ORIGINAL ARTICLE

Association of change in physical activity and body weight with quality of life and mortality in colorectal cancer: a systematic review and meta-analysis

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Abstract

Purpose A systematic review and a meta-analysis were performed to assess the associations between change over time in physical activity and weight and quality of life and mortality in colorectal cancer patients.

Methods The PubMed, Embase, and Cochrane Central Register of Controlled Trials databases were searched for English language articles published between January 1, 1990 and October 7, 2013. These articles reported results for changes in physical activity and body weight, assessed at pre- to postdiagnosis or at post-diagnosis only. A random effects model was used to analyze pooled quality of life and mortality estimates.

Results Seven eligible studies were identified and analyzed. Increased physical activity was associated with higher overall quality of life scores (N=3 studies; standardized mean difference (SMD)=0.74, 95 % confidence interval (CI)=0.66–0.82), reduced disease-specific mortality risk (hazard ratio (HR_{pooled})=0.70, 95 % CI=0.55–0.85), and reduced overall mortality (HR_{pooled}=0.75, CI=0.62–0.87) (N=2 studies). Weight gain was not associated with disease-specific (HR_{pooled}=1.02, CI=0.84–1.20) or overall (HR_{pooled}=1.03, CI=0.86–1.19) mortality (N=3 studies).

Conclusions Increased physical activity was associated with improved quality of life, a reduced risk of colorectal cancer, and overall mortality rate. Given the paucity of the literature published on this topic, this finding should be interpreted with caution.

Keywords Lifestyle \cdot Physical activity \cdot Weight gain \cdot Colorectal cancer \cdot Mortality \cdot Quality of life \cdot Systematic review

Introduction

Worldwide, colorectal cancer is ranked among the leading types of cancer that affect both women and men. In 2012, approximately 1.4 million new cases, or 10 % of all cancer sites, were of colorectal origin [1]. Advances in early detection, and in surgical and medical treatment, have led to improved survival of patients. In the USA, the relative 5-year survival rate is 65 % for all stages combined and is as high as 90 % for localized tumors [2]. In the USA, 1.1 million people were previously estimated to be living with a previous diagnosis of colorectal cancer [2]. In the UK, colorectal cancer survivors accounted for 26 % of all cancer survivors in 2008 [3]. The number of survivors is expected to increase further as a consequence of the implementation of screening programs.

Cancer survivors are usually encouraged to engage in healthier lifestyles that have positive effects on prognosis and survival [4–6]. A growing body of supporting evidence describes the beneficial effects of physical activity on health outcomes among cancer survivors [7–11]. For colorectal cancer survivors, suggestive evidence for the association between higher physical activity and lower mortality rates has emerged from studies that evaluated pre-diagnosis or post-diagnosis health behaviors of survivors [12, 13]. A higher amount of recreational physical activity before and after diagnosis is associated with lower mortality [14], and longer leisure time spent sitting is associated with a higher risk of death [15]. Some studies suggest an association between body weight of colorectal cancer survivors and survival probability [7]. Pre-diagnosis obesity is associated with poor overall and

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colorectal cancer-specific survival [16, 17]. A body mass index \geq 35 kg m⁻² at diagnosis is associated with an increased risk of recurrence of colorectal cancer and death [18].

Improvements in quality of life in colorectal cancer survivors are also positively associated with physical activity [19–22]. Healthy lifestyle, particularly physical activity, is also increasingly promoted to cancer survivors in an attempt to manage the psychosocial and physical consequences of the cancer and its treatment, which can negatively affect quality of life [8, 23–25]

There is growing evidence showing that physical inactivity and high body weight are associated with higher mortality and lower quality of life among colorectal cancer survivors. Yet, most studies have focused on assessing the amount or categories of physical activity and weight at one point of time with cancer outcome rather than the impact of actual changes of physical activity or body weight over time. While it is recommended that cancer survivors increase physical activity or made healthy changes in their body weight, we actually do not know if these changes will necessarily improve cancerrelated survival and quality of life. The evidence regarding a possible association of actual change over time in these behaviors with mortality and quality of life has not been summarized. Blanchard et al. [26] attempted to quantify the change in the amount of physical activity associated with quality of life, but this study included survivors of different cancer types, predominantly breast cancer survivors.

The purpose of this study was to systematically review the literature reporting on longitudinal changes in physical activity and weight on quality of life and mortality in colorectal cancer survivors.

Methods

Search strategy and study selection

We performed a literature search to identify empirical studies on the association of changes in physical activity and weight, overweight, and/or obesity with quality of life (i.e., physical, social, emotional, and functional well-being of the survivors) and mortality (i.e., disease-specific and overall mortality) among survivors. Searches of eligible English language articles were performed using the Medline (PubMed), Embase, and Cochrane Central Register of Controlled Trials databases. The search included all peer-reviewed articles that were published by October 7, 2013. Electronic search strategies were developed using the terms "(colorectal neoplasms AND survivors) OR colorectal cancer surviv* OR colorectal tumor surviv* OR colorectal tumour surviv* OR colorectal neoplasm surviv* OR colonic cancer surviv* OR colonic tumor surviv* OR colonic tumour surviv* OR colonic neoplasm surviv* and one of the following terms: lifestyle, change*

OR modif*, life change events OR life change event*, exerci* OR physical activity OR motor activity, body weight OR body weight* OR body mass*, or quetelet OR body mass index OR body mass index."

Survivors were defined as individuals diagnosed with cancer from the time of initial diagnosis and followed through their lifetime, using the definition of the National Coalition of Cancer Survivorship adopted by the Office of Cancer Survivorship Research of the National Cancer Institute [27].

We considered retrospective and prospective cohort studies, case control studies, and randomized controlled trials (RCTs) in which ancillary data were reported as observational studies. Physical activity and body weight were required to be assessed at least twice, before and after diagnosis, or during two follow-up periods after diagnosis. We included studies in which quality of life, measured by standardized instruments, and overall mortality, disease-specific mortality, disease-free or recurrence-free survival were the outcome measures. Studies retained eligibility if they also reported on adult men and women, aged ≥ 18 years, and diagnosed with a primary colorectal cancer (malignant neoplasm of the colon, rectum, or both). We excluded studies that included patients with familial adenomatous polyposis, hereditary non-polyposis colorectal cancer, or cancers that were not of colorectal cell origin (e.g., melanoma, Hodgkin's disease).

All authors participated in screening of the retrieved titles and review of the article abstracts. Disagreements were discussed by the group and resolved by consensus. SJO and IS selected the full papers for inclusion in the review. Any final discrepancies were resolved by consensus between these two coauthors or after consultation with the entire group of coauthors.

Data extraction

Study characteristics included in the analysis were extracted independently by SJO and IS. The extracted data included the title, the first author's name, publication year, type of design, study population origin, period of diagnosis, sample size, response rate, and age at diagnosis. Data on definitions and measures of changes in physical activity and body weight, comparison groups, quality of life scales, and unit outcomes (quality of life scores, mean differences, or mortality hazard ratios (HRs), 95 % confidence intervals (CI), and standard deviation or standard error of the mean values) were also extracted.

