Cancer Prev*. 2009;10:815-821.
 55. Atinafu BT, Bulti FA, Demelew TM. Survival status and predictors of mortality among colorectal cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: a retrospective followup study. *J Cancer Prev*. 2020;25:38-47.
 56. Aytac E, Lavery IC, Kalady MF, Kiran RP. Impact of obesity on operation performed, complications, and long-term outcomes in terms of restoration of intestinal continuity for patients with mid and low rectal cancer. *Dis Colon Rectum*. 2013;56:689-697.
 57. Azab B, Kedia S, Shah N, et al. The value of the pretreatment albumin/globulin ratio in predicting the long-term survival in colorectal cancer. *Int J Colorectal Dis*. 2013;28:1629-1636.
 58. Azizmohammad Loocha M, Zarean E, Maseabi F, Pourhoseingholi MA, Zali MR. Assessment of prognostic factors in long-term survival of male and female patients with colorectal cancer using non-mixture cure model based on the Weibull distribution. *Surg Oncol*. 2021;38:101562.
 59. Baghestani AR, Daneshvar T, Pourhoseingholi MA, Asadzade H. Survival of colorectal cancer patients in the presence of competing-risk. *Asian Pac J Cancer Prev*. 2014;15:6253-6255.
 60. Baird DLH, Simillis C, Pellino G, Kontovounisios C, Rasheed S, Tekkis PP. The obesity paradox in beyond total mesorectal excision surgery for locally advanced and recurrent rectal cancer. *Updates Surg*. 2019;71:313-321.
 61. Ballian N, Lubner MG, Munoz A, et al. Visceral obesity is associated with outcomes of total mesorectal excision for rectal adenocarcinoma. *J Surg Oncol*. 2012;105:365-370.
 62. Ballian N, Yamane B, Levenson G, et al. Body mass index does not affect postoperative morbidity and oncologic outcomes of total mesorectal excision for rectal adenocarcinoma. *Ann Surg Oncol*. 2010;17:1606-1613.
 63. Banaste N, Rousset P, Mercier F, et al. Preoperative nutritional risk assessment in patients undergoing cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy for colorectal carcinomatosis. *Int J Hyperthermia*. 2018;34:589-594.
 64. Bell S, Kong JC, Wale R, et al. The effect of increasing body mass index on laparoscopic surgery for colon and rectal cancer. *Colorectal Dis*. 2018;20:778-788.
 65. Biffi R, Botteri E, Bertani E, et al. Factors predicting worse prognosis in patients affected by pT3 N0 colon cancer: long-term results of a monocentric series of 137 radically resected patients in a 5-year period. *Int J Colorectal Dis*. 2013;28:207-215.
 66. Borumandnia N, Doosti H, Jalali A, et al. Nomogram to predict the overall survival of colorectal cancer patients: a multicenter national study. *Int J Environ Res Public Health*. 2021;18:7734.
 67. Caan BJ, Meyerhardt JA, Kroenke CH, et al. Explaining the obesity paradox: the association between body composition and colorectal cancer survival (C-SCANS study). *Cancer Epidemiol Biomarkers Prev*. 2017;26:1008-1015.
 68. Cao X, Zhao G, Yu T, An Q, Yang H, Xiao G. Preoperative prognostic nutritional index correlates with severe complications and poor survival in patients with colorectal cancer undergoing curative laparoscopic surgery: a retrospective study in a single Chinese institution. *Nutr Cancer*. 2017;69:454-463.
 69. Caycedo-Marulanda A, Lee L, Chadi SA, et al. Association of transanal total mesorectal excision with local recurrence of rectal cancer. *JAMA Netw Open*. 2021;4:e2036330.
 70. Cetin B, Kaplan MA, Berk V, et al. Prognostic factors for overall survival in patients with metastatic colorectal carcinoma treated with vascular endothelial growth factor-targeting agents. *Asian Pac J Cancer Prev*. 2012;13:1059-1063.
 71. Charette N, Vandeputte C, Ameys L, et al. Prognostic value of adipose tissue and muscle mass in advanced colorectal cancer: a post hoc analysis of two non-randomized phase II trials. *BMC Cancer*. 2019;19:134.
 72. Chen TC, Liang JT, Chang TC. Should surgical treatment be provided to patients with colorectal cancer who are aged 90 years or older? *J Gastrointest Surg*. 2018;22:1958-1967.
 73. Chen XQ, Wu PW, Liu DH, Yan SJ, Shen XM, Yang LY. Prognostic significance of high triglyceride and apolipoprotein B levels in patients with stage III and high-risk stage II colorectal cancer undergoing curative surgery. *Oncol Lett*. 2020;20:705-714.
 74. Cheng CC, Lai IL, Huang SH, et al. Association of preoperative physical activity with short- and long-term outcomes in patients undergoing palliative resection for metastatic colorectal cancer: an inverse probability of treatment weighting analysis. *Cancers (Basel)*. 2022;14:489.
 75. Cheng E, Ou FS, Ma C, et al. Diet- and lifestyle-based prediction models to estimate cancer recurrence and death in patients with stage III colon cancer (CALGB 89803/Alliance). *J Clin Oncol*. 2022;40:740-751.
 76. Chern H, Chou J, Donkor C, et al. Effects of obesity in rectal cancer surgery. *J Am Coll Surg*. 2010;211:55-60.

77. Choe EK, Park KJ, Ryoo SB, Moon SH, Oh HK, Han EC. Prognostic impact of changes in adipose tissue areas after colectomy in colorectal cancer patients. *J Korean Med Sci.* 2016;31:1571-1578.
78. Choi Y, Lee YH, Park SK, Cho H, Ahn KJ. Association between obesity and local control of advanced rectal cancer after combined surgery and radiotherapy. *Radiat Oncol J.* 2016;34:113-120.
79. Chu D, Zhang ZX, Li YM, et al. Prediction of colorectal cancer relapse and prognosis by tissue mRNA levels of NDRG2. *Mol Cancer Ther.* 2011;10:47-56.
80. Chung E, Lee HS, Cho ES, et al. Changes in body composition during adjuvant FOLFOX chemotherapy and overall survival in non-metastatic colon cancer. *Cancers (Basel).* 2019;12:60.
81. Chung JW, Chung MJ, Bang S, et al. Assessment of the risk of colorectal cancer survivors developing a second primary pancreatic cancer. *Gut Liver.* 2017;11:728-732.
82. Croft B, Reed M, Patrick C, Kovacevich N, Voutsadakis IA. Diabetes, obesity, and the metabolic syndrome as prognostic factors in stages I to III colorectal cancer patients. *J Gastrointest Cancer.* 2019;50:221-229.
83. Cunningham D, Pyrhönen S, James RD, et al. Randomised trial of irinotecan plus supportive care versus supportive care alone after fluorouracil failure for patients with metastatic colorectal cancer. *Lancet.* 1998;352:1413-1418.
84. Cybulska-Stopa B, Lugowska I, Wisniowski R, et al. Overweight is associated with better prognosis in metastatic colorectal cancer patients treated with bevacizumab plus FOLFOX chemotherapy. *Contemp Oncol (Pozn).* 2020;24:34-41.
85. da Silva DD, Machado M, Trabulo C, Gosálbez B, Ravasco P. Impact of body composition on prognosis and dose-limiting toxicities on metastatic colorectal cancer. *Front Nutr.* 2021;8:671547.
86. Daitoku N, Miyamoto Y, Tokunaga R, et al. Controlling nutritional status (CONUT) score is a prognostic marker in metastatic colorectal cancer patients receiving first-line chemotherapy. *Anticancer Res.* 2018;38:4883-4888.
87. De Robles MS, O'Neill RS, Mourad AP, Winn R, Putnis S, Kang S. Survival in stage IIB/C compared to stage IIIA rectal cancer: an Australian experience affirming that size does matter. *ANZ J Surg.* 2021;91:1866-1873.
88. Denost Q, Quintane L, Buscaill E, Martenot M, Laurent C, Rullier E. Short- and long-term impact of body mass index on laparoscopic rectal cancer surgery. *Colorectal Dis.* 2013;15:463-469.
89. Dolan DR, Knight KA, Maguire S, Moug SJ. The relationship between sarcopenia and survival at 1 year in patients having elective colorectal cancer surgery. *Tech Coloproctol.* 2019;23:877-885.
