

# Gastric and colorectal cancer incidence attributable to dietary factors in Korea

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**Background:** Dietary factors play a role in the etiology of gastrointestinal cancer. We aimed to estimate the burden of gastric and colorectal cancer that can be attributable to dietary factors in adults aged 20 years and older in Korea in 2018.

**Methods:** Dietary intakes in 2000 were estimated using data from the 2001, 2005, and 2007–2018 Korea National Health and Nutrition Examination Survey (KNHANES). For counterfactual scenarios, the optimal level of intake suggested by the Global Burden of Disease (GBD) study was used if it was available. Otherwise, the average intake values of reference groups among published studies globally were used. Relative risks (RRs) were pooled through dose-response meta-analyses of Korean studies.

**Results:** In Korea in 2018, an estimated 18.6% of gastric cancer cases and 34.9% of colorectal cancer cases were attributed to the combined effect of evaluated dietary factors. High intake of salted vegetables accounted for 16.0% of gastric cancer cases, followed by salted fish at 2.4%. Low intakes of whole grains (16.6%) and milk (13.7%) were leading contributors to colorectal cancer cases, followed by high intakes of processed meat (3.1%) and red meat (5.9%), and a low intake of dietary fiber (0.5%).

**Conclusions:** These results suggest that a considerable proportion of gastric and colorectal cancer incidence might be preventable by healthy dietary habits in Korea. However, further research is needed to confirm the associations between dietary factors and gastric and colorectal cancers in Korea and to formulate and apply effective cancer prevention strategies to Koreans.

Keywords: Population attributable fraction (PAF); gastric cancer; colorectal cancer; dietary factors; Korean

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#### Introduction

Cancer is the leading cause of death in Korea, with an estimated 247,952 newly diagnosed cases and 82,204 deaths in 2020 (1). The economic burden of cancer is steadily increasing, showing from \$11,894.9 in 2011 to \$13,945.3 in 2015 (2). In Korea, gastric and colorectal cancer were two of the most common cancers, with age-standardized incidence rates of 25.7 and 27.1 per 100,000 in 2020 (1).

Cancer is caused by a combination of environmental and genetic factors. Diet has been long studied as a risk factor for cancer. Summary results of the association have been reported in the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) Continuous Update Project (CUP). In particular, a relatively larger number of dietary factors were found to be associated with gastrointestinal cancers compared to other cancer sites in the CUP. Foods preserved by salting, including salted vegetables and salted fish, have been suggested as a probable risk factor for gastric cancer (3). For colorectal cancer, red and processed meat were reported to increase the risk of

#### **Highlight box**

#### Key findings

- In total, 5,307 gastric cancer cases and 9,820 colorectal cancer cases were found to be attributable to dietary factors in 2018 in Korea.
- The primary contributors were a high intake of salted vegetables for gastric cancer and a low intake of whole grains for colorectal cancer.

#### What is known and what is new?

- Substantial contributions of dietary factors to cancer risk have been suggested in Western studies, but Asian studies remain scarce.
- Our study examined the population attributable fraction (PAF) of various dietary factors, including salted vegetables and salted fish, for gastric and colorectal cancer.

#### What is the implication, and what should change now?

- Adopting healthy dietary habits, including reducing the consumption of salted vegetables, salted fish, red meat, and processed meat, while ensuring an adequate intake of milk, whole grains, and dietary fiber, has the potential to prevent a substantial proportion of gastric and colorectal cancers.
- Continuous monitoring of PAFs for dietary factors linked to gastric and colorectal cancers is needed.

cancer (4). Dairy products, whole grains, dietary fiber, and calcium supplements have been reported as probable factors to decrease the risk of colorectal cancer (4).

The population attributable fraction (PAF) is a measure of the proportion of disease in a population that could be prevented by eliminating a selected risk factor (5). PAFs can help prioritize risk factors contributing to cancer prevention and develop effective intervention strategies. Given the high incidences of gastric cancer and colorectal cancer and changes in diet over time in Korea, it is necessary to estimate the impact of cancer-related dietary factors in the Korean population. Recently, red and processed meat as dietary factors were considered in the Korean PAF-colorectal cancer study (6). However, comprehensive dietary factors associated with colorectal and gastric cancer have not been examined for PAFs in the Korean population. We aimed to estimate the PAFs and the number of gastric and colorectal cancer cases attributable to dietary factors in adults aged 20 years and older using nationally representative data on dietary factors. We present this article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/ view/10.21037/jgo-24-10/rc).

