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Association Between Intake of Red and Processed Meat and Survival in Patients With Colorectal Cancer in a Pooled Analysis

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Abstract

Background & Aims: Red and processed meat intake is associated with colorectal cancer (CRC) incidence, but it is not clear if intake is associated with patient survival after diagnosis

Methods: We pooled data from 7627 patients with stage I-IV CRC from 10 studies in the International Survival Analysis in Colorectal Cancer Consortium. Cox proportional hazards regression models were used to evaluate the associations of intake of red and processed meat before diagnosis with overall and CRC-specific survival.

Results: Among 7627 patients with CRC, 2338 died, including 1576 from CRC, over a median follow-up time of 5.1 years. In multivariable-adjusted analyses, higher intake of red or processed meat was not associated with overall survival of patients with stage I-III CRC: Q4 vs Q1 red meat hazard ratio [HR], 1.08 (95% CI, 0.93–1.26) and Q4 vs Q1 processed meat HR, 1.10 (95% CI, 0.93–1.32) or with CRC-specific survival: Q4 vs Q1 red meat HR, 1.09 (95% CI, 0.89–1.33) and

Q4 vs Q1 processed meat HR, 1.11 (95% CI, 0.87–1.42). Results were similar for patients with stage IV CRC. However, patients with stage I–III CRC who reported an intake of processed meat above the study-specific medians had a higher risk of death from any cause (HR, 1.12; 95% CI, 1.01–1.25) than patients who reported eating at or less than the median.

Conclusion: In this large consortium of CRC patient cohorts, intake of red and processed meat before a diagnosis of CRC was not associated with shorter survival time after diagnosis, although a possible weak adverse association cannot be excluded. Studies that evaluate dietary data from several time points before and after cancer diagnosis are required to confirm these findings.

Keywords

ISACC; colon cancer; epidemiology; risk factor

Introduction

The role of diet and lifestyle factors in colorectal cancer (CRC) has been extensively studied and evidence suggests that red and processed meat intake is an important dietary risk factor^{1, 2}. Meta-analyses have concluded that high intake of red and processed meat is associated with increased risk of colorectal, colon and rectal cancers^{1, 3, 4}, and in 2015 the International Agency for Research on Cancer classified processed meat as carcinogenic to humans and red meat as probably carcinogenic to humans². The World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) in 2017 judged red meat to be a probable risk factor for CRC, while processed meat was judged to be a convincing risk factor for CRC, recommending to limit the intake of red meat and to avoid processed meat¹.

However, in contrast, limited evidence exists on the role of red and processed meat intake in survival after a diagnosis of CRC^{5, 6}. To our knowledge, few studies have investigated the association between meat consumption and overall survival among men and women diagnosed with CRC^{7–12} and results are inconclusive. In two studies, pre-diagnostic red and processed meat intake was not associated with overall survival or CRC-specific survival^{11, 12}. In another study, higher red and processed meat intake was associated with all-cause mortality and CVD-specific mortality, but not with CRC-specific mortality⁸. Two other studies which assessed the associations between pre-diagnostic meat intake (not limited to red and processed meat) and overall survival did not observe any associations^{7, 10}.

Hence, using individual patient data in ten observational epidemiological studies of the International Survival Analysis in Colorectal Cancer Consortium (ISACC), we aimed to evaluate the association of pre-diagnostic red meat and processed meat intake with overall and CRC-specific survival.

Methods

Study population

This analysis included 10 studies from the International Survival Analysis in Colorectal Cancer Consortium (ISACC). We included data from 7 prospective U.S cohort studies [Cancer Prevention Study II Nutrition cohort (CPSII)¹³; Health Professionals Follow-up

Study (HPFS) ¹⁴; Nurses' Health Study I (NHS I) ^{15–17}; Physician's Health Study (PHS) ¹⁸; Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) ^{19, 20}; VITamins And Lifestyle Study (VITAL) ²¹ and Woman's Health Initiative (WHI) ²² and 3 population based case-control studies from the US and Germany with follow-up of patients [Darmkrebs: Chancen der Verhuetung durch Screening (DACHS) ^{23, 24}; Diet, Activity and Lifestyle Survey (DALIS) ²⁵ and PostMenopausal Hormone Study within the Colorectal Cancer Family Registry (PMH- CCFR)]. These studies are also included in the Genetics and Epidemiology of Colorectal Cancer Consortium (GECCO) which was primarily responsible for the data harmonization^{26, 27} All CRC cases were confirmed by medical record, pathology report or death certificate and included follow-up for survival. Informed consent was obtained from all participants, and the studies were approved by their respective institutional review board.

