Meat intake and risk of colorectal polyps: results from a large population-based screening study in Germany[1,2]

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ABSTRACT

Background: Red and processed meats have been shown to be associated with colorectal adenomas in many, but not all, studies, and the association according to the type of colorectal adenoma or the location in the colorectum is unclear.

Objectives: We investigated the association of meat intake in relation to colorectal polyps and further investigated the association according to histologic subtypes and subsites in a large population-based screening study in Germany.

Design: In this cross-sectional study, 15,950 participants aged ≥55 y underwent a screening colonoscopy. We calculated prevalence ratios (PRs) and 95% CIs for associations between meat intake and the most-advanced findings from a colonoscopy with the use of log binomial regression.

Results: Overall, 3340 participants (20.4%) had nonadvanced adenomas, 1643 participants (10.0%) had advanced adenomas, and 189 participants (1.2%) had colorectal cancer. We observed no statistically significant association between red or processed meat consumption and the prevalence of any adenomas or advanced adenomas [highest compared with lowest: red meat, PR: 1.07 (95% CI: 0.83, 1.37); processed meat, PR: 1.11 (95% CI: 0.91, 1.36)]. In site-specific analyses, although no dose-response relation was observed, processed meat was positively associated with the prevalence of advanced adenomas in the rectum only (multiple times per day compared with <1 time/wk, PR: 1.87; 95% CI: 1.19, 2.95). Poultry intake was not associated with any outcome.

Conclusions: On the basis of this large colonoscopy-based study, there are no significant associations between red or processed meat intake and the prevalence of any adenomas or advanced adenomas. However, processed meat may be positively associated with the prevalence of advanced adenomas in the rectum, but prospective cohort studies are needed to further clarify this association. There is no association between poultry consumption and the prevalence of colorectal polyps in this study. *Am J Clin Nutr* 2017;105:1453–61.

Keywords: adenomas, meat, polyps, processed meat, red meat

INTRODUCTION

Evidence has accumulated that the consumption of red and processed meats is a risk factor for colorectal cancer (CRC)[7] (1–3). In 2015, the International Agency for Research on Cancer classified the consumption of processed meat as carcinogenic to humans, whereas intake of red meat was classified as probably carcinogenic to humans (4); however, not all studies have provided support of increased risk.

Many studies that have examined colorectal adenomas, which are the precursor lesions for the majority of CRCs, have also shown increased risk with red and processed meat intake (5–7). Although 2 recent meta-analyses concluded that intake of red and processed meat is associated with increased risk of colorectal adenomas, not all studies have shown increased risk, and there has often been inconsistency and heterogeneity by study design (5, 6). Most of the studies that were included in the meta-analyses were case-control studies in which diet was assessed after a colonoscopy, and ~50% of the previous studies relied on sigmoidoscopy to identify cases and controls. The largest colonoscopy-based case-control study to date included 1881 patients with adenomas and 3764 polyp-free control subjects (8). Furthermore, only a few of the previous studies differentiated between advanced and non-advanced adenomas and between specific locations in the colorectum. Therefore, because of the limited number of studies, it is uncertain whether the association varies according to the type of colorectal adenoma or the location in the colorectum. In contrast with intake of red and processed meat, on the basis of the limited available evidence, intake of poultry was not associated with risk of colorectal adenomas (9, 10).

Therefore, the aim of this analysis was to investigate the association of meat intake (red meat, processed meat, and poultry) in relation to the presence of colorectal polyps and to further investigate this association according to histologic subtypes and subsites in a large population-based screening study in Germany.

METHODS

Study design and study population

The KolosSal (Effektivität der Früherkennungs-Koloskopie: Eine Saarland-weite Studie) study is a statewide cohort study that was initiated in 2005 in Saarland, which is a federal state (population: 1.02 million in 2010) in the southwest of Germany. The primary aim of this study is to monitor the long-term reduction in CRC incidence and mortality in participants of a screening colonoscopy. Participants who underwent a screening colonoscopy and were recruited in 33 gastroenterology practices in Saarland were eligible for participation if they were residents of Saarland and aged ≥55 y. This cross-sectional analysis was based on baseline data of participants who were recruited between May 2005 and November 2014. More information about the study has been described elsewhere (11–14). The KolosSal study was approved by the ethics committees of the University of Heidelberg and the Medical Association of Saarland. Written informed consent was obtained from each participant.

Data collection

Patients were asked to fill out a standardized questionnaire on personal and family medical histories and sociodemographic and lifestyle factors at or after consultation for a colonoscopy in the practices. Results from the screening colonoscopy were extracted from colonoscopy and histology reports and were transferred to a standardized form by 2 trained investigators who were blinded with respect to questionnaire data. Results recorded included the number, location, size and histologic classification of the polyps. In addition, the completeness of the colonoscopy (cecum reached during the colonoscopy) and quality of the bowel preparation were recorded. Discrepancies in the recorded results between the 2 investigators were resolved by further review and discussion.

Dietary assessment

Participants completed a 6-item food-frequency questionnaire (FFQ) that included 3 specific meat items. Participants were asked to report their average frequency of consumption of red meat (fresh pork, beef, or lamb), processed meat (sausages or lunch meat made from either red meat or poultry), and poultry (fresh poultry) in the previous 12 mo (6 possible responses that ranged from never to >1 time/d). Other food items included fruit, vegetables and salad, and whole grains [whole-grain bread and whole-grain products (e.g., muesli)]. The FFQ did not assess portion sizes. We reduced the number of intake groups from 6 to 4 to have comparison groups of roughly equal sizes in terms of the number of participants. The categories were different for red meat, processed meat, and poultry because of the differences in the distribution of the participants for each meat subtype.

Statistical analysis

The demographic characteristics and further potential CRC risk factors of participants with and without neoplasms were compared with the use of chi-square and t tests. Participants were classified according to the occurrence of the most advanced of the following findings: CRC; advanced adenoma (defined as presence of at least one adenoma with at least one of the following features: ≥1 cm in diameter, tubulovillous or villous components, or high-grade dysplasia); other adenoma; hyperplastic polyp (HPP); or unspecified polyp. Participants with none of the aforementioned findings from a screening colonoscopy were used as the comparison group in this analysis.