Quality assessment

The methodological quality of each selected study was assessed using a 10-item checklist adapted from Mols et al. [28] (Table 1). Zero points were assigned to an item if it did not meet a criterion or was not sufficiently described. If the
 Table 1 Criteria list for assessing the methodological quality of the selected studies on the effect of lifestyle on outcome among colorectal cancer survivors

Items	Scoring and definition
1. Study design	3 Randomized trial 2 Cohort study 1 Case–control study 0 Other
2. Origin of study population	 Population-based Hospital-based, Other/not mentioned
3. Available information for non-responders	1 Yes 0 Not mentioned
4. Response rate	1 Reported 0 Not reported
 Available information on data collection with formulation for inclusion and exclusion criteria 	1 Reported 0 Not reported
 Time between colorectal cancer diagnosis and measurement(s) was defined 	1 Yes 0 Not mentioned
7. Standardized and valid estimation or questionnaire(s) for assessment of lifestyle	1 Yes 0 Not mentioned
8. Standardized and valid estimation or questionnaires for assessment of quality of life/mortality	1 Yes 0 Not mentioned
9. Variation in point estimates was reported (confidence interval, etc.)	1 Yes 0 Not mentioned/no
10. Correction of outcome measures for confounding	2 Fully corrected1 Not corrected, but separately presented by confounding categories0 No correction/not reported
Maximum score ^a	14

^a High quality, score ≥ 11 ; adequate quality, score 7–10; low quality ≤ 6

criteria were all met, the study was assigned the maximum value of 14 points. Studies that scored \geq 75 % of the maximum score (\geq 11 points) were considered to be of "high quality." Studies that scored 50–75 % of the maximum score (7–10 points) were rated as "adequate quality." Studies that scored <50 % (\leq 6 points) were considered to be of "low quality."

Statistical analysis

If ≥ 2 studies were available, the quality of life scores or adjusted HRs with the corresponding standard deviation or CI values that were measured after the changes in physical activity or body weight were pooled. Change was defined as the difference in the individual's physical activity level or weight between the baseline and the last reported measurement for the time period used in the study (i.e., pre-diagnosis to post-diagnosis or only post-diagnosis). Changes in physical activity level were conceptualized as an increase, decrease, or no change in the amount of physical activity between the two time points (Table 2), or an increase from a low to a higher category of physical activity level, a decrease from a high to a lower category or no change in category between the two time points (Table 2). In the meta-analysis, we compared increased with decreased (or unchanged) physical activity level (reference) and weight gain with stable weight (reference). For the meta-analysis, we considered only weight gain over time, as weight loss in cancer survivors can be unintentional and unrelated to changes in lifestyle, e.g., due to taste alterations [29], anorexia, and wasting syndrome [30].

For studies that reported quality of life data, we calculated the standardized mean difference (SMD) and compared patients that increased physical activity level (or maintained at active level) with patients that decreased physical activity level during follow-up or were unchanged (this was for one study in the group of inactive/insufficiently active at baseline, [31]) (Table 2).

For the studies that reported mortality data, the reported adjusted HRs with corresponding CIs were pooled, and physical activity or weight gain were compared with the reference group (no change or decrease).

Pooled effect estimates were calculated using a random effects model that accounted for within-study and betweenstudy variation [32]. Heterogeneity of effects across studies was tested using the l^2 statistic, which represented the percent of total variation across studies that was attributable to heterogeneity rather than to chance. The Chi-square statistic was also used to test heterogeneity. An l^2 statistic index >50 % and a Chi-square *p* value <0.10 indicated the presence of substantial heterogeneity in the data.

Small study effects (e.g., publication bias) were assessed using the Egger's regression asymmetry test [33] and funnel plot analysis. These effects were assumed to be present for p values <0.10. When they were present, the HR values were naturally logarithm-transformed, and standard errors calculated using the Greenland formula [34].

All statistical analyses were performed using STATA 12.0 software (StataCorp, College Station, TX, USA).

Results

Selection of studies

The search of the three databases yielded 2,053 article titles (excluding 1,406 duplicates) (Fig. 1). A total of 1,891 articles were excluded after screening the titles, and 110 were excluded after abstract reviews. Forty-five of the remaining 52 articles were excluded after reading the full text publications. Seven articles were included in the current review. Three (43 %) were ranked as high quality [31, 35, 36], and four (57 %) were ranked as adequate quality [37–40].

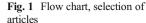
First author, year, study origin	Methodology quality score	Characteristics of participants: age, sample size (% males), tumor stage	Timing of physical activity (tools) and weight assessment and definition of change	Follow-up	Outcome: scores (quality of life) and adjusted HR, 95 % CI (mortality)
Quality of life endpoint Courneya, 1997 [37] Alberta Cancer Registry, Canada	×	Mean age: 62.1 (range 26–81); N=130 (65 % males); Stages 1.5 % I; 38.5 % II; 47.7 % II; 6.2 % IV (diagnosis 1992–1995)	Physical activity: recall pre-diagnosis, during treatment, post-treatment (self-reported; Leisure Score Index of the Godin Leisure-Time Exercise Questionnaire). Change measure: exercise pattern groups based on activity level, ≥16 MET/week (active) and <16 MET/ week (inactive), at each time point. Maintainers (31 %; <i>N</i> =41): active at all three time points; Temporary relapsers (16 %; <i>N</i> =21): inactive only during treatment; Permanent relapsers (14 %; <i>N</i> =29): active pre-diagnosis, but inactive both during treatment and post-treatment; Non exercisers (30 %; <i>N</i> =39): inactive at all three time point.	27.2±12.3 [9–51] months since diagnosis; (FACT-C)	<i>Pre- to post-diagnosis</i> Mean score (SD): Maintainers: 3.35 (0.42) Temporary relapsers: 3.37 (0.44) Permanent relapsers: 2.87 (0.70) Non exercisers: 3.31 (0.63)
Courneya, 2003 [38] 10 Alberta Cancer Registry, Canada	10	Ancillary study: Control: mean age 61.1; <i>N</i> =31 (65 % males) Intervention: mean age 59.9; <i>N</i> =62 (55 % males) Stage III-IV: 77.6 % (diagnosis period not reported)	Physical activity: at 3 months post-surgery and 16 week thereafter (self-reported; Leisure Score Index of the Godin Leisure-Time Exercise Questionnaire). Change measure: those who improved in treadmill time over the course of the intervention (Increased fitness: $N=58$) and those who decreased or showed no change (Decreased fitness: $N=35$).	approx. 7 months post-surgery; (FACT-C)	<i>Post-diagnosis</i> Mean score (SD) [change from baseline] Increased fitness: 110.9 (14.9) [+4.3 (13.2)] Decreased fitness: 103.7 (19.8) [-2.2(16.1)] Difference between groups in mean change [95 % CI]: 6.5 [0.4 to 12.6] (intention-to-treat analyses did not yield any significant differences between groups)
Lynch, 2008 [31] Queensland Cancer Registry, Australia	12	Age caregories: 9 % 20-49; 19 % 50-59; 34 % 60-69; 38 % 70-80; N=1,966 (60 % males) Duke's stages: 24.7 % A; 35.2 % B; 30 % C; 10.1 % D (diagnosis 2003–2004)	Physical activity: interviewed at approximately 6, 12, and 24 months post-diagnosis (self-reported; Active Australia Survey). Categories of physical activity level: inactive (0 min/ week), insufficiently active (1–149 min/week), sufficiently active (≥150 min/week). Change measure: intraindividual change in physical activity measured by calculating the difference between a participant's physical activity level at a certain point in time and his/her average physical activity level during the study.	24 months since diagnosis (FACT-C)	<i>Post-diagnosis</i> Proportional increase in quality of life for increase in physical activity category (95 % CI): 7.9 [4.9 to 11.0], corresponding to an increase of approximately 8 FACT-C points.
Mortality endpoint Meyerhardt, 2006 [39]10 Nurses' Health Study Cohort, US	9]10	median age: 63 to 66 dependent on exercise; <i>N</i> =573 ; (0 % males) Stages: 31.8 % I; 36.2 % II; 32.0 % III (diagnosis period 1986–2002)	Physical activity: self-reported duration of participation in walking and vigorous activities pre-diagnosis (median, 6 months before diagnosis) and post-diagnosis (>1 year-<4 years, median: 22 months), MET hrs/week. Change measure: change in physical activity calculated based on the difference in exercise categories (<3,	median: 9.6 years (with 95 % observed for ≥5 years)	<i>Pre to post-diagnosis</i> - Colorectal cancer–specific mortality ^a Increased: 0.48 (0.24 to 0.97) No change: 1.00 (reference) Decreased: 1.32 (0.74 to 2.34) - Overall mortality ^a

