

1 **Original Article**

2 **Adherence to the World Cancer Research Fund/American Institute for Cancer Research**
3 **and Korean Cancer Prevention Guidelines and cancer risk: a prospective cohort study**
4 **from the Health Examinees-Gem study**

5 **Cancer prevention recommendations and cancer risk**

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1 **Adherence to the World Cancer Research Fund/American Institute for Cancer**
2 **Research and Korean Cancer Prevention Guidelines and cancer risk: a prospective**
3 **cohort study from the Health Examinees-Gem study**

4
5 **Abstract**

6 **Objectives:** The purpose of this study was to explore the association between adherence to 2
7 cancer prevention recommendations and cancer risk.

8 **Methods:** In total, 104,386 individuals aged 40–69 years old who were recruited between 2004
9 and 2013 in the Health Examinees-Gem study were included. Adherence scores were
10 constructed based on 8 items from the World Cancer Research Fund/American Institute for
11 Cancer Research (WCRF/AICR) cancer prevention recommendations, including body weight,
12 physical activity, diet, alcohol consumption and breastfeeding, and on 6 items from the Korean
13 cancer prevention guidelines (smoking status, eating vegetables and fruits, salty foods, alcohol
14 intake, physical activity, and body weight). A Cox proportional hazards model was used to
15 estimate the associations between adherence scores and the risk of total and 5 major cancers.

16 **Results:** The multivariable hazard ratio (HR) for total cancer with the high adherence score
17 versus the lowest score (4.25-7 vs. 0-3.25) for the WCRF/AICR guidelines was 0.91 (95% CI,
18 0.82-1.00) in men. A reduced breast cancer risk was observed among women with the highest
19 score. Men within the highest category of the Korean cancer prevention guideline score (3.25-
20 6.00) had an HR of 0.80 (95% CI: 0.73-0.88) for developing total cancer compared to men
21 within the lowest score (0-2.50). The higher adherence group among men showed lower risks
22 of developing stomach, colorectal, and lung cancers.

23 **Conclusion:** Adhering to guidelines for cancer prevention can help to reduce the risk of
24 developing cancer in Korean men. The association might differ by cancer type and sex.

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26 **Keywords: cancer, Korea, cancer prevention recommendation, WCRF/AICR**

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28 **Introduction**

29 Previous studies have shown that many aspects of cancer pathogenesis are related to lifestyle
30 factors, including dietary habits [1]. It has also been reported that 30%-50% of cancer cases
31 worldwide can be prevented [2]. Countries and organizations around the world have published
32 guidelines for cancer prevention. Among them, the recommendations for cancer prevention
33 were updated in 2018 by the World Cancer Research Fund/American Institute for Cancer
34 Research (WCRF/AICR) based on a comprehensive literature review by expert panels [1]. Other
35 examples are the American Cancer Society guidelines [3] in the United States, the European
36 Code [4] in Europe, 6 cancer prevention recommendations proposed in Japan [5]. and 10 cancer
37 prevention recommendations in the Republic of Korea [6].

38 In 2018, the WCRF/AICR updated their cancer prevention guidelines, revising the
39 recommendations made in 2007 [1]. The revised guidelines consist of 10 key points: (1)
40 maintain a healthy weight; (2) engage in regular physical activity; (3) eat a better diet; (4) limit
41 “fast foods”; (5) limit “consumption of red and processed meats”; (6) limit alcohol
42 consumption; (7) cut down on sugary drinks; (8) breastfeed one’s baby if possible; (9) avoid
43 using supplements; and (10) adhere to recommendations after a cancer diagnosis. These
44 guidelines primarily focus on dietary habits, nutrition, and physical activity. However, they do
45 not address other significant modifiable factors such as cigarette smoking or sun exposure. In
46 Korea, national cancer prevention regulations and practice guidelines were established and
47 disseminated in 2006, in line with the Cancer Prevention and Management Act, and were
48 subsequently updated in 2016 [6]. According to the literature, there are 10 key factors for
49 cancer prevention: smoking, consumption of vegetables and fruits, eat food without, alcohol
50 consumption, physical activity, weight management, vaccination, sexual health, occupational

51 safety, and cancer screening. Of these 10 factors, 4 are related to dietary habits, compared to
52 the 6 dietary-related factors in the WCRF/AICR guidelines. Notably, the Korean guidelines
53 include smoking, which is absent from the WCRF/AICR guidelines. Therefore, it would be
54 intriguing to investigate the association between cancer risk and these 2 sets of guidelines within
55 the same population.