#### Methods

#### Selection of dietary factors for gastric and colorectal cancer

We selected dietary risk factors for gastric and colorectal cancer that had evidence supporting a causal relationship by two selection criteria. Firstly, convincing or probable dietary risk factors as evidenced by the WCRF/AICR CUP on gastric and colorectal cancers were considered (3,4). Secondly, we considered the dietary risk factors with sufficient evidence in humans to be carcinogenic agents in groups 1 and 2A, as classified by the International Agency for Research on Cancer (IARC) Monograph (7).

We included high intakes of foods preserved by salting (mainly salted vegetables and salted fish) as dietary risk factors for gastric cancer (Table S1). Given the different serving sizes of salted vegetables and salted fish, we included them separately in this study. For colorectal cancer, we identified the following dietary risk factors: high intakes of

red meat and processed meat, low intakes of dairy products, whole grains, and dietary fiber, and non-use of calcium supplements. However, we excluded calcium supplements because there was insufficient representative data on the intake of calcium supplements. In the current analysis, we included milk instead of dairy products to use the optimal intake ranges suggested by the Global Burden of Disease (GBD) study (8).

# Current distribution and counterfactual scenarios for each dietary risk factor

We used the intake levels in 2000 as the current distribution of dietary factors for estimating the burden of cancers in 2018, considering the latency period of at least 15 years. We estimated the daily mean intake and the standard deviations (SDs) of dietary risk factors in the Korean population using 24-hour dietary recall data from the Korea National Health and Nutrition Examination Survey (KNHANES) for men and women aged 20 and older. The KNHANES is a nationwide surveillance system that has been designed to monitor the health and nutritional status of Koreans since 1998 (9). Due to the lack of KNHANES data in 2000, we used KNHANES data from 2001, 2005, and 2007–2018, and estimated the age-standardized intake levels using the census 2000.

For counterfactual scenarios, we used the optimal intake levels suggested by the GBD study 2017 (8) (Table S2). Because the optimal intake levels of salted vegetables and salted fish were not suggested by the GBD study, we used the average intake values of reference groups among published studies globally.

#### Relative risks (RRs)

We performed dose-response meta-analyses of global cohort studies to investigate the associations of salted vegetables and salted fish with gastric cancer risk, and the associations of red meat, processed meat, milk, whole grains, and dietary fiber with colorectal cancer risk. In the sensitivity analyses, we conducted dose-response metaanalyses of the Asian prospective cohort and case-control studies. We directly analyzed the data of the Korean Multi-center Cancer Cohort Study (KMCC) (10) and the Namwon Study and the Dong-gu Study (NWS/DGS) (11) and added the estimates in the meta-analyses. The RRs of the associations for dietary factors available in the KMCC and the NWS/DGS are presented in Table S3. We conducted a comprehensive literature search for observational studies published up to November 2019 in PubMed, EMBASE, and KoreaMed. The key search terms were 'salted vegetable', 'pickled vegetable', 'salted fish', 'red meat', 'processed meat', 'meat', 'milk', 'dairy products, 'whole grains', 'dietary fiber', 'gastric cancer', and 'colorectal cancer'. The detailed search terminology used in each literature database is listed in Table S4. Further, we manually identified articles from the reference lists of review articles and meta-analyses on the association between each dietary risk factor and gastric/colorectal cancer risk.

We included prospective cohort studies and Asian casecontrol studies in meta-analyses if (I) the exposure of interest was one of our selected dietary risk factors; (II) the outcome of interest was gastric/colorectal cancer incidence; (III) they were published in English or Korean; (IV) RRs and 95% confidence intervals (CIs) or data to estimate these parameters were provided; and (V) there were at least 1,000 cases if the study design was a hospital-based casecontrol study. If studies were duplicated, we included the study with the following priority; the study reporting a higher number of cases; or the study published most recently. For dose-response meta-analyses, studies were included if they met the following additional criteria; studies provided data on more than two levels of dietary risk factors; studies provided data on the number of cases and controls (if case-control study); studies provided data on person-time or number of participants (if cohort study); and they provided quantified data on each level of dietary risk factors.

#### Cancer incidence

We used cancer incidence data derived from the Korea Central Cancer Registry in the Korean Statistical Information Service (KOSIS). Cancer incidence data in 2018 were extracted for both sexes aged 20 years and older. Gastric and colorectal cancers were defined as C16 and C18–C20, respectively, by the International Classification of Diseases 10<sup>th</sup> Revision (ICD-10) codes.