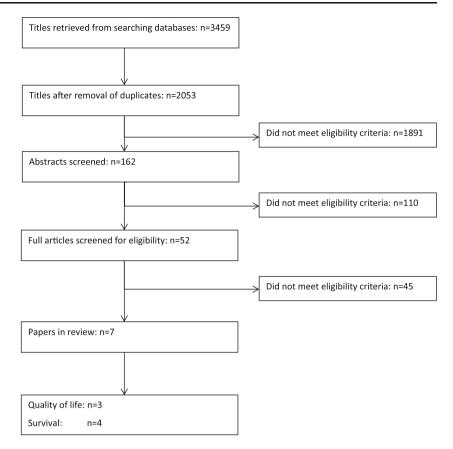
Table 2Characteristics of the studies included

Table 2 (continued)	_				
First author, year, study origin	Methodology quality score	Characteristics of participants: age, sample size (% males), tumor stage	Timing of physical activity (tools) and weight assessment and definition of change	Follow-up	Outcome: scores (quality of life) and adjusted HR, 95 % CI (mortality)
Baade, 2011 [35] Queensland Cancer Registry, Australia	=	median age 67; <i>N</i> =1,825 (60 % males), Stages: 24.5 % I; 32.3 % II; 30.8 % II; Unknown: 12.3 % (diagnosis period 2003–2004)	3–8.9, 9–17.9, ≥18 MET-hours per week) at those two time points; Increase (from low to high category): <i>N</i> = 144 (27.5 %); No change: <i>N</i> =203 (38.8 %); Decrease (from high to low category): <i>N</i> =176 (33.7 %) Physical activity: recall pre-diagnosis (time 0), and interviewed at approximately 5 (time 1) and 12 months post-diagnosis (time 2) (self-reported; Active Australia Survey). Change measure: change in physical activity from time 0 to time 1 and from time 1 to time 2; change assessed by grouping patients into 3 groups: no change or decreased, increased by 2 h per week.	median: 4.9 years [4.0-6.0]	Increased: 0.51 (0.30 to 0.85) No change: 1.00 (reference) Decreased: 1.23 (0.79 to 1.91) - Colorectal cancer-specific mortality ^b <i>Pre to post-diagnosis</i> Increased ≥ 2 h/week: 1.03 (0.59 to 1.80) Increased ≤ 2 h/week: 1.32 (0.89 to 1.98) No change or decreased: 1.00 (reference) <i>Post-diagnosis</i> Increased ≥ 2 h/week: 0.64 (0.44 to 0.93) Increased ≥ 2 h/week: 0.68 (0.48 to 0.97) No change or decreased: 1.00 (reference) <i>Post-diagnosis</i> Increased ≥ 2 h/week: 1.66 (0.65 to 1.71) Increased ≥ 2 h/week: 1.27 (0.88 to 1.83) No change or decreased: 1.00 (reference) <i>Post-diagnosis</i> Increased ≥ 2 h/week: 1.27 (0.88 to 1.83) No change or decreased: 1.00 (reference) <i>Post-diagnosis</i> Increased ≥ 2 h/week: 0.69 (0.5 to 0.94) Increased ≥ 2 h/week: 0.79 (0.50 to 1.04) No change or decreased: 1.00 (reference) <i>Post-diagnosis</i> Increased ≤ 2 h/week: 0.79 (0.50 to 1.04) No change or decreased: 1.00 (reference)
Meyerhardt, 2008 [40] 10 Cancer and Leukemia Group B (CALGB 89803) adjuvant therapy Trial, US	0]10 8	age not reported; <i>N</i> =836 (~58 % males) Stage: 100 % III (diagnosis period not reported)	Weight: self-reported weight during adjuvant therapy (4 months after surgery; time 1) and 6 months after adjuvant therapy (14 months after surgery; time 2). Change measure: change in weight as measured from time 1 to time 2 (weight gain or weight loss); change assessed by grouping patients into 5 groups: ≥ 5 kg gain, 2 to 4.9 kg gain, 2 kg gain or loss (reference), 2.1 to 5 km loss ≤ 5 km loss	median: 5.3 years (from time 1 to end follow-up)	<i>Post-diagnosis</i> - Overall mortality ° ≥5 kg gain: 1.23 (0.65 to 2.31) 2-49 kg gain: 0.97 (0.43 to 2.18) ±2 kg: 1.00 (reference) 2.1-5 kg loss: 0.89 (0.31 to 2.57) >5 kg loss: 1.13 (0.44 to 2.93)
Baade, 2011 [35] Queensland Cancer Registry, Australia	=	median age 67; N=1,825 (60 % males), Stages: 24.5 % I; 32.3 % II; 30 8 % III; Unknown: 12.3 % (diagnosis period 2003–2004)	Weight: self-reported weight recall pre-diagnosis (time 0), and interviewed at approximately 5 (time 1) and 12 months post-diagnosis (time 2) Change measure: change in weight from time 0 to time 1 and from time 1 to time 2; change assessed by grouping patients into 5 groups: >5 kg gain, 2 to 4.9 kg gain, 2 kg gain or loss (reference), 2 to 4.9 kg loss, >5 kg loss.	4.9 years [4.0 - 6.0]	 Colorectal cancer-specific mortality ^d <i>Pre to post-diagnosis</i> 5 kg gain: 1.63 (1.02 to 2.61) 2-4.9 kg gain: 1.12 (0.60 to 2.09) ±2 kg: 1.00 (reference) 2-4.9 kg loss: 1.10 (0.83 to 1.46) 55 kg loss: 1.10 (0.83 to 1.20) <i>Post-diagnosis</i> 5 kg gain: 0.91 (0.69 to 1.20) ±2 kg: 1.00 (reference) ±2 kg: 1.00 (reference) ±2 kg: 1.00 (reference)