56 A previous study found that strict adherence to the 2018 WCRF/AICR cancer prevention
57 recommendations reduced the risk of total cancer [7] and mortality [8]. An inverse association
58 between the WCRF/AICR cancer prevention recommendations adherence score and the
59 incidence of cancer was reported for several cancers, including colorectal cancer [9-11]
60 pancreatic cancer [12], prostate cancer [13] and breast cancer [14-16]. However, most of these
61 studies were conducted in Western countries, such as the United States and European nations,
62 and no studies have investigated these issues in Asia. In Korea, prospective studies have been
63 conducted on individual factors of cancer prevention recommendations, such as cigarette
64 smoking, alcohol consumption, and obesity, in relation to cancer risk [17]; however, none of
65 those studies comprehensively addressed guideline adherence as a whole.

66 Therefore, our study aimed to determine whether adherence to the Korean cancer prevention
67 guidelines and WCRF/AICR cancer prevention recommendations is associated with total
68 cancer risk and the risk for 5 major cancers (lung, stomach, colorectal, breast, and prostate
69 cancer) in the Korean population through a large-scale, population-based, prospective cohort
70 study.

71

72 **Materials and Methods**

73 **Study population**

74 The Health Examinees Study, a component of the Korean Genome and Epidemiology Study
75 (KoGES) funded by the Korea Disease Control and Prevention Agency, is a large-scale
76 population-based prospective cohort study aimed at identifying environmental and genetic
77 factors for major chronic diseases. From 2004 to 2013, a total of 173,202 men and women were
78 recruited from 38 hospitals and regional health check-up centers in 8 regions across Korea,
79 selected according to a rigorous standardized research protocol. Details about the study design
80 can be found in previous publications [18, 19].

81 The Health Examinees-Gem (HEXA-G) cohort was created by applying additional
82 qualification criteria for participating organizations [20]. Of the 139,267 participants aged 40-
83 69 years old in the HEXA-G cohort, 34,881 were excluded for the following reasons: (1) people
84 who disagreed with linkage between the Korea Central Cancer Registry and death certificates
85 (n=23,221); (2) people diagnosed with cancer before the date of enrollment (n=4,175); (3)
86 those without food frequency questionnaire (FFQ) information (n=1,339); (4) people with daily
87 energy intake <500 or > 4,000 kcal (n=769); and (5) people who had missing data on the main
88 variables (body mass index [BMI], waist circumference, physical activity, breastfeeding, and
89 smoking status) (n=5,377). The final analysis included 104,386 participants, consisting of
90 36,266 men and 68,130 women (Figure 1).

91 The present study guidelines were approved by the Institutional Review Boards of the Seoul
92 National University Hospital in Seoul, Korea (IRB number E-2212-006-1381), and the Ethics
93 Committee of the KoGES of the Korea National Institute of Health (IRB number 2014-08-02-
94 3C-A). After providing a detailed description of the study, prior written consent was collected

95 from all participants.

96 **WCRF/AICR score construction**

97 Information including participants' general demographic characteristics, physical activity,
98 lifestyle habits, and medical history was collected at baseline using structured questionnaires.
99 For dietary information, an individual's usual eating habits were estimated through the 106-
100 food item semiquantitative food frequency questionnaire (SQFFQ), which has been tested for
101 validity and reliability [21]. Each nutrient intake and daily energy intake were calculated by
102 the food composition table developed by the Korea Health Industry Development Institute [22].
103 A standardized scoring system developed by the National Cancer Institute (NCI) of the US and
104 members of the AICR and WCR International team, based on the 2018 version of the
105 WCRF/AICR cancer prevention recommendations, was used to facilitate international
106 comparisons between study results [23]. Eight items, excluding supplement use and
107 recommendations for cancer survivors, constituted the proposed 2018 WCRF/AICR cancer
108 prevention recommendations score: (1) maintain a healthy weight; (2) engage in regular
109 physical activity; (3) eat a better diet; (4) limit fast food; (5) limit “consumption of red and
110 processed meats”; (6) cut down on sugary drinks; (7) limit alcohol consumption; and (8)
111 breastfeed if possible. One point was assigned to complete adherence to each recommendation,
112 0.5 points for partial adherence, and 0 points for nonadherence [23]. When there were 2
113 subitems, such as the healthy weight item, the score was equally divided to maintain a total of
114 1 point. According to the guidelines of the Steering Committee of the Regional Office for the
115 Western Pacific Region of the World Health Organization [24], the BMI criterion was assigned
116 0.5 points if it was satisfied (18.5-22.9 kg/m²), 0.25 points if it was partially satisfied (23.0-
117 24.9 kg/m²), and 0 points if it was not satisfied (<18.5 or >25 kg/m²). The waist circumference

118 score was based on the criteria of the Korean Society for the Study of Obesity; 0.5 points were
119 assigned if the criterion was met (men: <90 cm, women: <80 cm), and 0 points was assigned
120 if it was not met (men: \geq 90 cm, women: \geq 80 cm). Details of each score component are
121 presented in Table S1.