Data collection and follow-up

Information on demographic and lifestyle factors was collected by self-report using in person interviews and/or structured questionnaires as detailed previously²⁸. As previously described, a multistep data harmonization procedure was carried out to combine the data across the studies for pooled analyses²⁸. Red meat intake (unprocessed red meat including processed red meat, i.e. sausages, in some studies) and processed meat (processed red meat and processed white meat) intake from all participating studies was classified as number of servings per day. Other variables collected by the studies included: age at diagnosis, sex, body mass index (BMI) (kg/m²), smoking status (ever/never at reference time), non-steroidal anti-inflammatory drug (NSAID) use including aspirin (yes/no for regular use at reference time), education (< high school graduate, high school graduate, some college or technical school, college graduate or graduate degree), alcohol intake (nondrinker, 1–28 g/day, >28g/day), family history of CRC in a first degree relative (yes, no), history of diabetes (yes, no), and physical activity (yes: vigorous and moderate physical activity 1 hour/week, no: vigorous and moderate physical activity < 1 hour/week). Additional dietary variables included dietary intake of calcium, folate, fiber, fruit, and vegetables. Information on cancer site (proximal colon, distal colon, or rectal) and cancer stage as determined by AJCC or SEER (AJCC stage 1 or SEER local, AJCC stage 2/3 or SEER regional, AJCC stage 4 or SEER distant) was available for all studies.

The details of assessing survival in the included studies have been described previously ^{13, 14, 17, 21, 23, 25, 29–32} Briefly, half of the studies used active follow-up to ascertain vital status (HPFS, NHS, PHS, PLCO, and WHI); dates and cause of death were confirmed via review of death certificates and/or medical records. For the other studies (VITAL, CPS-II, DACHS, DALIS, PMH-CCFR), vital status was determined through linkage to the National Death Index, state cancer registries, state death records, or population registries with cause of death verified by death certificates. In all studies, patients alive at the most recent follow-up or data linkage were censored on that date in the survival analysis.

Statistical analysis

All statistical analyses were performed at the central ISACC coordinating center using the individual level harmonized data pooled across studies. We used Cox proportional hazards

regression to calculate hazard ratios (HRs) and 95% confidence intervals (CI) for the association of baseline red meat and processed meat intake with overall and CRC-specific survival. Survival time was calculated as the time from diagnosis of CRC to death or end of follow-up. In analyses of CRC-specific survival, patients who died from causes other than CRC were censored at the time of death. We decided *a priori* to stratify results for patients by disease stage analyzing stages I-III and stage IV separately because the overall survival for stage IV patients is poor. Median follow-up time was calculated based on the Kaplan Meier estimate of potential follow-up³³

We constructed separate models for overall and CRC-specific survival. A combination of forwards and backwards variable selection was used to determine variables that were significantly associated with survival for inclusion in the multivariable adjusted model. All models included age at diagnosis, sex, cancer stage, cancer site and study. The multivariable model included additionally: BMI, smoking status, family history of CRC, aspirin/NSAID use and education. Other potential confounding variables that were considered but not included in the models were: physical activity, history of diabetes, total energy intake, alcohol intake, and intake of calcium, folate, fruit, vegetables and fiber. We examined Schoenfeld residuals and included strata variables for those which violated the proportional hazards assumption. Missing data for BMI, smoking status, family history of CRC, regular use of aspirin/NSAID use and education (all less than 8%) were accounted for by mean and mode imputation, and a missing indicator variable was used for missing stage at diagnosis.

We used study- and sex-specific quartiles of red meat and processed meat intake, using the lowest quartile as the referent category. We also examined the association with red meat and processed meat intake modelled as a dichotomous variable (< or > study-specific medians) and as a continuous variable (servings/day) (see Supplementary Table 1 for study-specific median intake). Tests for trend across quartiles were conducted by assigning participants the study and sex specific median value per quartile. We also conducted analyses stratified by age (<70 years, >70 years), sex (male, female), cancer site (colon, rectum), family history of CRC (yes, no), BMI (18.5–24.9, >24.9–<30, >30) and study design (cohort, case-control). We tested the significance of multiplicative interaction with age, sex, family history and BMI using the likelihood ratio tests. All analyses were performed using R 2.15.3.