Table 2 (continued)	1)				
First author, year, study origin	Methodology quality score	Characteristics of participants: age, sample size (% males), tumor stage	Timing of physical activity (tools) and weight assessment and definition of change	Follow-up	Outcome: scores (quality of life) and adjusted HR, 95 % CI (mortality)
					 >5 kg loss: 2.92 (1.89 to 4.49) - Overall mortality ^d <i>Pre to post-diagnosis</i> >5 kg gain: 1.46 (0.84 to 2.53) 2-4.9 kg gain: 1.02 (0.69 to 1.50) ±2 kg: 1.00 (reference) 2-4.9 kg loss: 1.02 (0.73 to 1.42) >5 kg gloss: 1.64 (1.24 to 2.15) <i>Post-diagnosis</i> >5 kg gain: 0.89 (0.64 to 1.25) 2-4.9 kg gain: 1.02 (0.69 to 1.50) ±2 kg: 1.00 (reference) 2-4.9 kg gain: 1.02 (0.51 to 2.68) >5 kg loss: 1.59 (0.95 to 2.68) >5 kg loss: 3.21 (1.95 to 5.31)
Campbell, 2012 [36] 11 Cancer Prevention Study-II Nutrition Cohort, US	n 5] 11	40–93 years at diagnosis; N=2303 (56 % males), SEER summary stage: 51 % localized, 49 % regional (diagnosis period 1992–2007)	Weight: self-reported weight pre-diagnosis (mean 7 years pre-diagnosis) and post-diagnosis period (mean 18 months after diagnosis) Change measure: change in weight from pre-diagnosis to the post-diagnosis period: weight gain or loss of \leq 10 lbs between two periods 10 lbs≈4.5 kg	median: 6.4 years [2 days–16.1 year]	Pre to post-diagnosis - Colorectal cancer-specific mortality ° >10 lbs gain: 1.34 (0.92 to 1.94) ± 10 lb: 1.00 (reference) >10 lbs loss: 1.65 (1.24 to 2.19) - Overall mortality ° >10 lbs gain: 1.09 (0.85 to 1.40) ± 10 lbs loss: 1.96 (1.63 to 2.34) >10 lbs loss: 1.96 (1.63 to 2.34)
MET metabolic equ ^a Adjusted for body J	iivalents, FACT-C mass index, stage	Functional Assessment of Cancer of disease (I, II, III), grade of tunn ement of honor in hody more in the	<i>MET</i> metabolic equivalents, <i>FACT-C</i> Functional Assessment of Cancer Therapy-Colorectal, <i>SD</i> standard deviation, <i>CI</i> confidence interval ^a Adjusted for body mass index, stage of disease (I, II, III), grade of tumor differentiation, colon or rectal primary, age at diagnosis, year of diagnosis, receipt of chemotherapy (yes, no, unknown), time from diagnosis to abrevial activity measument channel in body mass index.	nterval ur of diagnosis, receipt c	of chemotherapy (yes, no, unknown), time from
^b Adjusted for 5-moi 29.9, ≥ 30 , or unknow 2, or ≥ 3)	mth post-diagnosi wn), smoking stat	is PA level (sedentary, insufficient us (never smoked, current smoked	^b Adjusted for 5-month post-diagnosis PA level (sedentary, insufficient active, and sufficient active), age (<50, 50–59, 60–69, or ≥70 years), stage (stages I, II, III, or unknown), BMI (<18, 18–24.9, 25– 29.9, ≥30, or unknown), smoking status (never smoked, or former smoked), site (colon or rectum), treatment (surgery only, surgery and adjuvant, or unknown), sex and comorbidities (0, 1, 2, or ≥3)	0 years), stage (stages I / only, surgery and adju	, II, III, or unknown), BMI (<18, 18–24.9, 25– vant, or unknown), sex and comorbidities (0, 1,
^c Adjusted for sex, age, depth of invasion through bow time of surgery, baseline performance status (0 v 1–2 (current, past, and never), and physical activity level	tge, depth of invas eline performance tever), and physic	sion through bowel wall (T1-2 v T: a status (0 v 1–2), treatment arm, t al activity level	^c Adjusted for sex, age, depth of invasion through bowel wall (T1-2 v T3-4), number of positive lymph nodes (1–3 v \geq 4), presence of clinical perforation at time of surgery, presence of bowel obstruction at time of surgery attraction at time of surgery attraction at time of surgery presence of bowel obstruction at time of surgery baseline performance status (0 v 1–2), treatment arm, time between questionnaire one and questionnaire two, time-varying body mass index, smoking status at time of questionnaire two (current, past, and never), and physical activity level	clinical perforation at ti varying body mass inde	me of surgery, presence of bowel obstruction at ex, smoking status at time of questionnaire two
^d Adjusted for 5-mo.	onth post-diagnosi	is weight, height, PA level (sedent	^d Adjusted for 5-month post-diagnosis weight, height, PA level (sedentary, insufficient active, and sufficient active), age (<50, 50–59, 60–69, or ≥70 years), stage (stages I, II, III, or unknown), smoking	9, 60–69, or \geq 70 years)), stage (stages I, II, III, or unknown), smoking

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Characteristics of the studies

Descriptions of the characteristics of the studies described in the included articles are presented in Table 2. Except for one article [37], all were published after 2003. One article included results of an ancillary analysis of an RCT using data combined from two study arms [38]. Two articles reported studies of the same research group, using data from the same study cohort, but each examined a different endpoint (quality of life [31], mortality [35]). Quality of life was the endpoint in three reported studies [31, 37, 38], using the Functional Assessment of Cancer Therapy-Colorectal (FACT-C), which measures colorectal cancer-specific quality of life. Mortality was the endpoint in four reported studies [35, 36, 39, 40].

In five articles, the association of changes over time in physical activity level with quality of life or mortality was reported. Three articles focused on changes in weight and mortality over time. No articles examined associations between weight change and quality of life.

Both weight and physical activity were self-reported. In one study, physical activity was measured retrospectively [37]. The instruments for the assessment of physical activity varied among the studies. The Leisure Score Index (LSI) of Godin Leisure-Time Exercise Questionnaire was used in the studies reported by Courneya et al. [37, 38], while the Active Australia Survey was used in the study of Lynch et al. [31]. Meyerhardt et al. [39] used the self-reported data on time spent for walking and vigorous activities of the Nurses' Health Study. Physical activity measures were quantified as the number of metabolic equivalents (MET) per week, the number of minutes of physical activity per week, and meeting or not meeting a guideline for moderate to strenuous intensity exercise per week. A substantial proportion of survivors had a decline in physical activity during treatment and merely returned to pretreatment levels in the long term. Courneya et al. [37] found that there was a decrease in the proportion of physically active (≥ 16 MET week⁻¹) survivors. At pre-diagnosis, 61.5 % were physically active. This proportion declined to 36.9 % during treatment and to 53.1 % post-treatment. A decrease in the proportion of survivors that were sufficiently active (≥ 150 min week⁻¹) was observed in the Lynch et al. [31] cohort study. This proportion declined from 53 % at pre-diagnosis to 32 % at 6-month post-diagnosis, then increased to 37 % at 12 months and 39 % at 24-month post-diagnosis. Pooled HR estimates were not calculated for the association between decreased physical activity and mortality because these data were published in only one article [39]. A considerable proportion of survivors (64 % in the Meyerhardt et al. [40] and 27.8 % in the Baade et al. [35] studies) gained \geq 5 kg after completion of treatment.