122 **Korean cancer prevention guidelines score construction**

123 Among the 10 cancer prevention guidelines for Koreans, 6 items (smoking, vegetables and
124 fruits, salty foods, alcohol, physical activity, and weight) were included in the score. For
125 smoking, a score of 1 was assigned to never smokers, 0.5 to former smokers, and 0 to current
126 smokers. For salty food consumption, the 2020 Dietary Reference Intakes for Koreans was
127 used as a guide. A score of 1 was given for sodium intake less than 1500 mg/day, 0.5 for intake
128 between 1500 mg/day and 2300 mg/day, and 0 for intake of 2300 mg/day or more [25]. The
129 scoring for the remaining items was conducted in the same manner as the 2018 WCRF/AICR
130 cancer prevention recommendations. Consequently, the total score for the 2018 WCRF/AICR
131 cancer prevention recommendations, which is the aggregate of the scores for each
132 recommendation, ranged from 0 to 7 points for men and 0 to 8 points for women. The Korean
133 cancer prevention guideline score, however, had a maximum of 6 points for both genders. A
134 higher score signifies greater adherence to cancer prevention recommendations. More details
135 can be found in Supplementary Table S2.

136 **Ascertainment of cancer cases**

137 Cancer cases were ascertained through data linkage from the Korea Central Cancer Registry,
138 which has been supervising nationwide cancer registration since 1980 under the guidance of
139 the Ministry of Health and Welfare. Incident cases were classified as those diagnosed with
140 cancer after the baseline survey and up until December 31, 2018.

141 The top 5 major cancers were selected according to the Annual Report of Cancer Statistics in
142 Korea in 2019 [26]. The most common cancer among Korean men and women was thyroid
143 cancer, followed by lung cancer, stomach cancer, colorectal cancer, breast cancer, and prostate
144 cancer. However, thyroid cancer was omitted from our selection due to the lack of identifiable
145 preventable risk factors in comparison to the other cancers [1, 27].

146 Incident cancer cases were identified using the 10th revision of the International Classification
147 of Disease, 10th revision codes C33-C34 (lung cancer), C16 (stomach cancer), C18-C20
148 (colorectal cancer), C50 (breast cancer), and C61 (prostate cancer).

149 **Statistical analysis**

150 Tertile score groups were used, considering the distribution of the adherence scores and
151 examples from the previous literature [7, 10, 12, 14, 28-30]. The lowest group was analyzed
152 as the reference group. Because the breastfeeding category only applied to women, all analyses
153 were stratified by sex.

154 Participants' characteristics by cancer prevention recommendation score category and sex are
155 summarized using percentages for categorical variables and means and standard deviations for
156 continuous variables. General characteristics according to cancer prevention recommendation
157 scores were compared using the chi-square test for categorical variables and a generalized
158 linear model for continuous variables. The median score of each category of cancer prevention
159 guidelines was used as a continuous variable to test for trends. The proportional hazards
160 assumption was tested using the Schoenfeld residuals method, and no evidence of violating the
161 assumption was found ($p > 0.05$ for all). A Cox proportional hazards regression model was used
162 to evaluate the associations of cancer risk with WCRF/AICR cancer prevention
163 recommendation scores and Korean cancer prevention guideline scores. The results are

164 presented as hazard ratios (HRs) and 95% confidence intervals (CIs). Age was chosen as the
165 time scale [31]. The entry time was age at baseline when recruiting cohorts, and the exit time
166 was age at the date of diagnosis of cancer, death, or the last date of follow-up (December 31,
167 2018), whichever came first.