90. Dolan RD, Almasaudi AS, Dieu LB, Horgan PG, McSorley ST, McMillan DC. The relationship between computed tomography-derived body composition, systemic inflammatory response, and survival in patients undergoing surgery for colorectal cancer. *J Cachexia Sarcopenia Muscle.* 2019;10:111-122.
91. Dray X, Boutron-Ruault MC, Bertrais S, Sapinho D, Benhamiche-Bouvier AM, Faivre J. Influence of dietary factors on colorectal cancer survival. *Gut.* 2003;52:868-873.
92. Feng JF, Zhou XM, Mao WM. Prognostic analysis of colorectal cancer patients with diabetes mellitus in China—the experience of a single institution. *Adv Clin Exp Med.* 2011;20:473-480.
93. Ferroni P, Formica V, Della-Morte D, et al. Prognostic value of glycated hemoglobin in colorectal cancer. *World J Gastroenterol.* 2016;22:9984-9993.
94. Fong AJ, Lafaro K, Ituarte PHG, Fong Y. Association of living in urban food deserts with mortality from breast and colorectal cancer. *Ann Surg Oncol.* 2021;28:1311-1319.
95. Fournel L, Maria S, Seminel M, et al. Prognostic factors after pulmonary metastasectomy of colorectal cancers: a single-center experience. *J Thorac Dis.* 2017;9:S1259-S1266.
96. Frostberg E, Pedersen MR, Manhoobi Y, Rahr HB, Rafaelsen SR. Three different computed tomography obesity indices, two standard methods, and one novel measurement, and their association with outcomes after colorectal cancer surgery. *Acta Radiol.* 2021;62:182-189.
97. Gallois C, Artru P, Lièvre A, et al. Evaluation of two nutritional scores' association with systemic treatment toxicity and survival in metastatic colorectal cancer: an AGEO prospective multicentre study. *Eur J Cancer.* 2019;119:35-43.
98. Garcia-Martinez S, Gonzalez-Gamo D, Fernandez-Marcelo T, et al. Obesity and telomere status in the prognosis of patients with colorectal cancer submitted to curative intention surgical treatment. *Mol Clin Oncol.* 2021;15:184.
99. Greenlee H, Unger JM, LeBlanc M, Ramsey S, Hershman DL. Association between body mass index and cancer survival in a pooled analysis of 22 clinical trials. *Cancer Epidemiol Biomarkers Prev.* 2017;26:21-29.
100. Guiu B, Petit JM, Bonnetain F, et al. Visceral fat area is an independent predictive biomarker of outcome after first-line bevacizumab-based treatment in metastatic colorectal cancer. *Gut.* 2010;59:341-347.
101. Gupta D, Lammersfeld CA, Vashi PG, Burrows J, Lis CG, Grutsch JF. Prognostic significance of subjective global assessment (SGA) in advanced colorectal cancer. *Eur J Clin Nutr.* 2005;59:35-40.
102. Han JS, Ryu H, Park IJ, et al. Association of body composition with long-term survival in non-metastatic rectal cancer patients. *Cancer Res Treat.* 2020;52:563-572.
103. Hasegawa H, Matsuda T, Arimoto A, et al. Does anastomotic leakage after rectal cancer resection worsen long-term oncologic outcome? *Int J Colorectal Dis.* 2020;35:1243-1253.
104. Hashemian AH, Garshasbi M, Pourhoseingholi MA, Eskandari S. A comparative study of cox regression vs. log-logistic regression (with and without its frailty) in estimating survival time of patients with colorectal cancer. *J Med Biomed Sci.* 2017;6:35-43.
105. Hayama T, Ozawa T, Tsukamoto M, et al. Predicting overall survival using preoperative nutritional and inflammation status for colorectal cancer. *In Vivo.* 2022;36:450-457.
106. Healy LA, Ryan AM, Sutton E, et al. Impact of obesity on surgical and oncological outcomes in the management of colorectal cancer. *Int J Colorectal Dis.* 2010;25:1293-1299.
107. Heise D, Bayings W, Tuinhof A, et al. Long-term outcome and quality of life after initial and repeat resection of colorectal liver metastasis: a retrospective analysis. *Int J Surg.* 2017;48:281-285.
108. Hopirtean C, Ciuleanu T, Cainap C, Todor N, Nagy V. Body mass index AS a prognostic factor for disease progression in patients with metastatic colorectal cancer treated with bevacizumab based systemic therapy. *Acta Endocrinol (Buchar).* 2017;13:425-430.
109. Hopkins JJ, Reif RL, Bigam DL, Baracos VE, Eurich DT, Sawyer MB. The impact of muscle and adipose tissue on long-term survival in patients with stage I to III colorectal cancer. *Dis Colon Rectum.* 2019;62:549-560.
110. Horii N, Sawda Y, Kumamoto T, et al. Impact of intramuscular adipose tissue content on short- and long-term outcomes of hepatectomy for colorectal liver metastasis: a retrospective analysis. *World J Surg Oncol.* 2020;18:68.
111. Hosseini SV, Rezaianzadeh A, Rahimikazerooni S, Ghahramani L, Bananzadeh A. Prognostic factors affecting short- and long-term recurrence-free survival of patients with rectal cancer using cure models: a cohort study. *Iran J Med Sci.* 2020;45:333-340.
112. Huang CW, Sun LC, Shih YL, et al. The impact on clinical outcome of high prevalence of diabetes mellitus in Taiwanese patients with colorectal cancer. *World J Surg Oncol.* 2012;10:76.
113. Huang H, Zhang L, Chen DB, et al. Validation of prognosis value of cumulative prognostic scores based on serum high-density

- lipoprotein cholesterol and albumin levels in patients with colorectal cancer. *J Cancer*. 2019;10:35-42.
114. Huang L, Liu J, Huang X, et al. Serum C-reactive protein-to-body mass index ratio predicts overall survival in patients with resected colorectal cancer. *Technol Cancer Res Treat*. 2021;20:15330338211037418.
 115. Ikuta S, Aihara T, Nakajima T, Kasai M, Yamanaka N. Computed tomography-measured bone mineral density as a surrogate marker of survival after resection of colorectal liver metastases. *Ann Transl Med*. 2021;9:21.
 116. Ishizuka M, Nagata H, Takagi K, Iwasaki Y, Kubota K. Combination of platelet count and neutrophil to lymphocyte ratio is a useful predictor of postoperative survival in patients with colorectal cancer. *Br J Cancer*. 2013;109:401-407.
 117. Ishizuka M, Nagata H, Takagi K, Iwasaki Y, Shibuya N, Kubota K. Clinical significance of tumor pathology for postoperative survival of patients undergoing surgery for stage IV colorectal cancer. *Anticancer Res*. 2012;32:3291-3297.
 118. Islam R, Khan R, Ali A, et al. Clinical factors affecting bevacizumab efficacy with and without conventional chemotherapy in metastatic colon cancer. *Am J Ther*. 2020;27:e500-e506.
 119. Jiang W, Fang YJ, Wu XJ, et al. Intraoperative blood loss independently predicts survival and recurrence after resection of colorectal cancer liver metastasis. *PLoS One*. 2013;8:e76125.
 120. Jung HW, Kim JW, Kim JY, et al. Effect of muscle mass on toxicity and survival in patients with colon cancer undergoing adjuvant chemotherapy. *Support Care Cancer*. 2015;23:687-694.
 121. Juszczak K, Kang S, Putnis S, et al. High body mass index is associated with an increased overall survival in rectal cancer. *J Gastrointest Oncol*. 2020;11:626-632.
 122. Kaidar-Person O, Badarna H, Bar-Sela G. Bevacizumab for metastatic colon cancer: does patient BMI influence survival? *Anticancer Drugs*. 2015;26:363-366.
 123. Kaneko M, Sasaki S, Ozaki K, et al. Underweight status predicts a poor prognosis in elderly patients with colorectal cancer. *Mol Clin Oncol*. 2016;5:289-294.
 124. Kang J, Baek SE, Kim T, et al. Impact of fat obesity on laparoscopic total mesorectal excision: more reliable indicator than body mass index. *Int J Colorectal Dis*. 2012;27:497-505.
 125. Karabulut S, Dogan I, Usul Afsar C, et al. Does nutritional status affect treatment tolerability, response and survival in metastatic colorectal cancer patients? Results of a prospective multicenter study. *J Oncol Pharm Pract*. 2021;27:1357-1363.