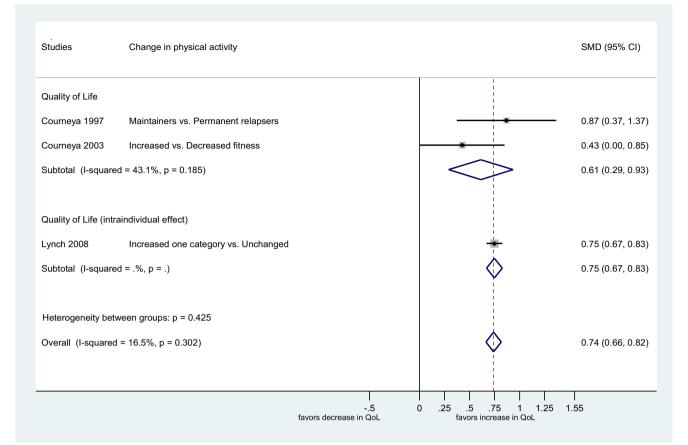


Fig. 2 Forest plot of the association between change in physical activity and quality of life among colorectal cancer survivors. The *squares* indicate the study-specific point estimates. *The width of the horizontal lines* indicates the 95 % confidence intervals (CIs). *The diamonds* represent the pooled estimates. *Maintainers* indicate those active throughout study

period and *permanent relapsers* those active pre-diagnosis, but inactive both during treatment and post-treatment (Courneya, 1997); unchanged physical activity indicates those inactive/insufficiently active at baseline (Lynch 2008)

Change in physical activity and quality of life

Patients that increased their physical activity level or remained active throughout the diagnosis and treatment phases had significantly higher quality of life scores than patients with reduced physical activity levels after treatment. In the individual studies, there was a clear association between change in physical activity level and quality of life when patients who increased, decreased, or did not change their activity levels were compared (Table 2). In their 1997 study, Courneya et al. [37] found that patients who maintained their pre-diagnosis activity levels had higher FACT-C scores compared with patients who decreased their activity levels. In the ancillary study performed within the RCT, Courneya et al. [38] found that FACT-C scores were lower in individuals that were less fit at the end of follow-up. FACT-C scores increased 4.3 points in individuals that increased their cardiovascular fitness, while a decrease of 2.2 points was observed in those who remained unchanged or showed a decrease in cardiovascular fitness. Fitness was assessed by the treadmill test. Lynch et al. [31] measured the intra-individual change in physical activity and found an increase of approximately 8 FACT-C points, from 109.9 (standard deviations (SD)=10.5) to 117.9 (SD=10.9) points in individuals who were inactive or insufficiently active at baseline but became more active during follow-up.

Figure 2 presents the results for the forest plot for the association between changes in physical activity level and quality of life. The meta-analysis revealed that compared with decreased physical activity post-diagnosis and/or post-treatment, increased physical activity was associated with significantly higher quality of life scores (SMD=0.74 (CI=0.66–0.82) with no heterogeneity between the studies (I^2 =16.5%, p value=0.302)). The analysis of publication bias indicated that no bias was present (Egger's test; p value=0.701).

Fig. 3 Forest plot of the association between increase in physical activity ► and disease-specific and overall mortality among colorectal cancer survivors. *The squares* indicate the study-specific point estimates. *The width of the horizontal lines* indicates the 95 % confidence intervals (CIs). *The diamonds* represent the pooled estimates. Reference group in Meyerhardt et al. (2006): unchanged activity category (MET h/week); reference group in Baade et al. (2011): unchanged or decreased in physical activity level

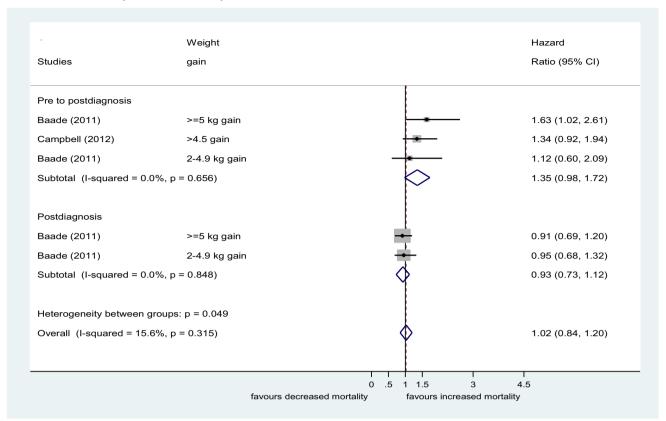
Colorectal cancer specific mortality

	Physical	
Studies	activity	HR (95% CI)
Pre to postdiagnosis		
Meyerhardt 2006	Increase physical activity	0.48 (0.24, 0.97
Baade 2011	Increased physical activity, <=2 h/wk	■ 1.32 (0.89, 1.98
Baade 2011	Increased physical activity, >2 h/wk	1.03 (0.59, 1.80
Subtotal (I-squared =	= 71.4%, p = 0.030)	0.80 (0.53, 1.07
Postdiagnosis		
Baade 2011	Increased physical activity, <=2 h/wk	0.68 (0.48, 0.97
Baade 2011	Increased physical activity, >2 h/wk	0.64 (0.44, 0.93
Subtotal (I-squared =	= 0.0%, p = 0.821)	0.66 (0.49, 0.83
Heterogeneity betwee	en groups: p = 0.399	
Overall (I-squared =	48.5%, p = 0.101)	0.70 (0.55, 0.85
	0.5	1 1.5 3 4.5
	favours decreased mortality	favours increased mortality

Overall mortality

-	Physical	
Studies	activity	HR (95% CI)
Pre to postdiagnosis		
Meyerhardt (2006)	Increase physical activity	0.51 (0.30, 0.85
Baade (2011)	Increased physical activity, <=2 h/wk	■ 1.27 (0.88, 1.83
Baade (2011)	Increased physical activity, >2 h/wk	1.06 (0.65, 1.71
Subtotal (I-squared =	77.4%, p = 0.012)	0.76 (0.54, 0.98
Postdiagnosis		
Baade (2011)	Increased physical activity, <=2 h/wk	0.79 (0.59, 1.04
Baade (2011)	Increased physical activity, >2 h/wk	0.69 (0.50, 0.94
Subtotal (I-squared =	0.0%, p = 0.533)	0.74 (0.58, 0.90
Heterogeneity between	groups: p = 0.871	
Overall (I-squared = 5	6.7%, p = 0.055)	0.75 (0.62, 0.87
	1 1 ¹ 0 .5	1 I I 1 1.5 3 4.5
	favours decreased mortality	favours increased mortality