Log binomial regression was used to calculate prevalence ratios (PRs) of the association between reported intake of meat (red meat, processed meat, and poultry) and the aforementioned findings from the colonoscopy (15). Poisson regression was used when the log binomial model failed to converge. We calculated basic models, which included age at colonoscopy and sex, and multivariate models, including the following known risk factors and factors that were differentially distributed between the different types of meat intake ($P < 0.10$) (in addition to age at colonoscopy and sex): school education (≤10 or >10 y); BMI (in kg/m^2; <25, 25–30, or >30); family history of CRC (yes or no); smoking (never, former, or current); alcohol consumption (none and quartiles of the amount of ethanol in grams); physical activity (quartiles of metabolic equivalents); current, regular use of nonsteroidal anti-inflammatory drugs (including aspirin) (yes or no); fruit intake (<1 or ≥1 time/d), vegetable intake (<1 or ≥1 time/d), and previous colonoscopy (yes or no). We also examined the associations between meat intake and adenomas that were stratified by the history of a previous colonoscopy, age, sex, BMI, and smoking status. We tested for interactive effects by including a cross-product term along with the main effect terms in the log binomial models. We performed subanalyses by subsite (proximal colon: cecum to splenic flexure; distal colon: descending colon to sigmoid colon; and rectum), morphology (tubular, and tubulovillous or villous), grade of dysplasia (mild, and moderate or high), size (<1 and ≥1 cm), and shape (flat, pedunculated, sessile, and other) of the adenomas. Most patients who were included in the study returned the completed questionnaire before their colonoscopy ($n = 8888$; 54%), some patients returned it after their colonoscopy ($n = 1707$; 11%), and approximately one-third of the participants were recruited by mail shortly after their screening colonoscopy because of overloads in the practices ($n = 5746$; 35%). To account for possible biases from this variance, additional sensitivity analyses were carried out by comparing subjects who completed the questionnaire before a colonoscopy and subjects who completed it after a colonoscopy. Statistical tests were 2 sided, with $\alpha = 0.05$. All analyses were performed with the use of SAS version 9.3 software (SAS Institute Inc.).

RESULTS

Overall, 19,177 participants were recruited during the study period. For this analysis, we excluded participants who did not complete the questionnaire ($n = 261$), had missing colonoscopy information ($n = 176$), did not know if they had a previous colonoscopy ($n = 67$), had an incomplete colonoscopy ($n = 276$), had poor bowel preparation ($n = 1375$), had a history of inflammatory bowel disease (Crohn disease, ulcerative colitis) ($n = 258$), had missing information on intakes of both red and processed meats ($n = 378$), were aged <55 y ($n = 45$), or had unspecified polyps ($n = 391$). A total of 15,950 participants were included in this analysis [5172 subjects with neoplasms
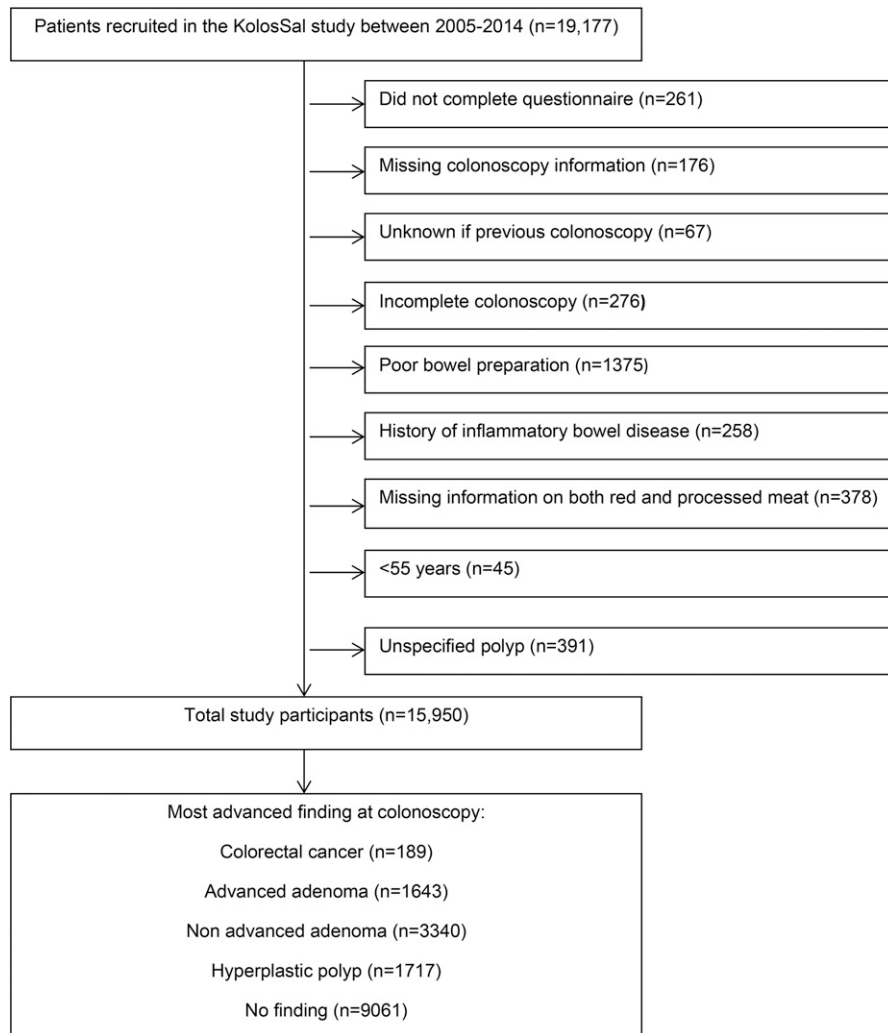
FIGURE 1 Flow diagram illustrating the exclusion of study participants from this analysis. KolosSal, Effektivität der Früherkennungs-Koloskopie: Eine Saarland-weite Studie.

(consisting of 3340 nonadvanced adenomas, 1643 adenomas, and 189 CRCs) and 10,778 subjects without neoplasms (including 1717 HPPs and 9061 subjects with no finding)] (**Figure 1**).

The characteristics of the study participants are presented in **Table 1**. Compared with participants without neoplasms, participants with neoplasms were more likely to be older, men, and current smokers; drink more alcohol; and to have higher intakes of red and processed meats, higher BMI, and a family history of CRC. Participants without neoplasms had significantly higher intakes of poultry, fruit, and vegetables, were more likely to have had a previous colonoscopy, and were more likely to have a higher level of physical activity than were participants with neoplasms. There was no difference between the 2 groups with respect to the current use of nonsteroidal anti-inflammatory drugs and years of education.