### Estimation of PAFs and the number of cancer cases attributed to dietary factors

We calculated the PAFs using pooled RRs from global cohort studies and RRs from Asian prospective cohort and case-control studies. When we assumed that dietary intakes were normally distributed, which could lead to the problem of having negative levels of intake, we assigned values below zero to a value of zero. To estimate incident cases of cancer attributable to dietary risk factors in each sex, we multiplied the sex-specific PAFs by the number of incident cases for cancer. The PAFs for both sexes attributable to each dietary risk factor were calculated by dividing the sum of attributable cases in men and women by the number of incident cases in both sexes.

#### Sensitivity analyses

In the sensitivity analysis, we used RRs only from Asian cohort studies and case-control studies to estimate Asianspecific PAFs. To consider the potential skewed distribution of dietary intakes, we conducted a sensitivity analysis assuming that dietary intakes followed a log-normal distribution. We also conducted a sensitivity analysis using the following modified Levin's formula (12) to estimate the PAF for continuous exposures.

$$PAF = \frac{P(e^{\beta*dose} - 1)}{P(e^{\beta*dose} - 1) + 1}$$
[1]

In the formula, P means the proportion exposed to each dietary risk level, and the dose is the daily mean intake (as a continuous variable). RR [ $\beta = \log(RR)$ ] was applied to this equation as a gram increase per day in each dietary risk factor. We used the RRs retrieved from the dose-response meta-analysis in this study. The prevalence of dietary risk factors in 2000 was predicted from the KNHANES 2001, 2005, and 2007–2018 using a linear regression model with optimal levels of intake, suggested by the GBD study 2017, or with the average intake values of reference groups among published studies.

#### Statistical analysis

The dietary intake levels in 2000 were predicted using a linear regression model. Since dietary fiber data were available from 2013 to 2018, we used these data to predict dietary fiber intake levels in 2000. For counterfactual scenarios, we assumed a uniform distribution of ±20% of the optimal levels for each dietary risk factor to account for the uncertainty of those levels (8). SD was estimated by the following formula:  $SD = \frac{mean \times 0.2}{\sqrt{3}}$  (13). All statistical analyses for the estimation of the daily mean intake and the SDs were conducted using SAS software (version 9.4, SAS Institute Inc., Cary, NC, USA).

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When conducting the meta-analyses of the association between each dietary factor and cancer risk, we pooled the RRs using a random-effects model (14). Test for heterogeneity across studies was conducted by Cochran's Q test (15). All meta-analyses were conducted with the use of R software (version 3.4.4, R Foundation for Statistical Computing, Vienna, Austria).

We estimated the PAFs of gastric and colorectal cancers using the following formula (16), assuming the causal relationship between each dietary risk factor and cancer.

$$PAF = \frac{\int_{x=0}^{m} RR(x)P(x)dx - \int_{x=0}^{m} RR(x)P'(x)dx}{\int_{x=0}^{m} RR(x)P(x)dx}$$
[2]

In the formula, x is the levels of each dietary risk factor, m is the maximum levels of those factors, RR(x) is the sexspecific RR at x level of exposure, P(x) is the sex-specific current distribution of exposure, and P'(x) represents the counterfactual distribution of exposure. If the sex-specific RR was not available, we used overall RR estimated from both sexes.

To estimate the total effect of all dietary factors on each cancer, we used the following equation (17,18).

$$PAF = 1 - \prod_{i=1}^{n} (1 - PAF_i)$$
[3]

In the equation, *i* mean individual dietary factors. We assumed that dietary factors were independently distributed and those RRs were multiplicative. To estimate the 95% CIs of PAFs, we applied Monte Carlo simulations (19). PAF calculations were repeated 10,000 times, with randomly selected RRs assuming a log-normal distribution. We then used 2.5<sup>th</sup> and 97.5<sup>th</sup> percentile values of the 10,000 values for 95% CIs. All statistical analyses for estimating PAFs were conducted using R software (version 3.4.4, R Foundation for Statistical Computing).

#### Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Seoul National University Hospital (No. C-1911-188-1084).