 126. Kim CH, Yeom SS, Kwak HD, et al. Clinical outcomes of patients with locally advanced rectal cancer with persistent circumferential resection margin invasion after preoperative chemoradiotherapy. *Ann Coloproctol*. 2019;35:72-82.
 127. Kim JM, Chung E, Cho ES, et al. Impact of subcutaneous and visceral fat adiposity in patients with colorectal cancer. *Clin Nutr*. 2021;40:5631-5638.
 128. Kim MS, Park EJ, Kang J, et al. Prognostic factors predicting survival in incurable stage IV colorectal cancer patients who underwent palliative primary tumor resection. Retrospective cohort study. *Int J Surg*. 2018;49:10-15.
 129. Kim WR, Han YD, Min BS. C-reactive protein level predicts survival outcomes in rectal cancer patients undergoing total mesorectal excision after preoperative chemoradiation therapy. *Ann Surg Oncol*. 2018;25:3898-3905.
 130. Kobayashi A, Kaido T, Hamaguchi Y, et al. Impact of visceral adiposity as well as sarcopenic factors on outcomes in patients undergoing liver resection for colorectal liver metastases. *World J Surg*. 2018;42:1180-1191.
 131. Kumar S, Burney IA, Zahid KF, et al. Colorectal cancer patient characteristics, treatment and survival in Oman—a single center study. *Asian Pac J Cancer Prev*. 2015;16:4853-4858.
 132. Kunizaki M, Sawai T, Takeshita H, et al. Clinical value of serum p53 antibody in the diagnosis and prognosis of colorectal cancer. *Anti-cancer Res*. 2016;36:4171-4175.
 133. Kuo YH, Shi CS, Huang CY, Huang YC, Chin CC. Prognostic significance of unintentional body weight loss in colon cancer patients. *Mol Clin Oncol*. 2018;8:533-538.
 134. Kuritzkes BA, Pappou EP, Kiran RP, et al. Visceral fat area, not body mass index, predicts postoperative 30-day morbidity in patients undergoing colon resection for cancer. *Int J Colorectal Dis*. 2018;33:1019-1028.
 135. Kwak HD, Ju JK, Kang DW, et al. Outcomes according to body mass index following laparoscopic surgery in patients with colorectal cancer. *J Minim Access Surg*. 2018;14:134-139.
 136. Kwak M, Kim C. Disparities by age, sex, tumor stage, diagnosis path, and area-level socioeconomic status in survival time for major cancers: results from the Busan Cancer Registry. *J Korean Med Sci*. 2017;32:1974-1983.
 137. Lee CS, Won DD, Oh SN, et al. Prognostic role of pre-sarcopenia and body composition with long-term outcomes in obstructive colorectal cancer: a retrospective cohort study. *World J Surg Oncol*. 2020;18:230.
 138. Lee GY, Lee SM, Jang JH, et al. Preoperative constipation is associated with poor prognosis of rectal cancer: a prospective cohort study. *J Korean Surg Soc*. 2013;85:35-42.
 139. Lee JH, Kim S, Lee HS, et al. Different prognostic impact of glucose uptake in visceral adipose tissue according to sex in patients with colorectal cancer. *Sci Rep*. 2021;11:21556.
 140. Lee KH, Kang BK, Ahn BK. Higher visceral fat area/subcutaneous fat area ratio measured by computed tomography is associated with recurrence and poor survival in patients with mid and low rectal cancers. *Int J Colorectal Dis*. 2018;33:1303-1307.
 141. Lee S, Song A, Eo W. Serum ferritin as a prognostic biomarker for survival in relapsed or refractory metastatic colorectal cancer. *J Cancer*. 2016;7:957-964.
 142. Lee SY, Jo JS, Kim HJ, Kim CH, Kim YJ, Kim HR. Prognostic factors for low rectal cancer patients undergoing intersphincteric resection after neoadjuvant chemoradiation. *J Surg Oncol*. 2015;111:1054-1058.
 143. Lee SY, Kim CH, Kim YJ, Kwak HD, Ju JK, Kim HR. Obesity as an independent predictive factor for pathologic complete response after neoadjuvant chemoradiation in rectal cancer. *Ann Surg Treat Res*. 2019;96:116-122.
 144. Levolger S, van Vledder MG, Alberda WJ, et al. Muscle wasting and survival following pre-operative chemoradiotherapy for locally advanced rectal carcinoma. *Clin Nutr*. 2018;37:1728-1735.
 145. Lino-Silva LS, Aguilar-Cruz E, Salcedo-Hernandez RA, Zepeda-Najar C. Overweight but not obesity is associated with decreased survival in rectal cancer. *Contemp Oncol (Pozn)*. 2018;22:158-164.
 146. Liu D, Li Q, Yang Z, et al. Association of body mass index and smoking on outcome of Chinese patients with colorectal cancer. *World J Surg Oncol*. 2013;11:271.
 147. Liu H, Wei R, Li C, et al. BMI may be a prognostic factor for local advanced rectal cancer patients treated with long-term neoadjuvant chemoradiotherapy. *Cancer Manag Res*. 2020;12:10321-10332.
 148. Liu YW, Lu CC, Chang CD, et al. Prognostic value of sarcopenia in patients with colorectal liver metastases undergoing hepatic resection. *Sci Rep*. 2020;10:6459.
 149. Liu Z, Lu S, Wang Y, et al. Impact of body composition during neoadjuvant chemoradiotherapy on complications, survival and tumor response in patients with locally advanced rectal cancer. *Front Nutr*. 2022;9:796601.
 150. Loosen SH, Roderburg C, Alizai PH, et al. Comparative analysis of circulating biomarkers for patients undergoing resection of colorectal liver metastases. *Diagnostics (Basel)*. 2021;11:1999.
 151. Makino T, Trencheva K, Shukla PJ, et al. The influence of obesity on short- and long-term outcomes after laparoscopic surgery for colon

- cancer: a case-matched study of 152 patients. *Surgery*. 2014;156:661-668.
152. Malietzis G, Currie AC, Athanasiou T, et al. Influence of body composition profile on outcomes following colorectal cancer surgery. *Br J Surg*. 2016;103:572-580.
 153. Mao Z, Sun J, Feng B, et al. The metastasis suppressor, N-myc downregulated gene 1 (NDRG1), is a prognostic biomarker for human colorectal cancer. *PLoS One*. 2013;8:e68206.
 154. Matsubara D, Arita T, Nakanishi M, et al. The impact of postoperative inflammation on recurrence in patients with colorectal cancer. *Int J Clin Oncol*. 2020;25:602-613.
 155. Matsumoto A, Shinohara H, Suzuki H. Laparoscopic and open surgery in patients with transverse colon cancer: short-term and oncological outcomes. *BJS Open*. 2021;5:5.
 156. McSorley ST, Black DH, Horgan PG, McMillan DC. The relationship between tumour stage, systemic inflammation, body composition and survival in patients with colorectal cancer. *Clin Nutr*. 2018;37:1279-1285.
 157. Min YW, Kim SA, Lee JH, et al. Overweight is associated with a favorable survival in patients with colorectal cancer: a prospective cohort study in an Asian population. *Ann Surg Oncol*. 2012;19:3460-3464.
 158. Ming-Sheng F, Mei-Ling D, Xun-Quan C, Yuan-Xin H, Wei-Jie Z, Qin-Cong P. Preoperative neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and CEA as the potential prognostic biomarkers for colorectal cancer. *Can J Gastroenterol Hepatol*. 2022;2022:3109165.
 159. Moamer S, Baghestani A, Pourhoseingholi MA, Hajizadeh N, Ahmadi F, Norouzinia M. Evaluation of prognostic factors effect on survival time in patients with colorectal cancer, based on Weibull competing-risks model. *Gastroenterol Hepatol Bed Bench*. 2017;10:54-59.
 160. Moein Y, Baghestani AR, Khadembashi N, Pourhoseingholi MA, Baghban AA, Khosrovirad A. Survival analysis of colorectal cancer patients using exponentiated Weibull distribution. *Int J Cancer Manag*. 2018;11:1-6.
 161. Mohri Y, Inoue Y, Tanaka K, Hiro J, Uchida K, Kusunoki M. Prognostic nutritional index predicts postoperative outcome in colorectal cancer. *World J Surg*. 2013;37:2688-2692.