In the basic model, which was adjusted for age and sex, the prevalence of advanced adenomas increased with higher intakes of processed meat (multiple times per day compared with ≤1 time/wk) and red meat (>1 time/d compared with ≤1 time/wk) (**Table 2**). After adjustment for potential confounders, red or processed meat intake was not significantly associated with the

prevalence of any adenomas or advanced adenomas, respectively. Poultry intake was not associated with the prevalence of any adenoma or advanced adenoma. Also, there were no associations with other findings or outcome definitions (HPP, nonadvanced adenoma, advanced neoplasm, and CRC) (**Supplemental Table 1**).

In site-specific analyses, processed meat intake (multiple times per day compared with ≤1 time/wk) was associated with the prevalence of advanced adenomas in the rectum (PR: 1.87; 95% CI: 1.19, 2.95) but not with the prevalence of advanced adenomas in the proximal colon (PR: 1.03; 95% CI: 0.71, 1.50) or distal colon (PR: 0.87; 95% CI: 0.62, 1.23), although no dose-response relation was observed (**Table 3**). A nonsignificant positive association was observed for processed meat intake and the prevalence of any adenomas (PR: 1.38; 95% CI: 0.99, 1.90) in the rectum, which were largely due to the higher prevalence of advanced adenomas (7.8% compared with 4.7%). No associations were observed between red meat or poultry intake and the prevalence of advanced adenomas or any adenomas with regard to their location in the colorectum.

In subgroup analyses, red meat intake (≥1 time/d compared with <1 time/wk) was positively associated with the prevalence

TABLE 1
Characteristics of the study participants[1]

Baseline characteristics	Total (*n* = 15,950)	Participants without neoplasms (*n* = 10,778)	Participants with neoplasms (*n* = 5172)
Age,[2] y	63.3 ± 6.8	62.9 ± 6.8	64.3 ± 7.0
Sex, F, *n* (%)	8070 (50.6)	6045 (56.1)	2025 (39.1)
Education ≥10 y, *n* (%)	5719 (36.2)	3908 (36.6)	1811 (35.4)
BMI, kg/m², *n* (%)			
<25	5048 (32.1)	3563 (33.5)	1485 (29.1)
25–29.9	7222 (45.9)	4762 (44.8)	2460 (48.2)
≥30	3453 (22.0)	2295 (21.6)	1158 (22.7)
Family history of CRC, yes, *n* (%)	2149 (13.7)	1394 (13.1)	755 (14.8)
Smoking, *n* (%)			
Never	7858 (50.9)	5595 (53.4)	2263 (45.6)
Former	5927 (38.4)	3900 (37.2)	2027 (40.9)
Current	1653 (10.7)	982 (9.4)	671 (13.5)
Alcohol quartiles (ethanol), g/d, *n* (%)			
0	3598 (23.9)	2599 (25.7)	999 (20.4)
0.1–5.6	2883 (19.2)	2025 (20.0)	858 (17.5)
5.7–10.3	2831 (18.8)	1960 (19.4)	871 (17.8)
10.4–19.0	2819 (18.8)	1826 (18.0)	993 (20.3)
≥19.1	2893 (19.3)	1715 (16.9)	1178 (24.1)
Physical activity quartiles, MET-h/wk, *n* (%)			
<48.2	3870 (24.7)	2517 (23.8)	1353 (26.7)
48.2 to <91.0	3925 (25.1)	2635 (24.9)	1290 (25.5)
91.0 to <150.4	3917 (25.0)	2735 (25.9)	1182 (23.3)
≥150.4	3835 (25.1)	2695 (25.5)	1240 (24.5)
Current regular NSAID use, *n* (%)	3261 (21.0)	2214 (21.1)	1047 (20.8)
Previous colonoscopy, yes, *n* (%)	4971 (31.2)	3476 (32.2)	1495 (28.9)
Red meat intake, *n* (%)			
<1 time/wk	2594 (16.3)	1832 (17.0)	762 (14.7)
1 time/wk	5463 (34.3)	3801 (35.3)	1662 (32.1)
Multiple times per week	7180 (45.1)	4689 (43.5)	2491 (48.2)
≥1 time/d	700 (4.4)	444 (4.1)	256 (4.9)
Processed meat intake, *n* (%)			
≤1 time/wk	3243 (20.3)	2315 (21.5)	928 (17.9)
Multiple times per week	6618 (41.5)	4482 (41.6)	2136 (41.3)
1 time/d	4961 (31.1)	3258 (30.2)	1703 (32.9)
Multiple times per day	1128 (7.1)	723 (6.7)	405 (7.8)
Poultry intake, *n* (%)			
Never	949 (6.1)	594 (5.6)	355 (7.1)
<1 time/wk	5780 (37.1)	3898 (37.0)	1882 (37.4)
1 time/wk	6038 (38.8)	4019 (39.0)	1929 (38.4)
>1 time/wk	2799 (18.0)	1935 (18.4)	864 (17.2)
Fruit intake, time/d, *n* (%)			
<1	5638 (35.4)	3655 (34.0)	1983 (38.4)
≥1	10267 (64.6)	7093 (66.0)	3174 (61.6)
Vegetable intake, time/d, *n* (%)			
<1	6783 (42.6)	4425 (41.1)	2358 (45.6)
≥1	9150 (57.4)	6341 (58.9)	2809 (54.4)

[1] Numbers of participants do not always equal total numbers because of missing values for some variables. CRC, colorectal cancer; NSAID, nonsteroidal anti-inflammatory drug; MET-h, metabolic equivalent task hours.
[2] Values are means ± SDs.

of advanced adenomas in participants aged ≥65 y (PR: 1.48; 95% CI: 1.06, 2.05) but not with the prevalence of advanced adenomas in participants aged <65 y. However, no trend in categorical prevalence estimates was observed for advanced adenomas in participants aged ≥65 y. Although the test for the multiplicative interaction between age and meat intake was not significant, power may have been limited because of the smaller subgroups (**Supplemental Table 2**). There was also no suggestion of an effect modification by sex, BMI, or smoking status (**Supplemental Tables 3–5**). A history of a previous

colonoscopy did not alter our main findings, and no differences were shown in PRs of all polyp types for red meat, processed meat, or poultry intake (**Supplemental Table 6**).