#### **Results**

#### Daily mean intake levels of dietary risk factors

The daily mean intake levels of dietary factors were

Table 1 Predicted daily mean intake levels of dietary factors in Korean adults aged 20 years or more in 2000

	Daily mean intake levels in 2000 (g/day), mean (95% Cl)					
Dietary risk factors —	All	Men	Women			
Salted vegetables	165.6 (159.3–171.9)	186.8 (178.2–195.3)	146.3 (140.5–152.1)			
Salted fish	4.1 (3.9–4.9)	4.7 (3.7–5.8)	3.6 (2.7–4.5)			
Red meat	57.2 (53.0–61.0)	73.9 (68.2–79.6)	41.8 (38.3–45.2)			
Processed meat	2.9 (2.3–3.5)	3.5 (2.5–4.5)	2.3 (1.8–2.9)			
Milk	37.1 (33.4–40.9)	34.4 (29.2–39.6)	39.6 (34.8–44.3)			
Whole grains	12.5 (10.2–14.8)	12.5 (9.6–15.4)	12.6 (10.1–14.9)			
Dietary fiber	22.8 (22.4–23.2)	24.5 (23.6–25.4)	21.2 (21.0–21.5)			

CI, confidence interval.

estimated to assess the difference between current and optimal intake levels (Table 1). The daily mean intake of salted vegetables was 165.6 g/d, with kimchi accounting for 96.2% of salted vegetables among Korean adults. The intake level of salted vegetables was higher than the optimal range of <9 g/d, as estimated by the mean of reference group ranges among published studies worldwide. The mean intake of salted fish (4.1 g/d) was slightly higher than the optimal range of <3 g/d, as estimated by the same protocols. The mean intake of red meat (57.2 g/d) was higher than the optimal range of 18–27 g/d, as suggested by the GBD study. The daily mean intake of processed meat was 2.9 g, close to the optimal range of 0-4 g/d. The daily mean intakes of milk and whole grains were 37.1 and 12.5 g, respectively, which were lower than the optimal ranges of 350-520 g/d for milk and 100-150 g/d for whole grains. The daily mean intake of dietary fiber (22.8 g) was within the optimal range of 19-28 g/d. When we estimated the dietary intake levels for each sex, the daily mean intake levels of dietary risk factors, except for milk and whole grains, were higher in men than in women. When we examined the trend of intake levels of dietary factors from 2000 to 2018, we found that the intake levels of salted vegetables and salted fish decreased, while the intake levels of red meat, processed meat, and milk increased (Figure S1).

# Estimation of the RRs of cancers associated with dietary risk factors

We performed a comprehensive literature search and identified relevant articles for inclusion in a meta-analysis investigating the associations of salted vegetables and salted fish with gastric cancer, as well as the associations of red meat, processed meat, milk, whole grains, and dietary fiber with colorectal cancer from the PubMed, EMBASE, and KoreaMed (Figures S2-S8).

The pooled RRs of gastric and colorectal cancer incidence associated with dietary risk factors are presented in Table 2. When pooling RRs from global cohort studies, we observed the following associations of each dietary factor with corresponding cancers. No significant associations were observed between gastric cancer and the intakes of salted vegetables [RR (95% CI): 1.04 (0.96-1.12) per increment of 40 g/d] or salted fish [RR (95% CI): 1.03 (0.92-1.15) per an increment of 20 g/d]. For colorectal cancer incidence, we found increased risks with a 120 g/d increment in red meat intake [RR (95% CI): 1.19 (1.08-1.31)] and a 50 g/d increment in processed meat intake [RR (95% CI): 1.13 (1.06-1.20)]. Conversely, we observed decreased risks with a 200 g/d increment in milk intake [RR (95% CI): 0.91 (0.89-0.94)], a 30 g/d increment in whole grains intake [RR (95% CI): 0.96 (0.94-0.99)], and a 10 g/d increment in dietary fiber intake [RR (95% CI): 0.93 (0.90-0.96)]. The results of meta-analyses, including Asian cohort studies and case-control studies, were consistent with those from the global cohort studies.

## *Gastric and colorectal cancers attributable to dietary risk factors*

When estimating PAFs using RR from global cohort studies, we found that an estimated 18.6% (95% CI: 0.0–51.5%) and 34.9% (95% CI: 12.0–58.6%) of new gastric and colorectal cancers in Korean adults aged 20 years and older were attributable to all combined dietary factors in 2018 (*Table 3*). The sex-specific PAFs of gastric and

Table 2 Summary estimates of gastric and colorectal cancer incidence by dietary risk factors