 162. Moon HG, Ju YT, Jeong CY, et al. Visceral obesity may affect oncologic outcome in patients with colorectal cancer. *Ann Surg Oncol*. 2008;15:1918-1922.
 163. Nakamura T, Miura H, Ikeda A, et al. Laparoscopic surgery for obese patients with colon cancer: a case-matched control study. *Surg Today*. 2013;43:763-768.
 164. Niemeläinen S, Huhtala H, Ehrlich A, Kössi J, Jämsen E, Hyöty M. Risk factors of short-term survival in the aged in elective colon cancer surgery: a population-based study. *Int J Colorectal Dis*. 2020;35:307-315.
 165. Novakova-Jiresova A, Kopeckova K, Boublikova L, et al. Regorafenib for metastatic colorectal cancer: an analysis of a registry-based cohort of 555 patients. *Cancer Manag Res*. 2020;12:5365-5372.
 166. O'Brien SJ, Kalbfleisch T, Srivastava S, et al. Decreased tumoral expression of colon-specific water channel aquaporin 8 is associated with reduced overall survival in colon adenocarcinoma. *Dis Colon Rectum*. 2021;64:1083-1095.
 167. Oh RK, Ko HM, Lee JE, Lee KH, Kim JY, Kim JS. Clinical impact of sarcopenia in patients with colon cancer undergoing laparoscopic surgery. *Ann Surg Treat Res*. 2020;99:153-160.
 168. Ottaiano A, Nappi A, Tafuto S, et al. Diabetes and body mass index are associated with neuropathy and prognosis in colon cancer patients treated with capecitabine and oxaliplatin adjuvant chemotherapy. *Oncology*. 2016;90:36-42.
 169. Pandey S, Fish SS, Roy HK. Increasing colorectal cancer in the young population and tailoring of the colorectal cancer screening recommendations in subpopulation: a retrospective single-center study. *Int J Colorectal Dis*. 2021;36:1515-1524.
 170. Park IJ, You YN, Skibber JM, et al. Oncologic and functional hazards of obesity among patients with locally advanced rectal cancer following neoadjuvant chemoradiation therapy. *Am J Clin Oncol*. 2017;40:277-282.
 171. Park JS, Sakai Y, Simon NSM, et al. Long-term survival and local relapse following surgery without radiotherapy for locally advanced upper rectal cancer: an international multi-institutional study. *Medicine (Baltimore)*. 2016;95:e2990.
 172. Partl R, Lukasiak K, Thurner EM, Renner W, Stranzl-Lawatsch H, Langsenlehner T. The elevated pre-treatment C-reactive protein predicts poor prognosis in patients with locally advanced rectal cancer treated with neo-adjuvant radiochemotherapy. *Diagnostics (Basel)*. 2020;10:10.
 173. Pathak S, Tang JM, Terlizzo M, Poston GJ, Malik HZ. Hepatic steatosis, body mass index and long term outcome in patients undergoing hepatectomy for colorectal liver metastases. *Eur J Surg Oncol*. 2010;36:52-57.
 174. Peng D, Liu XY, Cheng YX, Tao W, Cheng Y. Improvement of diabetes mellitus after colorectal cancer surgery: a retrospective study of predictive factors for type 2 diabetes mellitus remission and overall survival. *Front Oncol*. 2021;11:694997.
 175. Perrin T, Lenfant M, Boisson C, Bert M, Rat P, Facy O. Effects of body composition profiles on oncological outcomes and postoperative intraabdominal infection following colorectal cancer surgery. *Surg Obes Relat Dis*. 2021;17:575-584.
 176. Pian G, Oh SY. Comparison of nutritional and immunological scoring systems predicting prognosis in T1-2N0 colorectal cancer. *Int J Colorectal Dis*. 2022;37:179-188.
 177. Pisarska M, Torbicz G, Gajewska N, et al. Compliance with the ERAS protocol and 3-year survival after laparoscopic surgery for non-metastatic colorectal cancer. *World J Surg*. 2019;43:2552-2560.
 178. Polyzos KA, Karadima ML, Kosma AC, Lazaris A, Kavantzis N, Tsavaris N. Clinical influence of ploidy and cancer stem cells and other parameters in stage IV colorectal cancer. *In Vivo*. 2019;33:245-249.
 179. Pu H, Xie P, Chen Y, et al. Relationship between preoperative and postoperative serum carcinoembryonic antigen and prognosis of patients with stage I-III rectal cancer: a retrospective study of a multicentre cohort of 1022 rectal cancer patients. *Cancer Manag Res*. 2021;13:2643-2651.
 180. Ramjeesingh R, Orr C, Bricks CS, Hopman WM, Hammad N. A retrospective study on the role of diabetes and metformin in colorectal cancer disease survival. *Curr Oncol*. 2016;23:E116-E122.
 181. Reed M, Patrick C, Croft B, Walde N, Voutsadakis IA. The metabolic syndrome and its components as prognostic factors in metastatic colorectal cancer. *Indian J Gastroenterol*. 2019;38:15-22.
 182. Renfro LA, Grothey A, Xue Y, et al. ACCENT-based web calculators to predict recurrence and overall survival in stage III colon cancer. *J Natl Cancer Inst*. 2014;106:dju333.
 183. Rickles AS, Iannuzzi JC, Mironov O, et al. Visceral obesity and colorectal cancer: are we missing the boat with BMI? *J Gastrointest Surg*. 2013;17:133-143; discussion p. 43.
 184. Rieser CJ, Jones H, Hall LB, et al. Definition and prediction of early recurrence and mortality following cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for colorectal peritoneal metastases: towards predicting oncologic futility preoperatively. *Ann Surg Oncol*. 2021;28:9116-9125.
 185. Roxburgh CS, Platt JJ, Leitch EF, Kinsella J, Horgan PG, McMillan DC. Relationship between preoperative comorbidity, systemic inflammatory response, and survival in patients undergoing curative resection for colorectal cancer. *Ann Surg Oncol*. 2011;18:997-1005.
 186. Sakin A, Samanci NS, Secmeler S, et al. The effect of body mass index on location of recurrence and survival in early-stage colorectal cancer. *J Cancer Res Ther*. 2020;16:S176-S182.

187. Sasaki M, Miyoshi N, Fujino S, et al. The geriatric nutritional risk index predicts postoperative complications and prognosis in elderly patients with colorectal cancer after curative surgery. *Sci Rep.* 2020; 10:10744.
188. Scarpa M, Ruffolo C, Erroi F, et al. Obesity is a risk factor for multifocal disease and recurrence after colorectal cancer surgery: a case-control study. *Anticancer Res.* 2014;34:5735-5741.
189. Schreckenbach T, Zeller MV, El Youzouri H, Bechstein WO, Woeste G. Identification of factors predictive of postoperative morbidity and short-term mortality in older patients after colorectal carcinoma resection: a single-center retrospective study. *J Geriatr Oncol.* 2018;9:649-658.
190. Shah MS, Fogelman DR, Raghav KP, et al. Joint prognostic effect of obesity and chronic systemic inflammation in patients with metastatic colorectal cancer. *Cancer.* 2015;121:2968-2975.
191. Shan T, Chen S, Chen X, et al. Association of family history of tumors with clinicopathological characteristics and prognosis of colorectal cancer. *Eur J Cancer Prev.* 2019;28:258-267.
192. Shibakita M, Yoshimura H, Tachibana M, Ueda S, Nagasue N. Body mass index influences long-term outcome in patients with colorectal cancer. *Hepatogastroenterology.* 2010;57:62-69.
193. Shibata M, Fukahori M, Kasamatsu E, Machii K, Hamauchi S. A retrospective cohort study to investigate the incidence of cachexia during chemotherapy in patients with colorectal cancer. *Adv Ther.* 2020;37:5010-5022.
194. Singh A, Muthukumarasamy G, Pawa N, Riaz AA, Hendricks JB, Motson RW. Laparoscopic colorectal cancer surgery in obese patients. *Colorectal Dis.* 2011;13:878-883.
195. Sinicropo FA, Foster NR, Sargent DJ, O'Connell MJ, Rankin C. Obesity is an independent prognostic variable in colon cancer survivors. *Clin Cancer Res.* 2010;16:1884-1893.