High intake of processed meat (>1 time/d compared with ≤1 time/wk) was nonsignificantly associated with the prevalence of any adenoma (PR: 1.72; 95% CI: 0.88, 3.38) and advanced adenomas (PR: 1.76; 95% CI: 0.84, 3.66) with moderate or high dysplasia but was not associated with adenomas with mild dysplasia (**Supplemental Table 7**). No differences in PRs were observed for small or large advanced adenomas, and no differences

TABLE 2
Association between red meat, processed meat, and poultry and prevalence of any adenoma (nonadvanced and advanced adenoma) and advanced adenoma[1]

Meat intake	No finding (n = 9061), n (%)	Any adenoma (n = 4983)			Advanced adenoma (n = 1643)		
		n (%)	PR[2] (95% CI)[3]	PR (95% CI)[4]	n (%)	PR (95% CI)[3]	PR (95% CI)[4]
Red meat[5]							
<1 time/wk	1573 (60.6)	725 (27.9)	1.0 (reference)	1.0 (reference)	221 (8.5)	1.0 (reference)	1.0 (reference)
1 time/wk	3206 (58.7)	1609 (29.4)	1.02 (0.95, 1.10)	0.98 (0.91, 1.06)	536 (9.8)	1.09 (0.95, 1.26)	1.06 (0.91, 1.24)
Multiple times per week	3900 (54.3)	2401 (33.4)	1.09 (1.02, 1.17)	1.02 (0.95, 1.10)	797 (11.1)	1.18 (1.02,1.35)	1.07 (0.92, 1.24)
≥1 time/d	373 (53.3)	247 (35.3)	1.11 (0.99, 1.24)	1.03 (0.91, 1.16)	89 (12.7)	1.27 (1.02, 1.59)	1.07 (0.83, 1.37)
Per increase in group	—	—	1.04 (1.02, 1.07)	1.01 (0.98, 1.05)	—	1.08 (1.02, 1.14)	1.02 (0.96, 1.09)
Processed meat							
≤1 time/wk	1979 (61.0)	893 (27.5)	1.0 (reference)	1.0 (reference)	273 (8.4)	1.0 (reference)	1.0 (reference)
Multiple times per week	3779 (57.1)	2061 (31.1)	1.04 (0.97, 1.11)	1.02 (0.95, 1.09)	685 (10.4)	1.10 (0.97, 1.25)	1.05 (0.91, 1.21)
1 time/d	2714 (54.7)	1640 (33.1)	1.09 (1.02, 1.16)	1.02 (0.95, 1.10)	531 (10.7)	1.14 (1.00, 1.31)	1.02 (0.88, 1.19)
Multiple times per day	589 (52.2)	389 (34.5)	1.09 (1.00, 1.20)	0.98 (0.88,1.08)	154 (13.6)	1.34 (1.12, 1.61)	1.11 (0.91, 1.36)
Per increase in group	—	—	1.04 (1.01, 1.06)	1.00 (0.97, 1.03)	—	1.08 (1.03, 1.14)	1.02 (0.96, 1.08)
Poultry[6]							
Never	495 (52.2)	338 (35.6)	1.0 (reference)	1.0 (reference)	116 (12.2)	1.0 (reference)	1.0 (reference)
<1 time/wk	3297 (57.0)	1806 (31.2)	0.91 (0.84, 0.98)	0.93 (0.85, 1.01)	617 (10.7)	0.88 (0.76, 1.03)	0.97 (0.82, 1.15)
1 time/wk	3454 (57.2)	1869 (30.9)	0.92 (0.85, 1.00)	0.94 (0.86, 1.02)	595 (9.8)	0.86 (0.73, 1.00)	0.93 (0.78, 1.11)
>1 time/wk	1610 (57.5)	832 (29.7)	0.91 (0.83, 1.00)	0.95 (0.86, 1.05)	269 (9.6)	0.86 (0.72, 1.03)	0.92 (0.75, 1.12)
Per increase in group	—	—	0.98 (0.96, 1.01)	0.99 (0.97, 1.03)	—	0.96 (0.91, 1.02)	0.97 (0.91, 1.03)

[1] Log binomial regression was used to calculate PRs.
[2] PR, prevalence ratio.
[3] PRs were adjusted for age at colonoscopy and sex.
[4] PRs were adjusted for age at colonoscopy, sex, school education (<10 or >10 y), BMI (in kg/m^2; <25, 25–30, or >30), family history of CRC (yes or no), smoking (never, former, or current), alcohol (none and quartiles of the amount of ethanol in grams), physical activity (quartiles of metabolic equivalents), current regular use of nonsteroidal anti-inflammatory drugs (yes or no), fruit intake (<1 or ≥1 time/d), vegetable intake (<1 or ≥1 time/d), and previous colonoscopy (yes or no).
[5] Information was missing for 10 participants.
[6] Information was missing for 343 participants.

were observed when any adenomas and advanced adenomas were investigated according to morphology (tubular, and tubulovillous or villous), or shape (flat, pedunculated, sessile, and other) (**Supplemental Tables 8** and **9**). The results did not materially change in sensitivity analyses when we compared subjects who completed the questionnaire before a colonoscopy and those who completed it after a colonoscopy (**Supplemental Table 10**).

DISCUSSION

In this large colonoscopy-based screening study, we showed no significant overall association between red or processed meat consumption and the prevalence of any adenomas or advanced adenomas, respectively. In highest compared with lowest analyses, we showed a significant positive association for advanced rectal adenomas with processed meat intake although no dose-response relation was observed. In subgroup analyses, red meat was positively associated with the prevalence of advanced adenomas in participants aged ≥65 y only. To our knowledge, this is the largest colonoscopy-based study to date that has investigated meat intake and associations with colorectal polyps according to subsites and histologic subtypes.

Two meta-analyses that were published in 2013 provided evidence that red and processed meats are associated with increased risk of colorectal adenomas (5, 6). However, to date, only a limited number of studies, to our knowledge, have investigated the association between red or processed meat according to subsites within the colorectum, and the results have been inconsistent.