Dietary factors	Global (cohort only)			Asia (cohort + case-control)				
	Study, n	RR (95% CI)	l <sup>2</sup> (%)	P for heterogeneity	Study, n	RR (95% CI)	l <sup>2</sup> (%)	P for heterogeneity
Gastric cancer								
Salted vegetables (per 4	0 g/day)							
All	6	1.04 (0.96–1.12) <sup>†</sup>	27	0.23	10	1.06 (0.95–1.18) <sup>‡</sup>	43	0.06
Men	4	1.02 (0.96–1.09)	0	0.57	4	1.02 (0.96–1.09)	0	0.57
Women	3	0.92 (0.82–1.03)	0	0.50	3	0.92 (0.82–1.03)	0	0.50
Salted fish (per 20 g/day	()							
All	3	1.03 (0.92–1.15) <sup>†</sup>	25	0.27	5	1.07 (0.90–1.27) <sup>‡</sup>	49	0.08
Men	2	1.00 (0.84–1.21)	0	0.43	2	1.00 (0.84–1.21)	0	0.43
Women	2	0.73 (0.27–1.97)	38	0.20	2	0.73 (0.27–1.97)	38	0.20
Colorectal cancer								
Red meat (per 120 g/day	y)							
All	16	1.19 (1.08–1.31)	24	0.18	6	1.10 (0.93–1.31)	24	0.24
Men	7	1.02 (0.82–1.27) <sup>†</sup>	0	0.49	4	1.04 (0.72–1.49) <sup>‡</sup>	0	0.68
Women	10	1.21 (1.07–1.38) <sup>†</sup>	0	0.76	4	1.09 (0.87–1.36) <sup>‡</sup>	0	0.80
Processed meat (per 50	g/day)							
All	21	1.13 (1.06–1.20)	28	0.09	4	1.11 (0.97–1.27)	34	0.20
Men	7	1.05 (0.94–1.16) <sup>†</sup>	1	0.42	2	1.12 (0.70–1.77) <sup>‡</sup>	61	0.11
Women	12	1.27 (1.15–1.39) <sup>†</sup>	0	0.53	2	1.31 (1.04–1.65) <sup>‡</sup>	0	0.96
Milk (per 200 g/day)								
All	16	0.91 (0.89–0.94)	0	0.94	3	0.83 (0.69–0.99)	0	0.98
Men	8	0.91 (0.85–0.97) <sup>†</sup>	0	0.75	1	0.99 (0.50–1.95) <sup>‡</sup>	N/A	N/A
Women	8	0.93 (0.85–1.03) <sup>†</sup>	3	0.41	2	0.79 (0.60–1.05) <sup>‡</sup>	0	0.74
Whole grains (per 30 g/day)								
All	6	0.96 (0.94–0.99)	43	0.08	2	0.60 (0.29–1.24)	47	0.17
Men	4	0.92 (0.89–0.96) <sup>†</sup>	38	0.17	1	0.76 (0.32–1.79)‡	N/A	N/A
Women	7	0.96 (0.93–1.00) <sup>†</sup>	23	0.24	1	0.83 (0.29–2.38)‡	N/A	N/A
Dietary fiber (per 10 g/day)								
All	13	0.93 (0.90–0.96)	34	0.09	5	0.90 (0.75–1.06)	53	0.06
Men	10	0.94 (0.92–0.97) <sup>†</sup>	0	0.46	3	0.89 (0.66–1.20) <sup>‡</sup>	45	0.16
Women	15	0.94 (0.90–0.98) <sup>†</sup>	31	0.12	5	0.85 (0.71–1.02) <sup>‡</sup>	35	0.19

<sup>†</sup>, the values for the estimation of PAFs using RRs from global cohort studies; <sup>‡</sup>, the values for the estimation of PAFs using RRs from Asian cohort and case-control studies. Forest plots for meta-analyses are presented in Figures S9-S22. Reference lists for meta-analysis on the associations of dietary factors with gastric or colorectal cancer risk are presented in Tables S5-S11. RR, relative risk; CI, confidence interval; N/A, not applicable; PAF, population attributable fraction.

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Dietary factors	Men		Women		All		
	PAF (%)	Attributable cases	PAF (%)	Attributable cases	PAF (%)	Attributable cases	
Gastric cancer							
Salted vegetables	16.9 [0.0–46.7]	3,369 [0–9,319]	14.2 [0.0–41.0]	1,347 [0–3,875]	16.0 [0.0–44.9]	4,716 [0–13,195]	
Salted fish	2.4 [0.0–12.1]	481 [0–2,406]	2.4 [0.0–12.1]	223 [0–1,140]	2.4 [0.0–12.1]	704 [0–3,546]	
Total	18.9 [0.0–53.1]	3,769 [0–10,602]	16.3 [0.0–48.1]	1,538 [0–4,548]	18.6 [0.0–51.5]	5,307 [0–15,150]	
Colorectal cancer							
Red meat	2.2 [0.0–22.2]	378 [0–3,744]	11.3 [3.8–18.7]	1,280 [436–2,115]	5.9 [1.5–20.8]	1,658 [436–5,860]	
Processed meat	1.9 [0.0–5.1]	319 [0–860]	4.9 [2.9–6.9]	553 [327–778]	3.1 [1.2–5.8]	872 [327–1,639]	
Milk	15.2 [4.9–24.4]	2,566 [832–4,103]	11.4 [0.0–25.2]	1,293 [0–2,859]	13.7 [3.0–24.7]	3,859 [832–6,962]	
Whole grains	20.5 [10.9–29.1]	3,451 [1,836–4,899]	10.8 [0.2–20.4]	1,226 [26–2,312]	16.6 [6.6–25.6]	4,677 [1,862–7,211]	