Results

From 10 studies, data were harmonized for a total of 8316 (4502 female, 3814 male) patients. We excluded individuals from the present analyses with missing information on red meat (n=689) or processed meat (n=968) and those with missing follow up time (n=2). Consequently, the total study population for the current analyses comprised of 7625 CRC patients: 6695 CRC patients with stage I-III disease and 930 CRC patients with stage IV disease. More information on the individual studies is provided in Supplementary Table 1. Among the patients with stage I-IV CRC included in the analyses, 2338 (31%) died during follow-up and 1576 (21%) died from CRC. The median follow-up time was 5.1 years (IQR: 3.4–7.5 years).

The baseline characteristics of the study population according to red meat and processed meat intake are provided in Table 1. Patients were on average 68.9 years at diagnosis of CRC. Patients who frequently ate red meat and processed meat were more likely to smoke, they also tended to be younger, to have a higher BMI, to drink more alcohol, and to be less physically active. Family history of CRC did not differ according to red meat or processed meat intake (Table 1). Despite the observed difference among men and women in Table 1, females tended to eat less meat than men as seen in Supplementary Table 1. The higher percentages observed for females in Table 1 are mostly a function of there being more females in the included dataset than males.

In multivariable analyses among stage I-III patients, red meat and processed meat consumption in the highest versus the lowest quartile before CRC diagnosis was not associated with overall (red meat: HR:1.08, 95% CI:0.93–1.26; processed meat: HR:1.10, 95% CI:0.93–1.32) or CRC-specific (red meat: HR 1.09, 95% CI:0.89–1.33; processed meat: HR:1.11, 95% CI:0.87–1.42) survival (Table 2). No associations were observed for red meat or processed meat in the continuous analysis of servings per day for both overall and CRC-specific survival. However, stage I-III patients who reported intakes higher than the median amount of processed meat had a higher risk of death from any cause (HR:1.12, 95% CI: 1.01 –1.25), and a higher risk of CRC-specific mortality (HR:1.15, 95% CI:0.99–1.32) compared to patients who reported eating at or less than the median. In a separate analysis among patients with stage IV CRC, no associations were observed between red meat or processed meat intake and both survival endpoints (Table 3).

No statistically significant interactions were found between red meat and processed meat and overall or CRC-specific survival with sex, cancer site, family history of CRC, BMI, or study design (Supplementary Table 2 and 3). A statistically significant interaction was observed between age and red meat intake in relation to overall survival only ($p_{\text{interaction}} = 0.003$). Stratification by age revealed an association among those ≥ 70 years ($>$ median vs median, HR:1.14, 95% CI:1.00–1.30) but no association among those <70 years ($>$ median vs median, HR:0.88, 95% CI:0.74– 1.06).

Discussion

In this large international CRC consortium, we observed no association between the highest compared with the lowest intake of red or processed meat before diagnosis and overall and CRC-specific survival. However, patients with stage I-III CRC who reported intakes higher than the study-specific median amount of processed meat had a 12% higher risk of death compared to those who reported eating at or less than the median. We observed differences in the association between red meat and overall survival by age but no other significant effect modification was found. Higher intake of red meat ($>$ median) was associated with worse overall survival among patients ≥ 70 years but no association was observed among those <70 years.

To our knowledge only three studies have specifically examined red and processed meat in relation to CRC survival, and subsamples of two of these studies were included in the present analysis^{8,12}. In a cohort of 2315 patients diagnosed with CRC (CPS-II cohort), red

and processed meat intake before CRC diagnosis was associated with higher risk of all-cause mortality (Q4vsQ1, RR:1.29, 95% CI:1.05– 59) and cardiovascular disease (CVD) specific death (RR:1.63; 95% CI:1.00–2.67) but not CRC-specific death (RR:1.09; 95% CI: 0.79–1.51)⁸. Post-diagnostic red and processed meat intake was not associated with survival among CRC patients, however, those who consumed a higher amount both pre and post diagnosis, had a higher risk of CRC specific mortality (RR:1.79, 95% CI:1.11 –2.89) compared to those who had consistently lower intakes. In a larger study of 3122 CRC patients (DACHS study), red and processed meat intake was not associated with overall, CRC- specific, CVD-specific, non-CRC specific and recurrence free survival¹². Similarly, in the largest study to date, among 3789 CRC patients in the European Investigation into Cancer and Nutrition (EPIC) cohort, pre-diagnostic red and processed meat intake was not associated with overall or CRC-specific survival ¹¹.