Aune et al. (5) reported that red meat (per 100 g/d) was associated with adenomas in the colon (RR: 1.58; 95% CI: 1.03, 2.45; n = 2), distal colon (RR: 1.22; 95% CI: 1.03, 1.44; n = 3), and distal colon and rectum (RR: 1.23; 95% CI: 1.08, 1.40; n = 6) but not with adenomas in the proximal colon (RR: 1.25; 95% CI: 0.87, 1.80; n = 3) or with rectal adenomas (RR: 1.07; 95% CI: 0.74, 1.53; n = 2) when studies were pooled in a meta-analysis. Processed meat (per 50 g/d) was associated with adenomas in the distal colon (RR: 1.47; 95% CI: 1.10, 1.97; n = 2) and distal colon and rectum (RR: 1.38; 95% CI: 1.00, 1.91; n = 2) but not with rectal adenomas alone (RR: 1.10; 95% CI: 0.55, 2.16; n = 1). Xu et al. (6) did not provide results that were stratified by location in the colorectum. In our study, the association with processed meat intake was restricted to advanced adenomas in the rectum. Further large studies are warranted to clarify whether red or processed meat consumption varies according to colorectal subsites.

Both meta-analyses also reported summary estimates for the type of adenoma and red meat. Aune et al. (5) showed a positive association with both advanced adenomas [highest compared with lowest, RR: 1.38 (95% CI: 1.04, 1.84); n = 2] and non-advanced adenomas (RR: 1.31; 95% CI: 1.10, 1.57; n = 2), whereas Xu et al. (6) showed no associations for advanced adenomas [per 100 g/d, RR: 1.49 (95% CI: 0.89, 2.48); n = 4] or nonadvanced adenomas (RR: 1.26; 95% CI: 0.87, 1.83; n = 3). Xu et al. (6) reported results from one study on processed meat intake (per 50 g/d) and the type of adenoma but did not find an association (16).

TABLE 3
Red meat, processed meat and poultry intake and association with prevalence of any adenoma and advanced adenoma, stratified by adenoma location[1]

	Any adenoma						Advanced adenoma					
	Proximal colon		Distal colon		Rectum		Proximal colon		Distal colon		Rectum	
Meat intake	n (%)	PR[2] (95% CI)	n (%)	PR (95% CI)	n (%)	PR (95% CI)	n (%)	PR (95% CI)	n (%)	PR (95% CI)	n (%)	PR (95% CI)
Red meat[3]												
<1 time/wk	367 (14.2)	1.0 (reference)	317 (12.2)	1.0 (reference)	151 (5.8)	1.0 (reference)	71 (2.7)	1.0 (reference)	111 (4.3)	1.0 (reference)	62 (2.4)	1.0 (reference)
1 time/wk	782 (14.3)	0.96 (0.84, 1.11)	744 (13.7)	1.03 (0.88, 1.20)	301 (5.5)	1.00 (0.79, 1.27)	209 (3.8)	1.32 (0.97, 1.81)	260 (4.8)	0.94 (0.73, 1.21)	124 (2.3)	0.96 (0.67, 1.39)
Multiple times per week	1166 (16.3)	1.00 (0.87, 1.14)	1097 (15.3)	1.08 (0.93, 1.25)	481 (6.7)	1.05 (0.83, 1.33)	294 (4.1)	1.29 (0.94, 1.76)	381 (5.3)	0.97 (0.76, 1.23)	198 (2.8)	1.04 (0.73, 1.48)
≥1 time/d	113 (16.2)	1.08 (0.86, 1.36)	116 (16.6)	1.10 (0.85, 1.41)	50 (7.2)	0.97 (0.63, 1.51)	35 (5.0)	1.53 (0.95, 2.49)	41 (5.9)	0.88 (0.56, 1.36)	20 (2.9)	0.80 (0.40, 1.60)
Per increase in group	—	1.02 (0.96, 1.08)	—	1.04 (0.97, 1.10)	—	1.01 (0.92, 1.12)	—	1.10 (0.97, 1.24)	—	0.98 (0.88, 1.09)	—	1.00 (0.86, 1.16)
Processed meat												
≤1 time/wk	460 (14.2)	1.0 (reference)	404 (12.5)	1.0 (reference)	152 (4.7)	1.0 (reference)	105 (3.2)	1.0 (reference)	138 (4.3)	1.0 (reference)	56 (1.7)	1.0 (reference)
Multiple times per week	1008 (15.3)	1.01 (0.90, 1.15)	923 (14.0)	0.96 (0.84, 1.10)	425 (6.4)	1.28 (1.01, 1.60)	254 (3.8)	1.07 (0.84, 1.37)	313 (4.7)	0.92 (0.73, 1.16)	178 (2.7)	1.36 (0.95, 1.94)
1 time/d	778 (15.8)	1.03 (0.90, 1.17)	774 (15.7)	1.04 (0.91, 1.20)	318 (6.4)	1.13 (0.88, 1.45)	195 (3.9)	1.00 (0.78, 1.30)	271 (5.5)	0.98 (0.77, 1.24)	122 (2.5)	1.15 (0.78, 1.69)
Multiple times per day	183 (16.3)	1.00 (0.82, 1.21)	174 (15.5)	0.85 (0.69, 1.06)	88 (7.8)	1.38 (0.99, 1.90)	55 (4.9)	1.03 (0.71, 1.50)	71 (6.3)	0.87 (0.62, 1.23)	48 (4.3)	1.87 (1.19, 2.95)
Per increase in group	—	1.00 (0.95, 1.06)	—	0.99 (0.94, 1.05)	—	1.05 (0.96, 1.15)	—	0.99 (0.88, 1.10)	—	0.98 (0.89, 1.08)	—	1.12 (0.98, 1.29)
Poultry[4]												
Never	166 (17.6)	1.0 (reference)	148 (15.7)	1.0 (reference)	69 (7.3)	1.0 (reference)	46 (4.8)	1.0 (reference)	50 (5.3)	1.0 (reference)	29 (3.1)	1.0 (reference)
<1 time/wk	872 (15.1)	0.87 (0.74, 1.02)	852 (14.8)	0.97 (0.82, 1.16)	358 (6.2)	0.87 (0.66, 1.16)	231 (4.0)	0.82 (0.60, 1.12)	305 (5.3)	1.16 (0.84, 1.60)	147 (2.6)	0.91 (0.59, 1.41)
1 time/wk	930 (15.4)	0.91 (0.78, 1.07)	843 (14.0)	0.98 (0.82, 1.16)	348 (5.8)	0.86 (0.64, 1.14)	222 (3.7)	0.77 (0.56, 1.06)	285 (4.7)	1.12 (0.81, 1.55)	142 (2.3)	0.97 (0.63, 1.49)
>1 time/wk	396 (14.2)	0.91 (0.76, 1.09)	368 (13.2)	0.89 (0.73, 1.09)	179 (6.4)	1.03 (0.75, 1.41)	93 (3.3)	0.73 (0.50, 1.06)	129 (4.6)	0.99 (0.69, 1.43)	72 (2.6)	1.03 (0.64, 1.67)
Per increase in group	—	1.00 (0.95, 1.06)	—	0.97 (0.91, 1.03)	—	1.03 (0.93, 1.14)	—	0.92 (0.82, 1.03)	—	0.96 (0.87, 1.06)	—	1.03 (0.90, 1.20)