1.1 [0.3-2.2]

Table 3 Gastric and colorectal cancers attributable to dietary factors in Korea in 2018 using pooled RRs from global cohort studies

Data are presented as % or n [95% confidence interval]. RR, relative risk; PAF, population attributable fraction.

35.4 [15.3-60.4] 5,956 [2,577-10,175] 34.1 [7.1-55.9] 3,864 [807-6,335]

0 [0-0] 0

colorectal cancers attributable to all combined dietary factors were 18.9% (95% CI: 0.0–53.1%) and 35.4% (95% CI: 15.3–60.4%) among men, and 16.3% (95% CI: 0.0–48.1%) and 34.1% (95% CI: 7.1–55.9%) among women, respectively.

0.0 [0.0-0.0]

Dietary fiber

Total

Out of the 29,405 (19,948 for men and 9,457 for women) newly diagnosed gastric cancer cases among Korean adults aged 20 years and older, 5,307 cases (3,769 for men and 1,538 for women) were attributable to all dietary factors. High intakes of salted vegetables and salted fish accounted for 16.0% (95% CI: 0.0-44.9%) and 2.4% (95% CI: 0.0-12.1%) of incident gastric cancers, respectively. The PAFs of gastric cancer attributable to salted vegetables were slightly higher among men [PAF (95% CI): 16.9% (0.0-46.7%)] than among women [PAF (95% CI): 14.2% (0.0-41.0%)]. Considering the high intake of salted vegetables in Korea, we estimated the burden of gastric cancer attributable to salted vegetables using optimal intake levels derived from the average intake values of reference groups, focusing specifically on data from published Korean studies. A similar PAF was observed; the PAFs (95% CIs) of gastric cancer attributable to salted vegetables were 13.7% (0.0-40.6%) (cut-off levels for risk: <39 g/d) compared to 16.0% (0.0–44.9%) (cut-off levels for risk: <9 g/d).

When estimating the burden of colorectal cancer attributable to dietary factors, we found that among the 28,174 newly diagnosed cases (16,836 for men and 11,338 for women), 9,820 cases (5,956 for men and 3,864 for

women) were attributable to all dietary factors. The primary contributors to all incident colorectal cancers attributable to dietary factors were a low intake of whole grains [PAF (95% CI): 16.6% (6.6–25.6%)], followed by a low intake of milk [PAF (95% CI): 13.7% (3.0–24.7%)], a high intake of red meat [PAF (95% CI): 5.9% (1.5–20.8%)], a high intake of processed meat [PAF (95% CI): 3.1% (1.2–5.8%)], and a low intake of dietary fiber [PAF (95% CI): 0.5% (0.1–0.9%)].

0.5 [0.1-0.9]

128 [34-246]

34.9 [12.0-58.6] 9,820 [3,384-16,510]

#### Sensitivity analyses

128 [34-246]

We used RRs from the Asian cohort and case-control studies to estimate the burden of gastric and colorectal cancers attributable to dietary factors. We observed higher PAFs for gastric cancer [PAF (95% CI): 29.6% (0.0–67.3%)] and colorectal cancer [PAF (95% CI): 63.1% (0.4–99.5%) for Asian RR] compared to results based on global cohort studies (Table S12). The primary contributor to incident gastric and colorectal cancer remained consistent when compared to PAFs obtained from global cohort studies: a high intake of salted vegetables [PAF (95% CI): 25.0% (0.0–59.0%)] for gastric cancer and a low intake of whole grains [PAF (95% CI): 51.3% (0.0–97.6%)] for colorectal cancer.