Colorectal cancer specific mortality



Overall mortality

	Weight		Hazard
Studies	gain		Ratio (95% CI)
Pre to postdiagnosis			
Baade (2011)	>=5 kg gain		1.46 (0.84, 2.53)
Campbell (2012)	>4.5 gain	÷	1.09 (0.85, 1.40)
Baade (2011)	2-4.9 kg gain		0.90 (0.41, 1.96)
Subtotal (I-squared = 0.0	%, p = 0.619)	\diamond	1.10 (0.85, 1.35)
Postdiagnosis			
Meyerhardt (2008)	>=5 kg gain		1.23 (0.65, 2.31)
Baade (2011)	>=5 kg gain		0.89 (0.64, 1.25)
Meyerhardt (2008)	2-4.9 kg gain		0.97 (0.43, 2.18)
Baade (2011)	2-4.9 kg gain	.	1.02 (0.69, 1.50)
Subtotal (I-squared = 0.0%, p = 0.875)		\diamond	0.96 (0.74, 1.19)
Heterogeneity between grou	ups: p = 0.408		
Overall (I-squared = 0.0%	b, p = 0.886)	\diamond	1.03 (0.86, 1.19)
		0.511.5 3	4.5

Fig. 4 Forest plot of the association between weight gain and disease-specific and overall mortality among colorectal cancer survivors. *The squares* indicate the study-specific point estimates, and *the width of the horizontal lines* indicates the 95 % confidence intervals (CIs). *The diamonds* represent the pooled estimates. Reference group in Meyerhardt et al. (2008) and Baade et al. (2011): ±2 kg; reference group in Campbell (2012): weight stable

Change in physical activity and survival

There was a significant association between increases in physical activity in the post-diagnosis period and reduced colorectal cancer death, but increases from pre-diagnosis to 5-month post-diagnosis were not significant (Table 2, Fig. 3). However, the overall pooled HR estimate of 0.70 (CI=0.55–0.85) indicated that the change was significant. The tests for heterogeneity among the studies for the effect of increased physical activity on disease-specific mortality were not significant (I^2 = 48.5 %, *p* value=0.101). A similar pattern was observed for overall mortality (pooled HR=0.75, CI=0.62–0.87; I^2 = 56.7 %, *p* value=0.055; Fig. 3).

The results of the Egger's test indicated that no publication bias (p value=0.885) was present in the studies that examined the effect of physical activity on disease-specific mortality.

Weight gain and survival

The Meyerhardt et al. [40] study was the only study that assessed the impact of change in body weight on diseasefree and recurrence-free survival (Table 2). Recurrence was defined as tumor recurrence, occurrence of a new primary colon tumor, or death from any cause. These survival endpoints were not included in the comparisons of the three studies that reported data on weight and mortality changes. In the studies included, there was a tendency for a U-shape for the association between change in weight and either diseasespecific or overall mortality (Table 2). As aforementioned, we considered only weight gain over time for the meta-analysis, as weight loss in cancer survivors can be unintentional and unrelated to health behaviors. Despite a tendency toward an association between weight gain from pre- to post-diagnosis and mortality, weight gain did not significantly affect diseasespecific mortality (pooled HR=1.02, CI=0.84–1.20; I^2 = 15.6 %, p value=0.315) or overall mortality (pooled HR= 1.03, CI=0.86–1.19; $I^2=0.0$ %, p value=0.886) (Fig. 4).

The results for the Egger's test indicated that no publication bias was present (p values=0.249).

Discussion

We systematically reviewed the literature for studies examining the association between longitudinal change in physical activity level and weight and quality of life and mortality among colorectal cancer patients. Despite the general focus on adoption of healthier lifestyles and its effect on quality of life for cancer survivors, we retrieved only seven studies that examined this issue. Increase in physical activity level was associated with an improved quality of life and improved prognosis. There was no association between weight gain and mortality among survivors.

Two recent systematic reviews and meta-analyses of RCTs also concluded that physical activity interventions during active treatment and post-treatment may improve quality of life of cancer survivors [10, 11], but this finding was mostly based on RCTs conducted among breast cancer survivors. Two recently published RCTs evaluating an intervention aimed at increasing physical activity in colorectal cancer survivors failed to find an intervention effect on quality of life despite significant improvements in physical activity level in the intervention group compared with the control group [41, 42]. Hawkes et al. [42] found that participation in the CanChange intervention program (Cancer Council Queensland, Brisbane, Australia) yielded significant between-group difference in physical activity at 12-month post-diagnosis, which did not translate into differences in quality of life characteristics between the intervention and control groups. Similarly, Pinto et al. [41] found no significant between-group differences in quality of life characteristics despite increases in physical activity and fitness in the intervention group, which also received telephone counseling to support physical activity. Assessment of individual change would probably have been more likely to capture the effects of change in physical activity level on quality of life in these RCTs. Based on the results of three observational studies, in this current metaanalysis, we did find a positive association between an increase in physical activity level and quality of life. These contrasting findings from the observational studies might have been a consequence of selection bias as the RCTs probably included colorectal cancer survivors who experienced fewer disease-related symptoms or physical side effects of treatment or survivors who were more able and willing to engage into physical activity post-treatment. Pre-diagnosis exercise and exercise intention were found to be significant determinants of post-treatment physical activity, which was predominantly mediated by the individual's attitude [43]. However, as recently stated by Inoue-Choi et al. [44], it is also possible that individuals with higher quality of life post-treatment were more capable of physical activity.

A limited number of studies evaluated change in physical activity over time and prognosis [35, 39]. The results of our current meta-analysis suggested that an increase in physical activity, particularly during the post-diagnosis period, is associated with a decrease in colorectal cancer-specific and overall mortality. The observed findings for change in physical activity measured from pre- to post-diagnosis were seemingly dependent on the length of the interval. Meyerhardt et al. [39] found that at approximately 22-month post-diagnosis, there was a significant decrease in disease-specific mortality among women who had increased their pre-diagnosis physical activity category compared with women who remained in the same category or shifted to a lower category. However, in a population with a comparable age and stage distribution, Baade et al. [35] found that at 5-month post-diagnosis, there was no association between an increase in physical activity level and disease-specific mortality.

There are also few studies of weight change over time and potential effects on quality of life and survival in colorectal cancer patients. Only three studies have addressed the association between weight change and colorectal cancer-specific and overall mortality. The results of this current meta-analysis suggested that there were no beneficial or detrimental effects of weight gain on mortality. In studies with breast cancer survivors, women who gain weight after diagnosis were significantly more likely to experience cancer recurrence and mortality [45], which has been attributed to a simultaneous increase in fat mass and a decrease in lean body mass [46]. A possible explanation for this contradictory observation in colorectal cancer survivors might be, as suggested by Lynch et al. [31], that their weight gain is not related to health behavior, but instead is a reflection of the recovery of experienced weight loss related to the cancer, treatment, or both, which could have led to changes in body composition.