168 We adjusted for potential confounding variables, including education level (categorized as less
169 than high school, high school, college or more, and missing), smoking status (divided into
170 never smoker, ex-smoker, current smoker, and missing), total energy intake (grouped into
171 tertiles), and family history of cancer (classified as yes, no, or missing). These variables were
172 chosen based on previous literature. Missing data in categorical covariates were included in the
173 multivariable Cox proportional hazards regression models as a dummy category. We estimated
174 individual associations for each component of the WCRF/AICR cancer prevention
175 recommendations score and the Korean Cancer Prevention Guidelines score in relation to
176 cancer risk. To determine risk estimates and 95% CIs per 1-point increment, the WCRF/AICR
177 cancer prevention recommendations scores and the Korean Cancer Prevention Guidelines score
178 were also modeled as direct continuous variables. To exclude potential reverse causation due
179 to the prevalent cancers not diagnosed at baseline, a sensitivity analysis was conducted
180 excluding the initial 2 years of follow-up. All analyses were carried out using SAS software
181 (version 9.4; SAS Institute Inc., Cary, NC, USA).

182 **Results**

183 Table 1 shows the general characteristics of the participants according to adherence to the
184 WCRF/AICR cancer prevention recommendations. Those with high adherence tended to be
185 older, engage in more physical activity, and consume more fruits and vegetables compared to
186 those with low adherence. Both men and women with high adherence had lower BMI, alcohol
187 consumption, red meat consumption, and total energy intake. The baseline characteristics for
188 adherence to the Korean cancer prevention guidelines were largely similar to those for the
189 WCRF/AICR cancer prevention recommendations. However, in contrast to the WCRF/AICR
190 cancer prevention recommendations, those in the highest tertiles for adherence to the Korean
191 cancer prevention guidelines had higher education and income levels (Table S3).

192 During a median follow-up period of 9.04 years, we identified a total of 6,987 cancer cases,
193 comprised of 2,758 men and 4,229 women. Tables 2-3 display the risk of cancer in relation to
194 the adherence score of the WCRF/AICR cancer prevention recommendation. In models
195 adjusted for confounding factors, a high adherence score to the WCRF/AICR cancer prevention
196 recommendations was associated with a 9% reduction in total cancer risk (HR, 0.91; 95% CI,
197 0.82-1.00) in men. A high adherence score to the Korean cancer prevention guidelines was
198 associated with a reduced risk of total cancer (HR, 0.80; 95% CI, 0.73-0.88), stomach cancer
199 (HR, 0.68; 95% CI, 0.54-0.84), colorectal cancer (HR, 0.74; 95% CI, 0.58-0.95), and lung
200 cancer (HR, 0.37; 95% CI, 0.27-0.51) in men. In women, no association was found between
201 total cancer and other types of cancer, but an inverse association was observed with breast
202 cancer (HR, 0.80; 95% CI, 0.67-0.95). However, for stomach cancer in women, the risk
203 increased by 13% for each 1-point increase in the WCRF/AICR cancer prevention
204 recommendation score (HR, 1.13; 95% CI, 1.02-1.25)

205 Table 4 and Tables S4-5 present the associations between cancer risk and adherence to the
206 individual components of the cancer prevention guideline score. The group with normal weight
207 exhibited a 12% (HR, 0.88; 95% CI, 0.81-0.97) reduction in total cancer risk for men and a 10%
208 (HR, 0.90; 95% CI, 0.83-0.96) reduction for women, compared to the underweight or obese
209 group. Participants who met the optimal criteria for abdominal obesity (men: <90 cm, women:
210 <80 cm) demonstrated a 13% (HR, 0.87; 95% CI, 0.81-0.95) decrease in total cancer risk for
211 men and a 12% (HR, 0.88; 95% CI, 0.81-0.94) decrease for women, compared to those with
212 abdominal obesity (men: ≥ 90 cm, women: ≥ 80 cm). Our findings also revealed that men who
213 have never smoked had a 27% (HR, 0.73; 95% CI, 0.66-0.81) reduction in total cancer risk
214 compared to current smokers.

215 In a sensitivity analysis, we examined data from 35,659 men and 67,112 women, excluding the
216 first 2 years of follow-up (Table S6-7). The findings were generally similar to the results from
217 the main analysis. In the main analysis, women who scored highly on the WCRF/AICR cancer
218 prevention recommendation adherence scale demonstrated a 20% decrease in breast cancer risk.
219 However, this association was not significant in the sensitivity analysis. Conversely, women
220 who scored highly on the Korean cancer prevention guideline scale exhibited a 25% decrease
221 in colorectal cancer risk in the sensitivity analysis (HR, 0.75; 95% CI, 0.57-0.98).