For sensitivity analysis, we estimated the PAFs assuming that dietary intakes followed a log-normal distribution (Table S13). A lower PAF for gastric and colorectal cancers attributable to all dietary factors was observed compared to assuming that dietary intakes followed a zero-truncated normal distribution (as per our primary results from global cohort studies). The PAF (95% CI) for gastric cancer was 0.0% (0.0-38.1%) in the sensitivity analysis vs. 18.6% (0.0-51.5%) in the primary results. Similarly, the PAF (95% CI) for colorectal cancer was 33.5% (11.3-52.2%) in the sensitivity analysis vs. 34.9% (12.0-58.6%) in the primary results. Nevertheless, a low intake of whole grains consistently accounted for the highest proportion of colorectal cancers across all assumptions of dietary intake distribution.

When using the modified Levin's formula to calculate the PAFs, we observed lower PAFs compared to our primary results. Specifically, the PAFs (95% CIs) of gastric and colorectal cancers attributable to all dietary risk factors were 14.3% (0.0–39.3%) and 10.8% (4.0–20.8%), respectively (Table S14). The primary contributor to colorectal cancer was a low intake of dietary fiber [PAF (95% CI): 5.5% (2.9–8.1%)]. Nevertheless, a low intake of whole grains, as the second contributor, still accounted for a higher proportion of colorectal cancer than other dietary factors [PAF (95% CI): 3.1% (1.6–4.9%)].

#### Discussion

We found that in 2018, 18.6% of gastric cancer cases (5,307 cases) and 34.9% of colorectal cancer cases (9,820 cases) in the Korean population were attributed to inadequate or excess intake of specific dietary factors. Among these, a high intake of salted vegetables accounted for the highest proportion of gastric cancer cases (16.0%), followed by a high intake of salted fish (2.4%). For colorectal cancer, a low intake of whole grains was the leading dietary factor contributing to 16.6% of cases, followed by a low intake of milk (13.7%), a high intake of red meat (5.9%), a high intake of processed meat (3.1%), and a low intake of dietary fiber (0.5%). The proportion of gastric cancer cases attributable to dietary factors was slightly higher in men (18.9%) compared to women (16.3%), which can be attributed in part to higher intakes of salted vegetables and salted fish among men. For colorectal cancer, the proportion of cases attributable to dietary factors was similar across sexes (men: 35.4% of PAF, women: 34.1% of PAF). Notably, the PAFs for red meat and processed meat were higher among women than among men, while the PAFs of milk and whole grains were higher among men than among women. The higher RRs (far from null) of red

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meat and processed meat among women and the higher RRs (far from null) of milk and whole grains among men in global cohort studies contributed to a higher burden of new colorectal cancer cases in each sex.

Several studies have estimated the PAFs of gastric and colorectal cancers attributable to dietary factors. For gastric cancer, PAFs were reported as 6.8% in the US in 2015 (including red meat, processed meat, whole grains, fruits, vegetables, and sugar-sweetened beverages) (20), 7.1% in France in 2015 (including processed meat only) (21), and 8.7% in Germany in 2018 (including salt only) (22). In terms of colorectal cancer, studies have reported PAFs attributable to dietary factors as follows: 56% in Italy from 1985 to 1992 (including red meat, β-carotene, vitamin C, and major seasoning fats) (23); 38.3% in the US in 2015 (including red meat, processed meat, dairy products, whole grains, fruits, vegetables, and sugar-sweetened beverages) (20); 22.9% in France in 2015 (including red meat, processed meat, dairy products, and dietary fiber) (21); and 29.1% in Germany in 2018 (including red meat, processed meat, dietary fiber, fruit and non-starchy vegetable, and salt) (22). The PAF of gastric cancer due to dietary factors in Korea was higher than in other countries, attributed to the high intake of salted vegetables in Korea. Regarding colorectal cancer, low intakes of whole grains were identified as the primary contributing factor in Korea. Compared to countries that did not include whole grains in their analysis, our PAF (34.9%) was slightly higher. However, it was similar to the level observed in the US study (38.9%) that did include whole grains. This comparison not only underscores the unique dietary patterns and cancer risks in the Korean population but also emphasizes the need for tailored public health strategies that address these specific risk factors.

We observed a higher PAF for dietary factors contributing to gastric cancer compared to previous studies. This elevated PAF might be attributed to a high intake of salted vegetables, including Kimchi. However, it is noteworthy that the daily mean intake levels of salted vegetables have gradually decreased over time in Korea, from 165.6 g/d in 2000 to 104.9 g/d in 2018. Similarly, the intake of salted fish has also shown a decline, decreasing from 4.1 g/d in 2000 to 1.7 g/d in 2018.