A recent systematic review and meta-analysis investigating the association between food intake and dietary patterns and overall mortality among patients with cancer, reported results with regard to meat intake (not limited to red and processed meat). Meta-analysis of four studies (including the CPS-II study and the DACHS study) revealed no significant association with overall mortality among patients with CRC when comparing the highest versus the lowest category of meat intake (RR: 1.10, 95% CI: 0.84–1.43), also similar to the findings of the current study³⁴.

In this large pooled analysis of 10 epidemiological studies we did not find an association between higher red meat or processed meat intake and overall survival or CRC-specific survival, but, we found an association with overall survival and CRC- specific survival among stage I-III patients who reported eating above the median intake of processed meat compared to those who reported eating at or below the median intake. Although none of the three previous studies examined the association with meat intake when modeled as a dichotomous exposure (> median or < median intake), an analysis within the CPS-II cohort found that survivors with consistently above median red and processed meat intake both before and after CRC diagnosis had a higher risk of CRC specific mortality compared to those with consistently low intakes ⁸ Unfortunately, we were not able to examine associations with post-diagnostic intake within the ISACC consortium. However, for some patients it is likely that temporary if not permanent dietary modifications are required after a CRC diagnosis. Limited evidence is currently available which examines dietary changes after a CRC diagnosis, although, a recent analysis of the DACHS cohort found that five years after diagnosis there was a dramatic decrease in the proportion of CRC survivors who consumed red and processed meat more than 1 time per day (from 28.7% to 2.9%) or 1 time per day (from 37.4% to 14.5%)¹². Future studies with several dietary measurements both before and after cancer diagnosis are necessary to evaluate and clarify the relationship between consistency in pre- and post-diagnostic meat consumption and survival.

In subgroup analyses, higher red meat intake (> median) was significantly associated with worse overall survival in patients aged ≥ 70 years. One previous study (DACHS), of which a subset was included in this current analysis, also conducted analyses stratified by age but found no difference among survivors of CRC ≥ 70 years or <70 years¹². However, because of the many subgroup analyses we conducted in this analysis or because of the small group

sizes in some subgroup analyses, the results may be due to chance. Subgroup analyses in two studies^{8, 9} also found that among those with a family history of CRC, those with the highest meat consumption had a higher risk of death compared to those with the lowest intake, and no association was observed for those without a family history of CRC. In contrast to these findings, our large study as well as previously published results from the DACHS study, were not able to confirm these results¹².

Previous research has suggested that several factors such as heterocyclic amines, N-nitroso compounds, or the use of nitrate or nitrites in the preservation of meat, may help explain the observed association between higher red and processed meat intake and risk of CRC^{35, 36}. However, there is currently no evidence as to whether increased exposure to these factors will lead to more aggressive cancers³⁷. Furthermore, evidence on the association between red and processed meat and known molecular pathological subtypes of CRC is currently limited and inconsistent^{38,39}. More studies are necessary to evaluate novel molecular tumor subtypes associated with red and processed meat intake. Nevertheless, other lifestyle factors such as physical inactivity, and a Western dietary pattern, which often includes red and processed meat, refined grains and sugar-sweetened beverages, are associated with increased mortality risk^{37, 40}. Also, a lifestyle contributing to an unfavorable energy balance and hyperinsulinemia may lead to the development of more aggressive cancers^{37,41,42}.

Current dietary guidelines for cancer survivors are based on guidelines for cancer and heart disease prevention⁴³. The findings from the current pooled analysis are an important contribution to the limited knowledge on the role of diet and CRC survival. Although our study focuses on pre-diagnostic (rather than post-diagnostic) meat consumption, and may not directly inform clinical recommendations for patients, our results suggest that meat consumption before diagnosis has no or only a weak impact on survival after CRC. There is a need for well-designed patient cohort studies focusing on red and processed meat intake after diagnosis to better inform dietary guidelines for patients with CRC.