[1] Log binomial regression was used to calculate PRs. PRs were adjusted for age at colonoscopy, sex, school education (<10 or >10 y), BMI (in kg/m^2; <25, 25–30, or >30), family history of CRC (yes or no), smoking (never, former, or current), alcohol (none and quartiles of the amount of ethanol in grams), physical activity (quartiles of metabolic equivalents), current regular use of nonsteroidal anti-inflammatory drugs (yes or no), fruit intake (<1 or ≥1 time/d), vegetable intake (<1 or ≥1 time/d), and previous colonoscopy (yes or no). There was missing information on adenoma location for 30 participants.
[2] PR, prevalence ratio.
[3] Information was missing for 10 participants.
[4] Information was missing for 343 participants.

Although we detected a positive association between red meat and the prevalence of advanced adenomas in participants ≥65 y of age, it is difficult to draw a conclusion because we did not observe a significant effect modification. A number of studies have presented results that were stratified by sex but either did not find significant interactions (17–19) or had mixed results (20–25). To our knowledge, this is the first study to present results that were stratified by BMI. Fu et al. (8) showed that cigarette smoking and high meat intake were more strongly associated with increased risk of adenomas and with HPPs than in nonsmokers with lowest intake of red meat. However, if analyses were stratified by smoking status, such as in our study, both studies suggest that there is no effect modification by smoking. We did not observe differences according to adenoma size despite one of the systematic reviews having reported only increased risk of large adenomas (≥1 cm diameter) with higher red meat intake (5). To our knowledge, this is the first study to report associations by adenoma shape and the largest to report results by morphology.

As identified in the review by Aune et al. (5), none of the previous case-control studies conducted analyses that were restricted to participants with a previous colonoscopy. We hypothesized that, by analyzing the association stratified by a history of a previous colonoscopy, the results should give us an idea about recent meat consumption in individuals with a previous colonoscopy and the potential removal of precursors than with lifetime consumption in individuals who never had a colonoscopy. In stratified analyses, we did not observe a difference in the association. The FFQ that was used in our study asked about dietary intake in the previous 12 mo, which might not be the most relevant time period for the development of adenomas, although we hypothesize that the time period reflected by the FFQ is much longer. However, meat intake may be more relevant for the progression of polyps to carcinomas rather than for polyp initiation (9).

Although some evidence has suggested that red and processed meats are associated with CRC and adenomas, not all studies have been consistent, and moreover, the mechanisms to explain these associations remain unclear. One hypothesis relates to the formation of N-nitroso compounds, which can be formed in processed meats from the addition of nitrate and nitrites (26). Positive associations for nitrate or nitrite intakes from meat in relation to colorectal adenomas were observed in some (19, 27) but not all (28) studies. Red meat also contains heme iron, which likewise promotes the formation of N-nitroso compounds (29). Some epidemiologic evidence has suggested an association between heme-iron intake (which is often derived from meat-intake variables on FFQs) and CRC (30, 31); however, only a limited number of studies have investigated the association of heme iron with adenomas and have shown mixed results (19, 28, 32–35). Furthermore, many other studies have also investigated meat-derived mutagens (such as 2-amino-1-methyl-6-phenyl-imidazo [4,5-b] pyridine or benzo[a] pyrene) and colorectal adenomas; however, not all results were consistent (8, 16, 25, 28, 36–42). Because the mechanisms of potential effects of meat consumption on the development of colorectal neoplasms are not clear, further studies are warranted to clarify the potential difference in association by location.

In contrast with red and processed meats, the World Cancer Research Fund/American Institute for Cancer Research, in 2007, concluded that the evidence for poultry and CRC was too limited to draw any conclusion (26). However, limited evidence has suggested that poultry intake is not associated with colorectal adenomas (9, 10). In agreement with these results, poultry intake was not associated with the prevalence of any colorectal adenomas in this large study. To date, only a few studies, to our knowledge, have investigated meat intake and risk of HPP and have shown mixed results (8, 21, 43, 44). In our large study, we consistently did not find any association between meat intake and HPP. Although growing evidence suggests that a small proportion of HPPs may progress to cancer via an alternative pathway (serrated pathway) to the adenoma-carcinoma sequence (45–48), we had no specific information about serrated precursors for a more-detailed analysis.

This study has several strengths. The large number of participants in this statewide cohort study allowed us to perform many stratified analyses on specific adenoma features that were not reported previously. Also, because all participants underwent a complete colonoscopy in this study, polyp status was known for all participants. Despite the large size of this study, it was not possible to detect small-to-moderate effects in subgroup analyses. Although this analysis was cross-sectional, we were able to include a large range of covariates in our adjusted models. Our study also has some limitations. Although most participants completed the questionnaire before their colonoscopy, a large proportion completed it after their colonoscopy. However, we conducted a sensitivity analysis that was stratified according to the timing of questionnaire completion, which showed very similar results. Because the presence of adenomas is rather asymptomatic, diets in the preceding 12 mo should not have been affected. Furthermore, the FFQ that was used in our study did not assess portion sizes, has not been previously validated, and was limited in the number of food items. Because of these limitations, it is possible that some misclassification occurred when grouping participants by meat intake. Because this study included participants who underwent a screening colonoscopy, we may have recruited a generally healthier population, which, therefore, potentially limited the representativeness of these results. Finally, we could not exclude the possibility of residual confounding.