Our review has several limitations resulting from the availability and the methodology of the published data, and these limitations should be considered when interpreting our results. First, the number of studies on the effects of change over time in physical activity and body weight on quality of life and mortality was very limited. Except for one study in which physical activity was based on changes in physical fitness as measured in treadmill test over the course of the study [38], data on both body weight and physical activity in most studies were self-reported instead of objective assessments. Having been diagnosed with colorectal cancer, and probably subsequently having acquired the knowledge on physical inactivity and weight being risk factors for colorectal cancer, might have influence on their reporting. Asking participants to recall their pre-diagnosis physical activity levels and weight is also subjected to bias. Second, there were large variations in the lengths of the interval used for measuring change over time in physical activity and weight as well as variations in baseline time points of measurements, either pre-diagnosis, post-diagnosis, or post-treatment (surgery or adjuvant therapy). These variations make recommendations for a specific timing to engage into healthy behaviors (soon after diagnosis or short after treatment) and specific duration for colorectal cancer survivors difficult. Third, the follow-up periods after diagnosis and subsequent timing of endpoint variations in physical activity categories differed between studies. The length of follow-up after diagnosis for quality of life measurement was often limited to 2 years (median of 7 to 24 months), while the greatest impact on quality of life among colorectal cancer survivors seems to occur in the first 2-3 years after diagnosis and stabilizes beyond 3-year post-diagnosis [47]. Hence, both physical activity and quality of life could have been affected by clinical, medical, and psychological factors experienced by survivors [20, 48, 49]. However, despite these short follow-up periods after diagnosis, the three studies included in current meta-analysis indicated a beneficial effect of physical activity on quality of life. The median length of follow-up for the endpoint mortality varied between 5 and 10 years. Although the study design were prospective observational and adjustments were made in the analyses, it is possible that changes in health behaviors other than physical activity or weight have influenced the observed association. Outcome from recent studies suggest that the effect of combination of healthy behaviors rather than the effect of a single healthy behavior should be examined [50]. Effect of combination of healthy behaviors, including maintaining normal body weight, staying physically active, and eating healthy diet, is associated with low risk of mortality [51] and high quality of life [21, 23, 44, 50]. However, results from prospective studies should provide evidence on whether change over time into healthier behavior combination among cancer survivors is also associated with positive effects on survival and quality of life.

In conclusion, based on an analysis of seven studies, we found that an increase in physical activity levels was associated with improved quality of life and reduced risk of diseasespecific mortality in colorectal cancer survivors. Our study showed neither positive nor negative effects of weight gain on mortality. Given the paucity of the literature published on this topic, our findings should be interpreted with caution. More prospective studies with large sample sizes are needed, which apply objective assessments to quantify the change in physical activity level and weight post-diagnosis, and which account for the individual's initial activity and weight status from the moment of cancer diagnosis, to understand what level of physical activity provides prognostic effects. Such studies may support the development of appropriate health education and (personalized) intervention strategies to improve the health and quality of life for colorectal cancer survivors.

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References

- Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D and Bray F (2013) GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer, http://globocan.iarc.fr, accessed on 18/02/ 2014.
- 2. SEER Stat Fact Sheets: colon and rectum (2010). vol 2011. National Cancer Institute, Bethesda
- Maddams J, Brewster D, Gavin A, Steward J, Elliott J, Utley M, Moller H (2009) Cancer prevalence in the United Kingdom: estimates for 2008. Br J Cancer 101(3):541–547
- Demark-Wahnefried W, Pinto BM, Gritz ER (2006) Promoting health and physical function among cancer survivors: potential for prevention and questions that remain. J Clin Oncol 24(32):5125– 5131
- Doyle C, Kushi LH, Byers T, Courneya KS, Demark-Wahnefried W, Grant B, McTiernan A, Rock CL, Thompson C, Gansler T, Andrews KS (2006) Nutrition and physical activity during and after cancer treatment: an American Cancer Society guide for informed choices. CA Cancer J Clin 56(6):323–353
- Demark-Wahnefried W, Jones LW (2008) Promoting a healthy lifestyle among cancer survivors. Hematol Oncol Clin N Am 22(2):319– 342, viii
- 7. Vrieling A, Kampman E (2010) The role of body mass index, physical activity, and diet in colorectal cancer recurrence and survival: a review of the literature. Am J Clin Nutr 92(3):471–490
- Davies NJ, Batehup L, Thomas R (2011) The role of diet and physical activity in breast, colorectal, and prostate cancer survivorship: a review of the literature. Br J Cancer 105(Suppl 1):S52–S73. doi:10.1038/bjc.2011.423
- Ballard-Barbash R, Friedenreich CM, Courneya KS, Siddiqi SM, McTiernan A, Alfano CM (2012) Physical activity, biomarkers, and disease outcomes in cancer survivors: a systematic review. J Natl Cancer Inst 104(11):815–840
- Mishra SI, Scherer RW, Geigle PM, Berlanstein DR, Topaloglu O, Gotay CC, Snyder C (2012) Exercise interventions on health-related quality of life for cancer survivors. Cochrane Database Syst Rev 8, CD007566
- Mishra SI, Scherer RW, Snyder C, Geigle PM, Berlanstein DR, Topaloglu O (2012) Exercise interventions on health-related quality of life for people with cancer during active treatment. Cochrane Database Syst Rev 8, CD008465. doi:10.1002/14651858. CD008465.pub2
- Meyerhardt JA, Heseltine D, Niedzwiecki D, Hollis D, Saltz LB, Mayer RJ, Thomas J, Nelson H, Whittom R, Hantel A, Schilsky RL, Fuchs CS (2006) Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: findings from CALGB 89803. J Clin Oncol 24(22):3535–3541
- Meyerhardt JA, Giovannucci EL, Ogino S, Kirkner GJ, Chan AT, Willett W, Fuchs CS (2009) Physical activity and male colorectal cancer survival. Arch Intern Med 169(22):2102–2108
- Kuiper JG, Phipps AI, Neuhouser ML, Chlebowski RT, Thomson CA, Irwin ML, Lane DS, Wactawski-Wende J, Hou L, Jackson RD, Kampman E, Newcomb PA (2012) Recreational physical activity, body mass index, and survival in women with colorectal cancer. Cancer Causes Control 23(12):1939–1948. doi:10.1007/s10552-012-0071-2
- Campbell PT, Patel AV, Newton CC, Jacobs EJ, Gapstur SM (2013) Associations of recreational physical activity and leisure time spent sitting with colorectal cancer survival. J Clin Oncol 31(7):876–885
- Haydon AM, Macinnis RJ, English DR, Giles GG (2006) Effect of physical activity and body size on survival after diagnosis with colorectal cancer. Gut 55(1):62–67