There are a number of strengths of the present study. First, pooling studies from a large consortium with harmonized exposure and outcome resulted in the largest sample size to date to investigate associations of red and processed meat and survival after a diagnosis with CRC. Second, we were able to adjust for a wide range of potentially confounding variables. Other strengths of the present study include the comprehensive follow-up procedures carried out by each individual study which ensured thorough vital status assessment, completeness of follow-up, and a long duration of follow-up in each study. However, as this study includes harmonized data from 10 epidemiological studies, we cannot rule out differences in the completeness of follow-up between studies. We also acknowledge some limitations of our study. Among the studies included in the consortium, there were differences in dietary assessment and the ascertainment of red and processed meat intake. Some studies had much more detailed dietary information, whilst others were more limited. There were also differences between the studies in the timing of the dietary assessment due to the different study designs. However, we found no differences in overall results when stratified by original study design (i.e. cohort and case-control design). Furthermore, the studies also differed in their definitions of red and processed meat, meaning that we could not create a combined variable of red and processed meat and could therefore only analyse red meat

(unprocessed red meat including processed red meat, i.e. sausages, in some studies) and processed meat (processed red meat and processed white meat) separately. Additionally, we did not have information harmonized on post-diagnostic dietary intake, therefore, it was not possible to assess potential changes in dietary intake which could have affected the overall results. Further limitations include the limited availability of harmonized treatment information and information on CRC recurrence. Finally, we cannot rule out the possibility of residual confounding due to unmeasured or inaccurately measured variables.

In conclusion, in the largest study to date to examine the association between pre-diagnostic red meat and processed meat intake and CRC survival, we found no significant associations between intake of red or processed meat with overall and CRC-specific survival. However, we cannot exclude a possible weak adverse association with survival for intakes higher than the study-specific median amount of red and processed meat. Future studies with dietary data at a number of time points both before and after cancer diagnosis, are required to confirm and build upon the current findings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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<http://www.whi.org/researchers/Documents%20%20Write%20a%20Paper/WHI%20Investigator%20Short%20List.pdf>

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What You Need To Know**Background**

Red and processed meat intake is associated with colorectal cancer (CRC) incidence. We investigated whether intake is associated with patient survival after diagnosis.

Findings

In this large pooled consortium, intake of red and processed meat before a diagnosis of CRC was not associated with shorter survival time after diagnosis, although a weak adverse association cannot be excluded.

Implications for patient care

The findings from the current pooled analysis suggest no relevant impact of red and processed meat intake before diagnosis on CRC survival. Further studies are needed of diets before and after CRC diagnosis.

Table 1.Baseline characteristics of study participants according to red meat and processed meat intake¹.