For colorectal cancer, we found a similar or slightly higher PAF compared to other studies. In our study, the primary and secondary contributors to colorectal cancer were low intakes of whole grains and milk, respectively. This aligns with findings from a study in the US where the highest PAFs for dietary factors contributing to colorectal cancer were whole grains (19.4%) and dairy products (13.2%) (20). In our study, the percentage of dietary fiber contributing to colorectal cancer was 0.5%, lower than reported in other PAF studies. This discrepancy can be attributed in part to the high dietary fiber intake from vegetables in Korea (24). The proportion of colorectal cancer cases attributable to insufficient dietary fiber intake has been reported to range from 6.0% to 28.0% in various studies (21,22,25-30).

In evaluating individual dietary factors contributing to gastric cancer incidence, high intakes of processed meat and salt have been predominantly studied, with estimates ranging from 2.6% to 7.1% (20,21,25,27,31) for processed meat and 8.7-24.0% (22,26,28) for salt in the Western population. In Japan, a high salt intake (8.9% of the PAF) and low intakes of vegetables (1.3% and 2.2% in men and women) and fruits (1.3% and 5.1% in men and women) were identified as contributors to gastric cancer incidence (32). In the Eastern Mediterranean region, salt was assessed as a contributor to gastric cancer incidence, accounting for 27.3-32.4% of the PAF (33). Even though salted food, including salted vegetables and salted fish, has been proposed as a probable risk factor for gastric cancer, research on its PAFs is limited. A study in China specifically assessed the contribution of salted vegetables to gastric cancer deaths (34). For colorectal cancer in the Western population, PAFs for individual dietary factors were reported as follows: 0.7-17% for high intake of red meat intake (20-23,25,27,31,35,36); 2.9-15% for high processed meat intake (20-22,25,27,29,31,35,36); 2.4-13.2% for low dairy product intake (20,21); 19.4% for low whole grain intake (20); and 6.0-28.0% for low dietary fiber intake (21,22,25,27-30,37). In China, high red and processed meat intakes (8.6% of the PAF) and low intakes of vegetables (17.9%) and fruits (6.4%) were assessed as contributors to colorectal cancer (38). In the Eastern Mediterranean region, high intakes of red meat (2.1–2.2% of the PAF) and processed meat (3.0-3.1% of the PAF) contributed to colorectal cancer incidence (33).

Several studies have estimated the PAFs of colorectal cancer attributed to the combined intake of red meat and processed meat, showing a range of 8.6–21.1% of colorectal cancer cases (6,28,38,39). In a previous study conducted in Korea, it was found that a high intake of red and processed meat contributed to 10.1% and 9.2% of colon cancer cases, as well as 9.2% and 8.3% of rectal cancer cases among men and women, respectively (6). However, we conducted separate calculations for red and processed meat since

they had the different optimal intake ranges suggested by the GBD study (18–27 g/d for red meat and 0–4 g/d for processed meat) and the different RRs for colorectal cancer. In our study, we estimated that 2.0% and 4.2% of colorectal cancer cases were attributable to high intakes of red meat and processed meat, respectively. In several studies that assessed the PAFs of colorectal cancer incidence attributable to red meat and processed meat separately, the PAFs ranged from 0.7% to 17% for red meat (20-23,25-27,31,33,36) and from 2.9% to 15% for processed meat (20-22,25-27,29,31,33,36), respectively. As the intake levels of red meat and processed meat have increased over time in Korea, there might be a need to consistently monitor the burden of cancer attributable to the rising intake of these foods.

To our knowledge, this is the first study to estimate the PAFs of gastric and colorectal cancers attributable to comprehensive dietary factors by estimating the RRs through a systematic approach and by using nationally representative exposure data in the Korean population. We estimated PAFs using the pooled RRs from global cohort studies and Asian cohort and case-control studies. Also, we performed Monte Carlo simulations to allow for uncertainty in the data. However, this study has several limitations. Firstly, dietary intake was evaluated using a single 24-hour dietary recall, which might not reflect the usual intake, in the KNHANES. Secondly, the number of Korean studies might not be sufficient to yield reliable and stable summary results.

#### Conclusions

In conclusion, an estimated 18.6% and 34.9% of gastric and colorectal cancer cases diagnosed in Korea in 2018 were attributable to selected dietary factors. A considerable proportion of gastric and colorectal cancer incidence might be preventable by healthy dietary habits, including low intakes of salted vegetables, salted fish, red meat, and processed meat and sufficient intakes of milk, whole grains, and dietary fiber. Our study highlights the need for continuous monitoring of the PAFs for dietary factors associated with colorectal and gastric cancers.

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#### Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-10/rc

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-10/coif). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Seoul National University Hospital (No. C-1911-188-1084).

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