- Doria-Rose VP, Newcomb PA, Morimoto LM, Hampton JM, Trentham-Dietz A (2006) Body mass index and the risk of death following the diagnosis of colorectal cancer in postmenopausal women (United States). Cancer Causes Control 17(1):63–70
- Dignam JJ, Polite BN, Yothers G, Raich P, Colangelo L, O'Connell MJ, Wolmark N (2006) Body mass index and outcomes in patients who receive adjuvant chemotherapy for colon cancer. J Natl Cancer Inst 98(22):1647–1654
- Mosher CE, Sloane R, Morey MC, Snyder DC, Cohen HJ, Miller PE, Demark-Wahnefried W (2009) Associations between lifestyle factors and quality of life among older long-term breast, prostate, and colorectal cancer survivors. Cancer 115(17):4001–4009
- Buffart LM, Thong MS, Schep G, Chinapaw MJ, Brug J, van de Poll-Franse LV (2012) Self-reported physical activity: its correlates and relationship with health-related quality of life in a large cohort of colorectal cancer survivors. PLoS One 7(5):e36164. doi:10.1371/ journal.pone.0036164
- Grimmett C, Bridgewater J, Steptoe A, Wardle J (2011) Lifestyle and quality of life in colorectal cancer survivors. Qual Life Res 20(8): 1237–1245
- Peddle CJ, Au HJ, Courneya KS (2008) Associations between exercise, quality of life, and fatigue in colorectal cancer survivors. Dis Colon Rectum 51(8):1242–1248
- Blanchard CM, Courneya KS, Stein K (2008) Cancer survivors' adherence to lifestyle behavior recommendations and associations with health-related quality of life: results from the American Cancer Society's SCS-II. J Clin Oncol 26(13):2198–2204
- Hawkes AL, Gollschewski S, Lynch BM, Chambers S (2009) A telephone-delivered lifestyle intervention for colorectal cancer survivors 'CanChange': a pilot study. Psycho-Oncology 18(4):449–455. doi:10.1002/pon.1527
- Pekmezi DW, Demark-Wahnefried W (2011) Updated evidence in support of diet and exercise interventions in cancer survivors. Acta Oncol 50(2):167–178. doi:10.3109/0284186X.2010.529822
- 26. Blanchard CM, Baker F, Denniston MM, Courneya KS, Hann DM, Gesme DH, Reding D, Flynn T, Kennedy JS (2003) Is absolute amount or change in exercise more associated with quality of life in adult cancer survivors? Prev Med 37(5):389–395
- Cancer Survivorship Research (NCI) http://cancercontrol.cancer.gov/ ocs/definitions.html; accessed 07 October 2013.
- Mols F, Vingerhoets AJ, Coebergh JW, van de Poll-Franse LV (2005) Quality of life among long-term breast cancer survivors: a systematic review. Eur J Cancer 41(17):2613–2619
- DeWys WD, Walters K (1975) Abnormalities of taste sensation in cancer patients. Cancer 36(5):1888–1896
- Tisdale MJ (2010) Cancer cachexia. Curr Opin Gastroenterol 26(2): 146–151. doi:10.1097/MOG.0b013e3283347e77
- Lynch BM, Cerin E, Owen N, Hawkes AL, Aitken JF (2008) Prospective relationships of physical activity with quality of life among colorectal cancer survivors. J Clin Oncol 26(27):4480–4487
- DerSimonian R, Kacker R (2007) Random-effects model for metaanalysis of clinical trials: an update. Contemp Clin Trials 28(2):105– 114
- Egger M, Davey Smith G, Schneider M, Minder C (1997) Bias in meta-analysis detected by a simple, graphical test. BMJ 315(7109): 629–634
- Greenland S (1987) Quantitative methods in the review of epidemiologic literature. Epidemiol Rev 9:1–30
- 35. Baade PD, Meng X, Youl PH, Aitken JF, Dunn J, Chambers SK (2011) The impact of body mass index and physical activity on mortality among patients with colorectal cancer in Queensland, Australia. Cancer Epidemiol Biomarkers Prev 20(7):1410–1420
- Campbell PT, Newton CC, Dehal AN, Jacobs EJ, Patel AV, Gapstur SM (2012) Impact of body mass index on survival after colorectal cancer diagnosis: the Cancer Prevention Study-II Nutrition Cohort. J Clin Oncol 30(1):42–52

 Courneya KS, Friedenreich CM (1997) Relationship between exercise pattern across the cancer experience and current quality of life in colorectal cancer survivors. J Altern Complement Med 3(3):215–226

 Courneya KS, Friedenreich CM, Quinney HA, Fields AL, Jones LW, Fairey AS (2003) A randomized trial of exercise and quality of life in colorectal cancer survivors. Eur J Cancer Care (Engl) 12(4):347–357

- Meyerhardt JA, Giovannucci EL, Holmes MD, Chan AT, Chan JA, Colditz GA, Fuchs CS (2006) Physical activity and survival after colorectal cancer diagnosis. J Clin Oncol 24(22):3527–3534
- 40. Meyerhardt JA, Niedzwiecki D, Hollis D, Saltz LB, Mayer RJ, Nelson H, Whittom R, Hantel A, Thomas J, Fuchs CS (2008) 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 26(25):4109–4115
- Pinto BM, Papandonatos GD, Goldstein MG, Marcus BH, Farrell N (2011) Home-based physical activity intervention for colorectal cancer survivors. Psycho-Oncology 22(1):54–64. doi:10.1002/pon.2047
- 42. Hawkes AL, Chambers SK, Pakenham KI, Patrao TA, Baade PD, Lynch BM, Aitken JF, Meng X, Courneya KS (2013) Effects of a telephone-delivered multiple health behavior change intervention (CanChange) on health and behavioral outcomes in survivors of colorectal cancer: a randomized controlled trial. J Clin Oncol 31(18):2313–2321
- 43. Courneya KS, Friedenreich CM, Arthur K, Bobick TM (1999) Understanding exercise motivation in colorectal cancer patients: a prospective study using the theory of planned behavior. Rehabil Psychol 44(1):68–84
- 44. Inoue-Choi M, Lazovich D, Prizment AE, Robien K (2013) Adherence to the World Cancer Research Fund/American Institute for Cancer Research recommendations for cancer prevention is associated with better health-related quality of life among elderly

female cancer survivors. J Clin Oncol 31(14):1758–1766. doi:10. 1200/JCO.2012.45.4462

- 45. Kroenke CH, Chen WY, Rosner B, Holmes MD (2005) Weight, weight gain, and survival after breast cancer diagnosis. J Clin Oncol 23(7):1370–1378
- 46. Demark-Wahnefried W, Peterson BL, Winer EP, Marks L, Aziz N, Marcom PK, Blackwell K, Rimer BK (2001) Changes in weight, body composition, and factors influencing energy balance among premenopausal breast cancer patients receiving adjuvant chemotherapy. J Clin Oncol 19(9):2381– 2389
- Ramsey SD, Andersen MR, Etzioni R, Moinpour C, Peacock S, Potosky A, Urban N (2000) Quality of life in survivors of colorectal carcinoma. Cancer 88(6):1294–1303
- Chambers SK, Lynch BM, Aitken J, Baade P (2009) Relationship over time between psychological distress and physical activity in colorectal cancer survivors. J Clin Oncol 27(10):1600–1606. doi: 10.1200/JCO.2008.18.5157
- 49. Chambers SK, Meng X, Youl P, Aitken J, Dunn J, Baade P (2012) A five-year prospective study of quality of life after colorectal cancer. Qual Life Res 21(9):1551–1564. doi:10. 1007/s11136-011-0067-5
- 50. Schlesinger S, Walter J, Hampe J, von Schonfels W, Hinz S, Kuchler T, Jacobs G, Schafmayer C, Nothlings U (2014) Lifestyle factors and health-related quality of life in colorectal cancer survivors. Cancer Causes Control 25(1):99–110. doi:10. 1007/s10552-013-0313-y
- Inoue-Choi M, Robien K, Lazovich D (2013) Adherence to the WCRF/AICR guidelines for cancer prevention is associated with lower mortality among older female cancer survivors. Cancer Epidemiol Biomarkers Prev 22(5):792–802. doi:10.1158/1055-9965.EPI-13-0054