	Red meat(servings/day) ²				P*	Processed meat (servings/day) ³				P*
	Q1 (n=2120)	Q2 (n=2073)	Q3 (n=1911)	Q4 (n=1523)		Q1 (n=1493)	Q2 (n=2846)	Q3 (n=1929)	Q4 (n=1080)	
Age at diagnosis, mean (SD)	69.8 (9.3)	69.3 (9.2)	69.2 (9.5)	67.6 (9.9)	<.001	69.9 (8.8)	69.3 (9.9)	69.1 (9.5)	68.3 (9.6)	<.001
Sex, n (%)					<.001					<.001
Male	884 (42)	1120 (54)	850 (44)	587 (39)		843 (56)	1129 (40)	958 (49)	506 (47)	
Female	1236 (58)	953 (46)	1061 (56)	936 (61)		650 (44)	1717 (60)	971 (51)	574 (53)	
BMI, kgm ² (SD)	26.4 (4.4)	27.2 (4.3)	27.6 (4.8)	28.6 (5.4)	<.001	26.6 (4.3)	27.0(4.3)	27.7 (4.8)	28.6 (5.7)	<.001
Ever smoker, n (%)					0.004					<.001
No	961 (45)	842 (41)	823 (43)	616 (40)		641 (43)	1328 (47)	767 (40)	384 (35)	
Yes	1148 (54)	1228 (59)	1079 (56)	901 (59)		841 (56)	1511 (53)	1156 (60)	691 (64)	
Alcohol, n (%)					<.001					<.001
Non drinker	911 (43)	743 (36)	710(37)	616 (40)		670 (45)	1136 (40)	712 (37)	459 (43)	
1–28g/day	877 (41)	958 (46)	857 (45)	643 (42)		641 (43)	1346 (47)	883 (46)	463 (43)	
>28g/day	191 (9)	297 (14)	294 (15)	209 (14)		176 (12)	336 (12)	324 (17)	155 (14)	
Education, n (%)					<.001					<.001
Less than high school	250 (12)	211 (10)	270 (14)	176 (12)		92 (6)	458 (16)	228 (12)	108 (10)	
High school graduate	684 (32)	754 (36)	648 (34)	459 (30)		437 (29)	1024 (36)	683 (35)	319 (30)	
Some college/technical school	440 (21)	469 (23)	418 (22)	374 (25)		420 (28)	438 (15)	424 (22)	329 (30)	
College graduate	736 (35)	634 (31)	572 (30)	512 (34)		539 (36)	916 (32)	591 (31)	322 (30)	
Family history of CRC, n (%)					0.25					0.23
No	1708 (81)	1682 (81)	1510 (79)	1179 (77)		1173 (79)	2308 (81)	1511 (78)	824 (76)	
Yes	303 (14)	295 (14)	307 (16)	233 (15)		206 (14)	430 (15)	310 (16)	175 (16)	
Regular aspirin/NSAID use, n (%)					0.09					0.004
No	1476 (70)	1427 (69)	1299 (68)	1007 (66)		992 (66)	1994 (70)	1300 (67)	707 (65)	
Yes	620 (29)	624 (30)	594 (31)	505 (33)		489 (33)	817 (29)	606 (31)	368 (34)	
History of diabetes, n (%)					0.03					0.01
No	1609 (76)	1543 (74)	1383 (72)	1068 (70)		1058 (71)	2216 (78)	1395 (72)	696 (64)	
Yes	195 (9)	222 (11)	229 (12)	145 (10)		117 (8)	324 (11)	223 (12)	86 (8)	
Physical activity ⁴ , n (%)					<.001					<.001
No	315 (15)	355 (17)	370 (19)	325 (21)		302 (20)	397 (14)	374 (19)	292 (27)	
Yes	1393 (66)	1342 (65)	1187 (62)	835 (55)		1001 (67)	1931 (68)	1227 (64)	598 (55)	

	Red meat(servings/day) ²				P*	Processed meat (servings/day) ³				P*
	Q1 (n=2120)	Q2 (n=2073)	Q3 (n=1911)	Q4 (n=1523)		Q1 (n=1493)	Q2 (n=2846)	Q3 (n=1929)	Q4 (n=1080)	
Tumor site, n (%)					<.001					<.001
Proximal colon	929 (44)	915 (44)	799 (42)	665 (44)		679 (45)	1195 (42)	794 (41)	502 (46)	
Distal colon	621 (29)	580 (28)	578 (30)	522 (34)		454(30)	811 (28)	597 (31)	372 (34)	
Rectum	526 (25)	542 (26)	498 (26)	311 (20)		328(22)	788 (28)	510 (26)	186 (17)	
Unknown	44 (2)	36 (2)	36 (2)	25 (2)		32 (2)	52 (2)	28 (1)	20 (2)	
Stage of CRC, n (%)					0.27					<.001
I	624 (29)	584 (28)	586 (31)	465 (31)		468 (31)	746 (26)	556 (29)	361 (33)	
II/III	1120 (53)	1150 (55)	1030 (54)	784 (51)		747 (50)	1634 (57)	1060 (55)	521 (48)	
IV	272(13)	255 (12)	214 (11)	189 (12)		192 (13)	347 (12)	230 (12)	134 (12)	

¹ Numbers of participants do not always equal total numbers because of missing values for some variables.