196. Sinicropo FA, Foster NR, Yoon HH, et al. Association of obesity with DNA mismatch repair status and clinical outcome in patients with stage II or III colon carcinoma participating in NCCTG and NSABP adjuvant chemotherapy trials. *J Clin Oncol.* 2012;30:406-412.
197. Sjoquist KM, Renfro LA, Simes RJ, et al. Personalizing survival predictions in advanced colorectal cancer: the ARCAD nomogram project. *J Natl Cancer Inst.* 2018;110:638-648.
198. Snyder RA, He J, Le-Rademacher J, et al. Racial differences in survival and response to therapy in patients with metastatic colorectal cancer: a secondary analysis of CALGB/SWOG 80405 (Alliance A151931). *Cancer.* 2021;127:3801-3808.
199. Son IT, Kim DW, Choe EK, et al. Oncologic evaluation of obesity as a factor in patients with rectal cancer undergoing laparoscopic surgery: a propensity-matched analysis using body mass index. *Ann Surg Treat Res.* 2019;96:86-94.
200. Song A, Eo W, Lee S. Comparison of selected inflammation-based prognostic markers in relapsed or refractory metastatic colorectal cancer patients. *World J Gastroenterol.* 2015;21:12410-12420.
201. Sun Y, Chi P. Impact of body mass index on surgical and oncological outcomes in laparoscopic total mesorectal excision for locally advanced rectal cancer after neoadjuvant 5-fluorouracil-based chemoradiotherapy. *Gastroenterol Res Pract.* 2017;2017:1509140.
202. Takeda Y, Akiyoshi T, Matsueda K, et al. Skeletal muscle loss is an independent negative prognostic factor in patients with advanced lower rectal cancer treated with neoadjuvant chemoradiotherapy. *PLoS One.* 2018;13:e0195406.
203. Tang S, Xie H, Kuang J, Gao F, Gan J, Ou H. The value of geriatric nutritional risk index in evaluating postoperative complication risk and long-term prognosis in elderly colorectal cancer patients. *Cancer Manag Res.* 2020;12:165-175.
204. Tartter PI, Slater G, Papatostas AE, Aufses AH Jr. Cholesterol, weight, height, Quetelet's index, and colon cancer recurrence. *J Surg Oncol.* 1984;27:232-235.
205. Toiyama Y, Hiro J, Shimura T, et al. The impact of body mass index on oncological outcomes in colorectal cancer patients with curative intent. *Int J Clin Oncol.* 2016;21:1102-1110.
206. Tokunaga R, Nakagawa S, Miyamoto Y, et al. The clinical impact of preoperative body composition differs between male and female colorectal cancer patients. *Colorectal Dis.* 2020;22:62-70.
207. Tokunaga R, Sakamoto Y, Nakagawa S, et al. Prognostic nutritional index predicts severe complications, recurrence, and poor prognosis in patients with colorectal cancer undergoing primary tumor resection. *Dis Colon Rectum.* 2015;58:1048-1057.
208. Uratani R, Toiyama Y, Shimura T, et al. Preoperative lower body mass index correlates with poorer prognosis in patients undergoing curative laparoscopic surgery for colorectal cancer. *Anticancer Res.* 2015;35:5639-5648.
209. Van Blarigan EL, Fuchs CS, Niedzwiecki D, et al. Association of Survival with adherence to the American Cancer Society nutrition and physical activity guidelines for cancer survivors after colon cancer diagnosis: the CALGB 89803/Alliance trial. *JAMA Oncol.* 2018;4:783-790.
210. van Vledder MG, Levolger S, Ayez N, Verhoef C, Tran TC, Ijzermans JN. Body composition and outcome in patients undergoing resection of colorectal liver metastases. *Br J Surg.* 2012;99:550-557.
211. van Vugt JLA, Coebergh van den Braak RRJ, Lalmahomed ZS, et al. Impact of low skeletal muscle mass and density on short and long-term outcome after resection of stage I-III colorectal cancer. *Eur J Surg Oncol.* 2018;44:1354-1360.
212. Volkova E, Willis JA, Wells JE, Robinson BA, Dachs GU, Currie MJ. Association of angiotensin-2, C-reactive protein and markers of obesity and insulin resistance with survival outcome in colorectal cancer. *Br J Cancer.* 2011;104:51-59.
213. Wang F, Liu Y, Jiang J, et al. High expression of AMPD2 and obesity are associated with poor prognosis in colorectal cancer. *Int J Clin Exp Pathol.* 2018;11:216-223.
214. Wang S, Xie H, Gong Y, et al. The value of L3 skeletal muscle index in evaluating preoperative nutritional risk and long-term prognosis in colorectal cancer patients. *Sci Rep.* 2020;10:8153.
215. Wei FZ, Mei SW, Chen JN, et al. Nomograms and risk score models for predicting survival in rectal cancer patients with neoadjuvant therapy. *World J Gastroenterol.* 2020;26:6638-6657.
216. Xie H, Gong Y, Kuang J, et al. Computed tomography-determined sarcopenia is a useful imaging biomarker for predicting postoperative outcomes in elderly colorectal cancer patients. *Cancer Res Treat.* 2020;52:957-972.
217. Xu X, Zhou L, Miao R, et al. Association of cancer mortality with postdiagnosis overweight and obesity using body mass index. *Oncotarget.* 2016;7:5023-5029.
218. Xu Y, Xu X, Xi C, Ye N, Wang Y. Prognostic value of preoperative albumin to globulin ratio in elderly patients with rectal cancer. *Medicine (Baltimore).* 2019;98:e16066.
219. Yamamoto N, Fujii S, Sato T, et al. Impact of body mass index and visceral adiposity on outcomes in colorectal cancer. *Asia Pac J Clin Oncol.* 2012;8:337-345.
220. Yang C, Wei C, Wang S, et al. Combined features based on preoperative controlling nutritional status score and circulating tumour cell status predict prognosis for colorectal cancer patients treated with curative resection. *Int J Biol Sci.* 2019;15:1325-1335.
221. Yang L, Chen H, Zhao M, Peng P. Prognostic value of circulating vitamin D binding protein, total, free and bioavailable 25-hydroxy vitamin D in patients with colorectal cancer. *Oncotarget.* 2017;8:40214-40221.
222. Yang M, Zhang Q, Ruan GT, et al. Association between serum creatinine concentrations and overall survival in patients with colorectal cancer: a multi-center cohort study. *Front Oncol.* 2021;11:710423.

223. Yang Z, Wei X, Pan Y, Min Z, Xu J, Yu B. Colon cancer combined with obesity indicates improved survival—research on relevant mechanism. *Aging (Albany NY)*. 2020;12:23778-23794.
224. Yoon J, Chung YE, Lim JS, Kim MJ. Quantitative assessment of mesorectal fat: new prognostic biomarker in patients with mid-to-lower rectal cancer. *Eur Radiol*. 2019;29:1240-1247.
225. You J, Huang S, Huang GQ, et al. Nonalcoholic fatty liver disease: a negative risk factor for colorectal cancer prognosis. *Medicine (Baltimore)*. 2015;94:e479.
226. You J, Zhu GQ, Xie L, et al. Preoperative platelet to lymphocyte ratio is a valuable prognostic biomarker in patients with colorectal cancer. *Oncotarget*. 2016;7:25516-25527.
227. Yu WD, Peng YF, Pan HD, Wang L, Li K, Gu J. Phosphatidylinositol 3-kinase CB association with preoperative radiotherapy response in rectal adenocarcinoma. *World J Gastroenterol*. 2014;20:16258-16267.
228. Yu YL, Fan CW, Tseng WK, et al. Correlation between the Glasgow prognostic score and the serum cytokine profile in Taiwanese patients with colorectal cancer. *Int J Biol Markers*. 2021;36:40-49.
229. Yu YL, Tseng WK, Fan CW, et al. Pretreatment nutrition-inflammation biomarkers correlated with differential cytokine profiles in Taiwanese patients with colorectal cancer. *Nutr Cancer*. 2022;74:1614-1624.
230. Zhang N, Ning F, Guo R, et al. Prognostic values of preoperative inflammatory and nutritional markers for colorectal cancer. *Front Oncol*. 2020;10:585083.