In conclusion, on the basis of this large colonoscopy-based screening study, we show no significant associations between the consumption of red or processed meat and the prevalence of any adenomas or advanced adenomas. However, processed meat may be positively associated with the prevalence of advanced adenomas in the rectum only. In contrast, data from this large study confirm that poultry intake is not associated with colorectal polyps. Despite the large size of our study, further prospective studies are still warranted to confirm our findings and to clarify the potential difference in the association by location.

data or performed the statistical analysis; and all authors: critically reviewed and approved the final manuscript. None of the authors reported a conflict of interest related to the study.

REFERENCES

1. World Cancer Research Fund/American Institute for Cancer Research. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. Washington (DC): AICR; 2007.
2. World Cancer Research Fund/American Institute for Cancer Research. Continuous update project report. Food, nutrition, physical activity, and the prevention of colorectal cancer. 2011. [cited 2016 Sep 27]. Available from: http://www.wcrf.org/sites/default/files/Colorectal-Cancer-2011-Report.pdf.
3. Chan DS, Lau R, Aune D, Vieira R, Greenwood DC, Kampman E, Norat T. Red and processed meat and colorectal cancer incidence: meta-analysis of prospective studies. PLoS One 2011;6:e20456.
4. Bouvard V, Loomis D, Guyton KZ, Grosse Y, Ghissassi FE, Benbrahim-Tallaa L, Guha N, Mattock H, Straif K. Carcinogenicity of consumption of red and processed meat. Lancet Oncol 2015;16:1599–600.
5. Aune D, Chan DS, Vieira AR, Navarro Rosenblatt DA, Vieira R, Greenwood DC, Kampman E, Norat T. Red and processed meat intake and risk of colorectal adenomas: a systematic review and meta-analysis of epidemiological studies. Cancer Causes Control 2013;24:611–27.
6. Xu X, Yu E, Gao X, Song N, Liu L, Wei X, Zhang W, Fu C. Red and processed meat intake and risk of colorectal adenomas: a meta-analysis of observational studies. Int J Cancer 2013;132:437–48.
7. Leslie A, Carey FA, Pratt NR, Steele RJ. The colorectal adenoma-carcinoma sequence. Br J Surg 2002;89:845–60.
8. Fu Z, Shrubsole MJ, Smalley WE, Wu H, Chen Z, Shyr Y, Ness RM, Zheng W. Association of meat intake and meat-derived mutagen exposure with the risk of colorectal polyps by histologic type. Cancer Prev Res (Phila) 2011;4:1686–97.
9. Carr PR, Walter V, Brenner H, Hoffmeister M. Meat subtypes and their association with colorectal cancer: systematic review and meta-analysis. Int J Cancer 2016;138:293–302.
10. Xu B, Sun J, Sun Y, Huang L, Tang Y, Yuan Y. No evidence of decreased risk of colorectal adenomas with white meat, poultry, and fish intake: a meta-analysis of observational studies. Ann Epidemiol 2013;23:215–22.
11. Brenner H, Haug U, Arndt V, Stegmaier C, Altenhofen L, Hoffmeister M. Low risk of colorectal cancer and advanced adenomas more than 10 years after negative colonoscopy. Gastroenterology 2010;138:870–6.
12. Hoffmeister M, Schmitz S, Karmrodt E, Stegmaier C, Haug U, Arndt V, Brenner H. Male sex and smoking have a larger impact on the prevalence of colorectal neoplasia than family history of colorectal cancer. Clin Gastroenterol Hepatol 2010;8:870–6.
13. Brenner H, Hoffmeister M, Arndt V, Stegmaier C, Altenhofen L, Haug U. Protection from right- and left-sided colorectal neoplasms after colonoscopy: population-based study. J Natl Cancer Inst 2010;102:89–95.
14. Tao S, Hoffmeister M, Brenner H. Development and validation of a scoring system to identify individuals at high risk for advanced colorectal neoplasms who should undergo colonoscopy screening. Clin Gastroenterol Hepatol 2014;12:478–85.
15. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. Am J Epidemiol 2005;162:199–200.
16. Sinha R, Peters U, Cross AJ, Kulldorff M, Weissfeld JL, Pinsky PF, Rothman N, Hayes RB. Meat, meat cooking methods and preservation, and risk for colorectal adenoma. Cancer Res 2005;65:8034–41.
17. Tantamango YM, Knutsen SF, Beeson WL, Fraser G, Sabate J. Foods and food groups associated with the incidence of colorectal polyps: the Adventist Health Study. Nutr Cancer 2011;63:565–72.
18. Tiemersma EW, Voskuil DW, Bunschoten A, Hogendoorn EA, Witteman BJ, Nagengast FM, Glatt H, Kok FJ, Kampman E. Risk of colorectal adenomas in relation to meat consumption, meat preparation, and genetic susceptibility in a Dutch population. Cancer Causes Control 2004;15:225–36.
19. Ferrucci LM, Sinha R, Huang WY, Berndt SI, Katki HA, Schoen RE, Hayes RB, Cross AJ. Meat consumption and the risk of incident distal colon and rectal adenoma. Br J Cancer 2012;106:608–16.
20. Probst-Hensch NM, Sinha R, Longnecker MP, Witte JS, Ingles SA, Frankl HD, Lee ER, Haile RW. Meat preparation and colorectal adenomas in a large sigmoidoscopy-based case-control study in California (United States). Cancer Causes Control 1997;8:175–83.
21. Shin A, Shrubsole MJ, Ness RM, Wu H, Sinha R, Smalley WE, Shyr Y, Zheng W. Meat and meat-mutagen intake, doneness preference and the risk of colorectal polyps: the Tennessee Colorectal Polyp Study. Int J Cancer 2007;121:136–42.
22. Breuer-Katschinski B, Nemes K, Marr A, Rump B, Leiendecker B, Breuer N, Goebell H. Colorectal adenomas and diet: a case-control study. Colorectal Adenoma Study Group. Dig Dis Sci 2001;46:86–95.
23. Senesse P, Boutron-Ruault MC, Faivre J, Chatelain N, Belghiti C, Meance S. Foods as risk factors for colorectal adenomas: a case-control study in Burgundy (France). Nutr Cancer 2002;44:7–15.
24. Sandler RS, Lyles CM, Peipins LA, McAuliffe CA, Woosley JT, Kupper LL. Diet and risk of colorectal adenomas: macronutrients, cholesterol, and fiber. J Natl Cancer Inst 1993;85:884–91.
25. Budhathoki S, Iwasaki M, Yamaji T, Sasazuki S, Takachi R, Sakamoto H, Yoshida T, Tsugane S. Dietary heterocyclic amine intake, NAT2 genetic polymorphism, and colorectal adenoma risk: the colorectal adenoma study in Tokyo. Cancer Epidemiol Biomarkers Prev 2015;24:613–20.
26. Cross AJ, Pollock JR, Bingham SA. Haem, not protein or inorganic iron, is responsible for endogenous intestinal N-nitrosation arising from red meat. Cancer Res 2003;63:2358–60.
27. Ward MH, Cross AJ, Divan H, Kulldorff M, Nowell-Kadlubar S, Kadlubar FF, Sinha R. Processed meat intake, CYP2A6 activity and risk of colorectal adenoma. Carcinogenesis 2007;28:1210–6.
28. Ferrucci LM, Sinha R, Graubard BI, Mayne ST, Ma X, Schatzkin A, Schoenfeld PS, Cash BD, Flood A, Cross AJ. Dietary meat intake in relation to colorectal adenoma in asymptomatic women. Am J Gastroenterol 2009;104:1231–40.
29. Sesink AL, Termont DS, Kleibeuker JH, Van der Meer R. Red meat and colon cancer: the cytotoxic and hyperproliferative effects of dietary heme. Cancer Res 1999;59:5704–9.
30. Qiao L, Feng Y. Intakes of heme iron and zinc and colorectal cancer incidence: a meta-analysis of prospective studies. Cancer Causes Control 2013;24:1175–83.
31. Bastide NM, Pierre FH, Corpet DE. Heme iron from meat and risk of colorectal cancer: a meta-analysis and a review of the mechanisms involved. Cancer Prev Res (Phila) 2011;4:177–84.
32. Chan AT, Ma J, Tranah GJ, Giovannucci EL, Rifai N, Hunter DJ, Fuchs CS. Hemochromatosis gene mutations, body iron stores, dietary iron, and risk of colorectal adenoma in women. J Natl Cancer Inst 2005;97:917–26.
33. Ruder EH, Berndt SI, Gilsing AM, Graubard BI, Burdett L, Hayes RB, Weissfeld JL, Ferrucci LM, Sinha R, Cross AJ. Dietary iron, iron homeostatic gene polymorphisms and the risk of advanced colorectal adenoma and cancer. Carcinogenesis 2014;35:1276–83.
34. Cross AJ, Sinha R, Wood RJ, Xue X, Huang WY, Yeager M, Hayes RB, Gunter MJ. Iron homeostasis and distal colorectal adenoma risk in the prostate, lung, colorectal, and ovarian cancer screening trial. Cancer Prev Res (Phila) 2011;4:1465–75.
35. Bastide N, Morois S, Cadeau C, Kangas S, Serafini M, Gusto G, Dossus L, Pierre FH, Clavel-Chapelon F, Boutron-Ruault MC. Heme iron intake, dietary antioxidant capacity, and risk of colorectal adenomas in a large cohort study of French women. Cancer Epidemiol Biomarkers Prev 2016;25:640–7.
36. Gunter MJ, Probst-Hensch NM, Cortessis VK, Kulldorff M, Haile RW, Sinha R. Meat intake, cooking-related mutagens and risk of colorectal adenoma in a sigmoidoscopy-based case-control study. Carcinogenesis 2005;26:637–42.
37. Rohrmann S, Hermann S, Linseisen J. Heterocyclic aromatic amine intake increases colorectal adenoma risk: findings from a prospective European cohort study. Am J Clin Nutr 2009;89:1418–24.
38. Sinha R, Kulldorff M, Chow WH, Denobile J, Rothman N. Dietary intake of heterocyclic amines, meat-derived mutagenic activity, and risk of colorectal adenomas. Cancer Epidemiol Biomarkers Prev 2001;10:559–62.
39. Sinha R, Kulldorff M, Gunter MJ, Strickland P, Rothman N. Dietary benzo[a]pyrene intake and risk of colorectal adenoma. Cancer Epidemiol Biomarkers Prev 2005;14:2030–4.
40. Wang H, Yamamoto JF, Caberto C, Saltzman B, Decker R, Vogt TM, Yokochi L, Chanock S, Wilkens LR, Le Marchand L. Genetic variation in the bioactivation pathway for polycyclic hydrocarbons and heterocyclic amines in relation to risk of colorectal neoplasia. Carcinogenesis 2011;32:203–9.