² Study and sex specific quartiles of red meat: WHI (women): <0.32, 0.32-<0.57, 0.57-<0.95, 0.95; DALIS (women): <0.41, 0.41-<0.65, 0.65-<0.95, 0.95; DALIS (men): <0.66, 0.66-<1.12, 1.12-<1.78, 1.78; PMH (women): <0.29, 0.29-<0.43, 0.43-<0.57, 0.57; VITAL (women): <0.23, 0.23-<0.48, 0.48-<0.77, 0.77; VITAL (men): <0.37, 0.37-<0.68, 0.68-<1.05, 1.05; PLCO (women): <0.38, 0.38-<0.62, 0.62-<0.89, 0.89; PLCO (men): <0.7, 0.7-<1.25, 1.25-<1.8, 1.8; DACHS (women): <0.42, 0.42-<0.64, 0.64-<0.84, 0.84; DACHS (men): <0.63, 0.63-<0.84, 0.84-<1.06, 1.06; HPFS (men): <0.41, 0.41-<0.73, 0.73-<1.31, 1.31; PHS (men): <0.46, 0.46-<0.56, 0.56-<0.86, 0.86; NHS (women): <0.34, 0.34-<0.62, 0.62-<1.08, 1.08; CPS2 (women): <0.3, 0.3-<0.48, 0.48-<0.79, 0.79; CPS2 (men): <0.45, 0.45-<0.70, 0.70-<1.12, 1.12.

³ Study and sex specific quartiles of processed meat: WHI (women): <0.07, 0.07-<0.16, 0.16-<0.36, 0.36; DALIS (women): <0.05, 0.05-<0.11, 0.11-<0.21, 0.21; DALIS (men): <0.11, 0.11-<0.24, 0.24-<0.44, 0.44; VITAL (women): <0.04, 0.04-<0.14, 0.14-<0.28, 0.28; VITAL (men): <0.14, 0.14-<0.27, 0.27-<0.54, 0.54; PLCO (women): <0.05, 0.05-<0.10, 0.10-<0.19, 0.19; PLCO (men): <0.12, 0.12-<0.25, 0.25-<0.49, 0.49; DACHS (women): <0.42, 0.42-<0.84, 0.84, 0.84; DACHS (men): <0.64, 0.64-<0.84, 0.84-<1.28, 1.28; HPFS (men): 0, 0-<0.04, 0.04-<0.07, 0.07; PHS (men): <0.09, 0.09-<0.20, 0.20-<0.26, 0.26; NHS (women): 0, >0-<0.07, 0.07, >0.07; CPS2 (women): <0.08, 0.08-<0.15, 0.15-<0.25, 0.25; CPS2 (men): <0.15, 0.15-<0.27, 0.27-<0.61, 0.61

⁴ Physical activity: no, vigorous and moderate physical activity < 1 hour/week; yes, vigorous and moderate physical activity 1 hour/week.

* P value for differences in frequencies across meat strata

Abbreviations: BMI, body mass index; CI, confidence interval; CRC, colorectal cancer; HR, hazard ratio; NSAID, non steroidal antiinflammatory drug; SD, standard deviation

Table 2.

Associations between meat intake and overall and colorectal cancer-specific survival after colorectal cancer diagnosis among stage I-III patients

Quartile of pre-diagnostic meat intake (servings/day)												
Q1			Q2			Q3			Q4			P _{for trend}
HR	95% CI		HR	95% CI		HR	95% CI		HR	95% CI		
Continuous meat intake (servings/day)												
			HR	95% CI		HR	95% CI		HR	95% CI		
Median ⁵												
			HR	95% CI		HR	95% CI		HR	95% CI		
>Median ⁵												
Overall survival												
Red meat												
n (deaths)	1847 (433)		1817 (437)			1697 (381)			1334 (319)			
Model 1 ¹	1.00	Ref.	1.07	0.94–1.23		1.04	0.91–1.20		1.14	0.99–1.32		0.10
Model 2 ²	1.00	Ref.	1.06	0.93–1.21		1.02	0.89–1.17		1.08	0.93–1.26		0.35
Processed meat												
n (deaths)	1300 (292)		2499 (569)			1698 (406)			946 (230)			
Model 1 ¹	1.00	Ref.	1.08	0.93–1.25		1.18	1.01–1.38		1.17	0.98–1.39		0.03
Model 2 ²	1.00	Ref.	1.05	0.90–1.22		1.13	0.97–1.32		1.10	0.93–1.32		0.16
CRC-specific survival												
Red meat												
n (deaths)	1845 (230)		1813 (229)			1695 (216)			1334 (184)			
Model 1 ³	1.00	Ref.	1.03	0.86–1.24		1.05	0.87–1.27		1.15	0.95–1.41		0.14
Model 2 ⁴	1.00	Ref.	1.02	0.85–1.22		1.03	0.85–1.24		1.09	0.89–1.33		0.39
Processed meat												
n (deaths)	1300 (150)		2494 (323)			1698 (229)			946 (126)			
Model 1 ³	1.00	Ref.	1.11	0.90–1.36		1.23	1.00–1.52		1.18	0.93–1.50		0.10
Model 2 ⁴	1.00	Ref.	1.08	0.88–1.33		1.18	0.96–1.46		1.11	0.87–1.42		0.27