231. Zhang Q, Liu Q, Chen J, Mei S, Liang J, Wang Z. Short-term outcomes for laparoscopic surgery for BMI ≥ 30 patients with rectal cancer. *Asian Pac J Cancer Prev*. 2021;22:3705-3709.
232. Zhang X, Wu Q, Gu C, Hu T, Bi L, Wang Z. The effect of increased body mass index values on surgical outcomes after radical resection for low rectal cancer. *Surg Today*. 2019;49:401-409.
233. Zheng J, Li Y, Zhu S, et al. NDRG4 stratifies the prognostic value of body mass index in colorectal cancer. *Oncotarget*. 2016;7:1311-1322.
234. Zhou S, Sheng N, Ren J, et al. Clinical significance of and predictive risk factors for the postoperative elevation of carcinoembryonic antigen in patients with non-metastatic colorectal cancer. *Front Oncol*. 2021;11:741309.
235. Zhou Y, Zhang Y, Guo R, Li C, Sun N. Identification of methyltransferase-like protein 11B as a new prognostic biomarker for colorectal cancer through an analysis of The Cancer Genome Atlas. *J Gastrointest Oncol*. 2021;12:2854-2871.
236. Andreyev HJ, Norman AR, Oates J, Cunningham D. Why do patients with weight loss have a worse outcome when undergoing chemotherapy for gastrointestinal malignancies? *Eur J Cancer*. 1998;34:503-509.
237. Woff E, Hendlitz A, Ameye L, et al. Validation of metabolically active tumor volume and total lesion glycolysis as 18F-FDG PET/CT-derived prognostic biomarkers in chemorefractory metastatic colorectal cancer. *J Nucl Med*. 2019;60:178-184.
238. Kuiper JG, Phipps AI, Neuhaus ML, et al. Recreational physical activity, body mass index, and survival in women with colorectal cancer. *Cancer Causes Control*. 2012;23:1939-1948.
239. Chin CC, Kuo YH, Yeh CY, et al. Role of body mass index in colon cancer patients in Taiwan. *World J Gastroenterol*. 2012;18:4191-4198.
240. Alipour S, Kennecke HF, Woods R, et al. Body mass index and body surface area and their associations with outcomes in stage II and III colon cancer. *J Gastrointest Cancer*. 2013;44:203-210.
241. Adachi T, Hinoi T, Kinugawa Y, et al. Lower body mass index predicts worse cancer-specific prognosis in octogenarians with colorectal cancer. *J Gastroenterol*. 2016;51:779-787.
242. Baade PD, Meng X, Youl PH, Aitken JF, Dunn J, Chambers SK. The impact of body mass index and physical activity on mortality among patients with colorectal cancer in Queensland, Australia. *Cancer Epidemiol Biomarkers Prev*. 2011;20:1410-1420.
243. Carlisle J, Swart M, Dawe EJ, Chadwick M. Factors associated with survival after resection of colorectal adenocarcinoma in 314 patients. *Br J Anaesth*. 2012;108:430-435.
244. Chiao EY, Nambi PV, Naik AD. The impact of diabetes process and outcome quality measures on overall survival in patients with co-morbid colorectal cancer. *J Cancer Surviv*. 2010;4:381-387.
245. Baghestani AR, Daneshva T, Pourhoseingholi MA, Asadzadeh H. Survival of colorectal cancer in the presence of competing-risks—modeling by Weibull distribution. *Asian Pac J Cancer Prev*. 2016;17:1193-1196.
246. Choi MH, Oh SN, Lee IK, Oh ST, Won DD. Sarcopenia is negatively associated with long-term outcomes in locally advanced rectal cancer. *J Cachexia Sarcopeni*. 2018;9:53-59.
247. You JF, Tang R, Changchien CR, et al. Effect of body mass index on the outcome of patients with rectal cancer receiving curative anterior resection: disparity between the upper and lower rectum. *Ann Surg*. 2009;249:783-787.
248. Kocarnik JM, Hua X, Hardikar S, et al. Long-term weight loss after colorectal cancer diagnosis is associated with lower survival: the Colon Cancer Family Registry. *Cancer*. 2017;123:4701-4708.
249. Vergidis J, Gresham G, Lim HJ, et al. Impact of weight changes after the diagnosis of stage III colon cancer on survival outcomes. *Clin Colorectal Cancer*. 2016;15:16-23.
250. Meyerhardt JA, Kroenke CH, Prado CM, et al. Association of weight change after colorectal cancer diagnosis and outcomes in the Kaiser permanente northern California population. *Cancer Epidemiol Biomarkers Prev*. 2017;26:30-37.
251. Sun Y, Xu Z, Lin H, et al. Impact of body mass index on treatment outcome of neoadjuvant chemoradiotherapy in locally advanced rectal cancer. *Eur J Surg Oncol*. 2017;43:1828-1834.
252. Tamakoshi A, Nakamura K, Ukawa S, et al. Characteristics and prognosis of Japanese colorectal cancer patients: the BioBank Japan project. *J Epidemiol*. 2017;27:536-542.
253. Walter V, Jansen L, Hoffmeister M, et al. Prognostic relevance of pre-diagnostic weight loss and overweight at diagnosis in patients with colorectal cancer. *Am J Clin Nutr*. 2016;104:1110-1120.
254. Meyerhardt JA, Niedzwiecki D, Hollis D, et al. Impact of body mass index and weight change after treatment on cancer recurrence and survival in patients with stage III colon cancer: findings from Cancer and Leukemia Group B 89803. *J Clin Oncol*. 2008;26:4109-4115.
255. Patel GS, Ullah S, Beeke C, et al. Association of BMI with overall survival in patients with mCRC who received chemotherapy versus EGFR and VEGF-targeted therapies. *Cancer Med US*. 2015;4:1461-1471.
256. Seishima R, Okabayashi K, Hasegawa H, et al. Obesity was associated with a decreased postoperative recurrence of rectal cancer in a Japanese population. *Surg Today*. 2014;44:2324-2331.
257. Renfro LA, Loupakis F, Adams RA, et al. Body mass index is prognostic in metastatic colorectal cancer: pooled analysis of patients from first-line clinical trials in the ARCAD database. *J Clin Oncol*. 2016;34:144-150.
258. Lee DW, Han SW, Cha Y, et al. Prognostic influence of body mass index and body weight gain during adjuvant FOLFOX chemotherapy in Korean colorectal cancer patients. *BMC Cancer*. 2015;15:690.
259. Sinicrope FA, Foster NR, Yothers G, et al. Body mass index at diagnosis and survival among colon cancer patients enrolled in clinical trials of adjuvant chemotherapy. *Cancer*. 2013;119:1528-1536.
260. Jafarabadi MA, Mohammadi SM, Hajizadeh E, Kazemnejad A, Fatemi SR. Does the prognosis of colorectal cancer vary with tumor site? *Gastroenterol Hepatol Bed Bench*. 2011;4:199-209.
261. Agyemang-Yeboah F, Yorke J, Obirikorang C, et al. Colorectal cancer survival rates in Ghana: a retrospective hospital-based study. *PLoS One*. 2018;13:e0209307.

262. Cong Z, Wang D, Cao Y. The relationship between body mass index changes during chemotherapy and prognosis of patients with advanced colorectal cancer: a retrospective cohort study. *Medicine (Baltimore)*. 2018;97:e10843.
263. Silva TH, Schilithz AOC, Peres WAF, Murad LB. Neutrophil-lymphocyte ratio and nutritional status are clinically useful in predicting prognosis in colorectal cancer patients. *Nutr Cancer*. 2020;72:1345-1354.
264. Lin J, Peng J, Qdaisat A, et al. Severe weight loss during preoperative chemoradiotherapy compromises survival outcome for patients with locally advanced rectal cancer. *J Cancer Res Clin Oncol*. 2016;142:2551-2560.
265. Ding PQ, Batra A, Xu Y, McKinnon GP, Cheung WY. Obesity and its impact on outcomes in patients with stage III colon cancer receiving adjuvant chemotherapy. *Clin Colorectal Cancer*. 2020;19:209-218.
266. Arkenbosch JHC, van Erning FN, Rutten HJ, Zimmerman D, de Wilt JHW, Beijer S. The association between body mass index and postoperative complications, 30-day mortality and long-term survival in Dutch patients with colorectal cancer. *Eur J Surg Oncol*. 2019;45:160-166.