41. Wu K, Giovannucci E, Byrne C, Platz EA, Fuchs C, Willett WC, Sinha R. Meat mutagens and risk of distal colon adenoma in a cohort of U.S. men. Cancer Epidemiol Biomarkers Prev 2006;15:1120–5.

42. Ho V, Peacock S, Massey TE, Ashbury JE, Vanner SJ, King WD. Meat-derived carcinogens, genetic susceptibility and colorectal adenoma risk. Genes Nutr 2014;9:430.

43. Burnett-Hartman AN, Newcomb PA, Mandelson MT, Adams SV, Wernli KJ, Shadman M, Wurscher MA, Makar KW. Colorectal polyp type and the association with charred meat consumption, smoking, and microsomal epoxide hydrolase polymorphisms. Nutr Cancer 2011;63: 583–92.

44. Erhardt JG, Kreichgauer HP, Meisner C, Bode JC, Bode C. Alcohol, cigarette smoking, dietary factors and the risk of colorectal adenomas and hyperplastic polyps–a case control study. Eur J Nutr 2002;41:35–43.

45. Snover DC. Update on the serrated pathway to colorectal carcinoma. Hum Pathol 2011;42:1–10.

46. Haque T, Greene KG, Crockett SD. Serrated neoplasia of the colon: what do we really know? Curr Gastroenterol Rep 2014;16:380.

47. Haque TR, Bradshaw PT, Crockett SD. Risk factors for serrated polyps of the colorectum. Dig Dis Sci 2014;59:2874–89.

48. Leggett B, Whitehall V. Role of the serrated pathway in colorectal cancer pathogenesis. Gastroenterology 2010;138:2088–100.