¹Model 1: adjusted for age at diagnosis, sex, cancer site, tumor stage; stratified by study and stage.²Model 2: adjusted for Model 1 plus BMI, smoking status, family history of colorectal cancer, aspirin/NSAIDs use, education³Model 1: adjusted for age at diagnosis, sex, cancer site, tumor stage, study; stratified by age categories⁴Model 2: adjusted for Model 1 plus BMI, smoking status, family history of colorectal cancer, aspirin/NSAIDs use, education

Abbreviations: CRC, colorectal cancer; HR, hazard ratio; CI, confidence interval.

Study-specific medians₅

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Table 3.

Association between meat intake and overall and colorectal cancer-specific survival after colorectal cancer diagnosis among stage IV patients

Quartile of pre-diagnostic meat intake (servings/day)														
Outcome	Q1		Q2		Q3		Q4		Continuous meat intake (servings/day)		Median		>Median	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI		
Overall survival														
Red meat														
n (deaths)	272 (225)		255 (209)		214 (174)		189 (160)				557 (453)	373 (315)		
Model 1 ¹	1.00	Ref.	1.00	0.83–1.22	0.92	0.75–1.13	0.98	0.80–1.21	1.01	0.87–1.17	1.00	Ref.	0.96	0.83–1.12
Model 2 ²	1.00	Ref.	1.01	0.83–1.23	0.92	0.75–1.14	0.95	0.76–1.17	0.98	0.84–1.14	1.00	Ref.	0.94	0.81–1.10
Processed meat														
n (deaths)	192 (157)		347 (287)		230 (188)		134 (111)				532 (437)	371 (306)		
Model 1 ¹	1.00	Ref.	1.07	0.86–1.33	1.01	0.81–1.26	1.01	0.79–1.29	0.84	0.68–1.04	1.00	Ref.	0.99	0.85–1.15
Model 2 ²	1.00	Ref.	1.08	0.87–1.35	1.02	0.81–1.28	0.98	0.76–1.26	0.81	0.66–1.01	1.00	Ref.	0.97	0.83–1.14
CRC-specific survival														
Red meat														
n (deaths)	272 (212)		255 (193)		214 (159)		189 (153)				553 (422)	373 (295)		
Model 1 ³	1.00	Ref.	1.00	0.82–1.22	0.91	0.74–1.12	0.98	0.79–1.21	1.00	0.86–1.17	1.00	Ref.	0.95	0.82–1.12
Model 2 ⁴	1.00	Ref.	1.01	0.83–1.24	0.92	0.75–1.14	0.96	0.77–1.19	0.98	0.84–1.14	1.00	Ref.	0.94	0.80–1.10
Processed meat														
n (deaths)	192 (149)		347 (266)		230 (177)		134 (103)				528 (409)	371 (286)		
Model 1 ³	1.00	Ref.	1.06	0.85–1.33	1.01	0.80–1.27	0.99	0.77–1.28	0.84	0.68–1.05	1.00	Ref.	0.98	0.84–1.14
Model 2 ⁴	1.00	Ref.	1.08	0.86–1.36	1.03	0.81–1.29	0.98	0.76–1.27	0.82	0.66–1.02	1.00	Ref.	0.97	0.83–1.14

¹Model 1: adjusted for age at diagnosis, sex, cancer site; stratified by study²Model 2: adjusted for Model 1 plus BMI, smoking status, family history of colorectal cancer, aspirin/NSAIDs use, education³Model 1: adjusted for age at diagnosis, sex, cancer site, study; stratified by age categories.

⁴Model 2: adjusted for Model 1 plus BMI, smoking status, family history of colorectal cancer, aspirin/NSAIDs use, education

Abbreviations: CRC, colorectal cancer; HR, hazard ratio; CI, confidence interval.