267. Al Omari A, Abdelkhaleq H, Al-Hussaini M, et al. Validation of the survival benefits of metformin in middle eastern patients with type II diabetes mellitus and colorectal cancer. *J Glob Oncol*. 2018;4:1-10.
268. Gebauer B, Meyer F, Ptok H, et al. Impact of body mass index on early postoperative and long-term outcome after rectal cancer surgery. *Visc Med*. 2017;33:373-382.
269. Kuo YH, Lee KF, Chin CC, Huang WS, Yeh CH, Wang JY. Does body mass index impact the number of LNs harvested and influence long-term survival rate in patients with stage III colon cancer? *Int J Colorectal Dis*. 2012;27:1625-1635.
270. Moghimi-Dehkordi B, Safaee A, Zali MR. Prognostic factors in 1,138 Iranian colorectal cancer patients. *Int J Colorectal Dis*. 2008;23:683-688.
271. Izadi N, Koohi F, Safarpour M, Naseri P, Rahimi S, Khodakarim S. Estimating the cure proportion of colorectal cancer and related factors after surgery in patients using parametric cure models. *Gastroenterol Hepatol Bed Bench*. 2020;13:125-132.
272. Zacharakis M, Xynos ID, Lazaris A, et al. Predictors of survival in stage IV metastatic colorectal cancer. *Anticancer Res*. 2010;30:653-660.
273. Mitry E, Douillard JY, Van Cutsem E, et al. Predictive factors of survival in patients with advanced colorectal cancer: an individual data analysis of 602 patients included in irinotecan phase III trials. *Ann Oncol*. 2004;15:1013-1017.
274. Vashi PG, Gorsuch K, Wan L, Hill D, Block C, Gupta D. Sarcopenia supersedes subjective global assessment as a predictor of survival in colorectal cancer. *PLoS One*. 2019;14:e0218761.
275. Lee DW, Cho S, Shin A, Han SW, Kim TY. Body mass index and body weight change during adjuvant chemotherapy in colon cancer patients: results from the AVANT trial. *Sci Rep*. 2020;10:19467.
276. Simkens LH, Koopman M, Mol L, et al. Influence of body mass index on outcome in advanced colorectal cancer patients receiving chemotherapy with or without targeted therapy. *Eur J Cancer*. 2011;47:2560-2567.
277. Looijaard S, Meskers CGM, Slee-Valentijn MS, et al. Computed tomography-based body composition is not consistently associated with outcome in older patients with colorectal cancer. *Oncologist*. 2020;25:e492-e501.
278. Kurk SA, Peeters PHM, Dorresteijn B, et al. Loss of skeletal muscle index and survival in patients with metastatic colorectal cancer: secondary analysis of the phase 3 CAIRO3 trial. *Cancer Med*. 2020;9:1033-1043.
279. Souwer ET, Moos SI, van Rooden CJ, et al. Physical performance has a strong association with poor surgical outcome in older patients with colorectal cancer. *Eur J Surg Oncol*. 2020;46:462-469.
280. Hu C, Zhang Q, Jin X, et al. A paradox between preoperative overweight/obesity and change in weight during postoperative chemotherapy and its relationship to survival in stage and colorectal cancer patients. *Clin Nutr*. 2021;40:2410-2419.
281. Baghestani AR, Moamer S, Pourhoseingholi MA, Khadem Maboudi AA, Ghoresli B, Zali MR. Demographic and pathological predictors of colorectal cancer survival in competing risk model, using generalized Weibull distribution. *Int J Cancer Manag*. 2017;10:e7352.
282. Hannisdal E, Tveit KM, Theodorsen L, Host H. Host markers and prognosis in recurrent rectal carcinomas treated with radiotherapy. *Acta Oncol*. 1994;33:415-421.
283. Hines RB, Shanmugam C, Waterbor JW, et al. Effect of comorbidity and body mass index on the survival of African-American and Caucasian patients with colon cancer. *Cancer*. 2009;115:5798-5806.
284. Van de Putte D, Van Daele E, Willaert W, et al. Effect of abdominopelvic sepsis on cancer outcome in patients undergoing sphincter saving surgery for rectal cancer. *J Surg Oncol*. 2017;116:722-729.
285. Abdel-Rahman O. Effect of body mass index on 5-FU-based chemotherapy toxicity and efficacy among patients with metastatic colorectal cancer; a pooled analysis of 5 randomized trials. *Clin Colorectal Cancer*. 2019;18:e385-e393.
286. Hajebi Khaniki S, Fakoor V, Shahid Sales S, Esmaily H, Heidarian MH. Risk of relapse and death from colorectal cancer and its related factors using non-Markovian multi-state model. *Gastroenterol Hepatol Bed Bench*. 2020;13:200-208.
287. Shahjehan F, Merchea A, Cochuyt JJ, Li Z, Colibaseanu DT, Kasi PM. Body mass index and long-term outcomes in patients with colorectal cancer. *Front Oncol*. 2018;8:8.
288. Zhang LM, Schuitevoerder D, White MG, et al. Combined mechanical and oral antibiotic bowel preparation is associated with prolonged recurrence-free survival following surgery for colorectal cancer. *J Surg Oncol*. 2021;124:1106-1114.
289. Safari M, Mahjub H, Esmaili H, Abbasi M, Roshanaei G. Determining the risk factors affecting on death due to colorectal cancer progression: survival analysis in the presence of competing risks. *J Gastrointest Cancer*. 2022;53:348-355.
290. Xu M, Zhao Z, Jia B, Liu R, Liu H. Perioperative and long-term outcomes of robot-assisted versus laparoscopy-assisted hemicolectomy for left-sided colon cancers: a retrospective study. *Updates Surg*. 2021;73:1049-1056.
291. Prejac J, Kekez D, Belev B, Prejac M, Pleština S. Frequency of body weight loss is an independent prognostic factor of first-line treatment outcomes in metastatic colorectal cancer. *Nutr Cancer*. 2022;74:520-526.
292. Fanipakdel A, Hosseini S, Javadinia SA, Afkhami Jeddi F, Vasei M. The prognostic role of body mass index in survival of non-metastatic postoperative patients with colorectal cancer. *Int J Cancer Manag*. 2021;14:e110257.
293. Falk W, Magnuson A, Eintrei C, et al. Comparison between epidural and intravenous analgesia effects on disease-free survival after colorectal cancer surgery: a randomised multicentre controlled trial. *Br J Anaesth*. 2021;127:65-74.
294. Wu HL, Tai YH, Lin SP, Yang SH, Tsou MY, Chang KY. Epidural analgesia does not impact recurrence or mortality in patients after rectal cancer resection. *Sci Rep*. 2021;11:913.
295. Park JW, Chang SY, Lim JS, et al. Impact of visceral fat on survival and metastasis of stage III colorectal cancer. *Gut Liver*. 2022;16:53-61.
296. Tojek K, Anaszewicz M, Szukay B, et al. Circulating leptin, adiponectin, and tumor necrosis factor-alpha in patients undergoing surgery due to colorectal cancer. *Digestion*. 2021;102:246-255.
297. Liu L, Erickson NT, Ricard I, et al. Early weight loss is an independent risk factor for shorter survival and increased side effects in patients with metastatic colorectal cancer undergoing first-line treatment

- within the randomized phase III trial FIRE-3 (AIO KRK-0306). *Int J Cancer*. 2022;150:112-123.
298. Eckberg SE, Dahlberg MJA, der Hagopian OS, et al. Perirenal fat surface area and oncologic outcome in elective colon cancer surgery. *Dis Colon Rectum*. 2021;64:171-180.
 299. Croese A, Gartrell R, Hiscock R, et al. The effect of smoking, obesity and diabetes on recurrence-free and overall survival in patients with stage III colon cancer receiving adjuvant chemotherapy. *Cancer Rep (Hoboken)*. 2021;4:e1346.
 300. Chai VW, Chia M, Cocco A, Bhamidipaty M, D'Souza B. Sarcopenia is a strong predictive factor of clinical and oncological outcomes following curative colorectal cancer resection. *ANZ J Surg*. 2021;91:E292-E297.
 301. Best TD, Roeland EJ, Horick NK, et al. Muscle loss is associated with overall survival in patients with metastatic colorectal cancer independent of tumor mutational status and weight loss. *Oncologist*. 2021;26:e963-e970.
 302. Sim JH, Bang JY, Kim SH, Kang SJ, Song JG. Association of preoperative prognostic nutritional index and postoperative acute kidney injury in patients with colorectal cancer surgery. *Nutrients*. 2021;13:1604.
 303. van Zutphen M, van Duijnhoven FJB, Wesselink E, et al. Identification of lifestyle behaviors associated with recurrence and survival in colorectal cancer patients using random survival forests. *Cancers (Basel)*. 2021;13:2442.
 304. Azizmohammad Looha M, Pourhoseingholi MA, Nasserinejad M, Najafimehr H, Zali MR. Application of a non-parametric non-mixture cure rate model for analyzing the survival of patients with colorectal cancer in Iran. *Epidemiol Health*. 2018;40:e2018045.
 305. Tokunaga R, Sakamoto Y, Nakagawa S, et al. CONUT: a novel independent predictive score for colorectal cancer patients undergoing potentially curative resection. *Int J Colorectal Dis*. 2017;32:99-106.
 306. Amanpour F, Akbari S, Azizmohammad Looha M, Abdehagh M, Pourhoseingholi MA. Mixture cure model for estimating short-term and long-term colorectal cancer survival. *Gastroenterol Hepatol Bed Bench*. 2019;12:S37-S43.
 307. Lee S, Lee DH, Lee JH, et al. Association of body mass index with survival in Asian patients with colorectal cancer. *Cancer Res Treat*. 2022;54:860-872.
 308. Giani A, Famularo S, Fogliati A, et al. Skeletal muscle wasting and long-term prognosis in patients undergoing rectal cancer surgery without neoadjuvant therapy. *World J Surg Oncol*. 2022;20:51.
 309. Okuno M, Goumar C, Kopetz S, et al. Loss of muscle mass during preoperative chemotherapy as a prognosticator for poor survival in patients with colorectal liver metastases. *Surgery*. 2019;165:329-336.
 310. Tarantino I, Warschkow R, Worni M, et al. Elevated preoperative CEA is associated with worse survival in stage I-III rectal cancer patients. *Br J Cancer*. 2012;107:266-274.
 311. Silva A, Pereira SS, Monteiro MP, Araujo A, Faria G. Effect of metabolic syndrome and individual components on colon cancer characteristics and prognosis. *Front Oncol*. 2021;11:631257.
 312. Kahn BB, Flier JS. Obesity and insulin resistance. *J Clin Invest*. 2000;106:473-481.
 313. Ellulu MS, Patimah I, Khaza'i H, Rahmat A, Abed Y. Obesity and inflammation: the linking mechanism and the complications. *Arch Med Sci*. 2017;13:851-863.
 314. Sandhu MS, Dunger DB, Giovannucci EL. Insulin, insulin-like growth factor-I (IGF-I), IGF binding proteins, their biologic interactions, and colorectal cancer. *J Natl Cancer Inst*. 2002;94:972-980.
 315. Renehan AG, Roberts DL, Dive C. Obesity and cancer: pathophysiological and biological mechanisms. *Arch Physiol Biochem*. 2008;114:71-83.
 316. Guercio BJ, Zhang S, Ou FS, et al. IGF-binding proteins, adiponectin, and survival in metastatic colorectal cancer: results from CALGB (Alliance)/SWOG 80405. *JNCI Cancer Spectr*. 2020;5:pkaa074.
 317. Wolpin BM, Meyerhardt JA, Chan AT, et al. Insulin, the insulin-like growth factor axis, and mortality in patients with nonmetastatic colorectal cancer. *J Clin Oncol*. 2009;27:176-185.
 318. Fuchs CS, Goldberg RM, Sargent DJ, et al. Plasma insulin-like growth factors, insulin-like binding protein-3, and outcome in metastatic colorectal cancer: results from intergroup trial N9741. *Clin Cancer Res*. 2008;14:8263-8269.
 319. Tuomisto AE, Makinen MJ, Vayrynen JP. Systemic inflammation in colorectal cancer: underlying factors, effects, and prognostic significance. *World J Gastroenterol*. 2019;25:4383-4404.
 320. Naszai M, Kurjan A, Maughan TS. The prognostic utility of pre-treatment neutrophil-to-lymphocyte-ratio (NLR) in colorectal cancer: a systematic review and meta-analysis. *Cancer Med*. 2021;10:5983-5997.
 321. Cupp MA, Cariolou M, Tzoulaki I, Aune D, Evangelou E, Berlanga-Taylor AJ. Neutrophil to lymphocyte ratio and cancer prognosis: an umbrella review of systematic reviews and meta-analyses of observational studies. *BMC Med*. 2020;18:360.
 322. Huang XZ, Chen WJ, Zhang X, et al. An elevated platelet-to-lymphocyte ratio predicts poor prognosis and clinicopathological characteristics in patients with colorectal cancer: a meta-analysis. *Dis Markers*. 2017;2017:1053125.
 323. Chambers P, Daniels SH, Thompson LC, Stephens RJ. Chemotherapy dose reductions in obese patients with colorectal cancer. *Ann Oncol*. 2012;23:748-753.
 324. Lee KC, Chung KC, Chen HH, Cheng KC, Wu KL, Song LC. The impact of obesity on postoperative outcomes in colorectal cancer patients: a retrospective database study. *Support Care Cancer*. 2022;30:2151-2161.
 325. Flegal KM, Graubard BI, Williamson DF, Gail MH. Cause-specific excess deaths associated with underweight, overweight, and obesity. *JAMA*. 2007;298:2028-2037.
 326. Renehan AG, Sperrin M. The obesity paradox and mortality after colorectal cancer: a causal conundrum. *JAMA Oncol*. 2016;2:1127-1129.
 327. Pin F, Couch ME, Bonetto A. Preservation of muscle mass as a strategy to reduce the toxic effects of cancer chemotherapy on body composition. *Curr Opin Support Palliat Care*. 2018;12:420-426.
 328. Schmidt SF, Rohm M, Herzig S, Berriel DM. Cancer cachexia: more than skeletal muscle wasting. *Trends Cancer*. 2018;4:849-860.
 329. Kalantar-Zadeh K, Rhee C, Sim JJ, Stenvinkel P, Anker SD, Kovesdy CP. Why cachexia kills: examining the causality of poor outcomes in wasting conditions. *J Cachexia Sarcopenia Muscle*. 2013;4:89-94.
 330. Kasi PM, Zafar SY, Grothey A. Is obesity an advantage in patients with colorectal cancer? *Expert Rev Gastroenterol Hepatol*. 2015;9:1339-1342.
 331. Lawlor DA, Hart CL, Hole DJ, Davey SG. Reverse causality and confounding and the associations of overweight and obesity with mortality. *Obesity (Silver Spring)*. 2006;14:2294-2304.
 332. Aune D, Sen A, Prasad M, et al. BMI and all cause mortality: systematic review and non-linear dose-response meta-analysis of 230 cohort studies with 3.74 million deaths among 30.3 million participants. *BMJ*. 2016;353:i2156.
 333. Winslow UC, Rode L, Nordestgaard BG. High tobacco consumption lowers body weight: a Mendelian randomization study of the Copenhagen general population study. *Int J Epidemiol*. 2015;44:540-550.
 334. Park Y, Peterson LL, Colditz GA. The plausibility of obesity paradox in cancer-patient. *Cancer Res*. 2018;78:1898-1903.
 335. Nuttall FQ. Body mass index: obesity, BMI, and health: a critical review. *Nutr Today*. 2015;50:117-128.

336. Caan BJ, Cespedes Feliciano EM, Kroenke CH. The importance of body composition in explaining the overweight paradox in cancer-counterpoint. *Cancer Res.* 2018;78:1906-1912.
337. Harrington M, Gibson S, Cottrell RC. A review and meta-analysis of the effect of weight loss on all-cause mortality risk. *Nutr Res Rev.* 2009;22:93-108.
338. De Stefani FDC, Pietraroia PS, Fernandes-Silva MM, Faria-Neto J, Baena CP. Observational evidence for unintentional weight loss in all-cause mortality and major cardiovascular events: a systematic review and meta-analysis. *Sci Rep.* 2018;8:15447.
339. McArdle CS, Hole DJ. Emergency presentation of colorectal cancer is associated with poor 5-year survival. *Br J Surg.* 2004;91:605-609.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: 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](https://doi.org/10.1002/ijc.34905)