222

223 **Discussion**

224 In this large-scale, prospective cohort study involving the Korean population, we found an
225 inverse association between total cancer incidence and adherence to the WCRF/AICR cancer
226 prevention guidelines among men. The Korean cancer prevention guidelines also showed an
227 inverse association with adherence scores for total cancer, stomach cancer, colorectal cancer,
228 and lung cancer. In women, only breast cancer showed an inverse association with adherence
229 to the WCRF/AICR cancer prevention recommendations.

230 No studies have yet explored the association between cancer risk and adherence to the 2007 or
231 2018 versions of the WCRF/AICR cancer prevention recommendations in Asian countries.
232 Furthermore, the effectiveness of Korean cancer prevention guidelines remains unexamined.
233 However, research has been conducted on the association between adherence to the 2007
234 version of the WCRF/AICR cancer prevention recommendations and cancer risk within the
235 European population [7, 32]. Despite variations in scoring systems, items, and racial and
236 population characteristics, numerous studies have consistently reported that adherence to
237 cancer prevention guidelines can help prevent cancer. Our findings align with these studies.
238 Higher adherence to the WCRF/AICR cancer prevention recommendations was associated
239 with a reduced risk of total cancer in the United States [33] and Sweden [7], breast cancer in
240 Europe [14, 16] and South Africa [15], and colorectal cancer in Spain [9] and the United
241 States [10, 11].

242 Among the individual factors of the WCRF/AICR cancer prevention recommendations and
243 Korean cancer prevention guidelines, strong adherence to weight management and smoking
244 was associated with a decrease in cancer risk. Previous studies have identified obesity [34] and
245 smoking [35] as significant risk factors among many for various types of cancer. Aside from

246 obesity and smoking, no significant association was found with cancer risk with other
247 individual components of the cancer prevention recommendation score.

248 There were no observed associations between adherence to Korean cancer prevention
249 guidelines and total cancers and 5 types of cancer in women. Similarly, no associations were
250 found with other types of cancer in the WCRF/AICR cancer prevention recommendations, with
251 the exception of breast cancer. Case-control studies conducted in South Africa [15] and Italy
252 [16] and a cohort study in Spain [14], found that a higher score on the 2018 WCRF/AICR
253 cancer prevention recommendations was associated with a lower risk of breast cancer. This
254 finding was corroborated by a meta-analysis [16]. Our study discovered that for women, each
255 one-point increase in the WCRF/AICR cancer prevention recommendations score
256 corresponded to a 13% higher risk of stomach cancer. The precise reason for this result remains
257 unclear, but it is plausible that the high rate of *Helicobacter pylori* infection, which is not
258 included in the WCRF/AICR cancer prevention recommendations, played a significant role.
259 The International Agency for Research on Cancer (IARC) classifies *Helicobacter pylori* as a
260 class 1 carcinogen [36]. The population-attributable fraction of *Helicobacter pylori* infection
261 for stomach cancer was 80.3% for men and 78.7% for women in Korea [37], which is higher
262 than in China (63%) and in European countries (20-30%) and similar to that in Japan [38]. The
263 main risk factors for gastric cancer among Korean women, such as age, BMI, having a family
264 history of cancer, and past smoking status, are not adequately reflected in the WCRF/AICR
265 recommendations [39]. In this study, we found that the risk of gastric cancer increased in
266 women who scored highly on the individual components of breastfeeding and fast food
267 restriction. As there are no other published studies for comparison, further research is required.
268 With the exception of breast cancer, our study found a reduced cancer risk only in men who

269 adhered to the cancer prevention recommendations, while no association was found in women.
270 A United States study similarly found a stronger inverse association for colorectal cancer in
271 men than in women [11]. The mechanisms behind these sex differences remain unclear, but we
272 present several potential explanations from various perspectives. One possibility is the
273 involvement of sex hormones. Prior research has indicated that the use of exogenous hormones,
274 such as postmenopausal hormone therapy and oral contraceptives, as well as the increase in
275 female hormones due to pregnancy and childbirth, may help prevent the development of
276 colorectal cancer in women [40-42]. Another potential explanation could be gender-based
277 differences in dietary intake and eating behavior. In Korean culture, women are more likely to
278 purchase and prepare food, which may lead to greater nutritional knowledge and a tendency
279 towards healthier dietary choices compared to men [43, 44]. Furthermore, the number of
280 current female smokers in our study population was extremely low (less than 5%), and the
281 percentage of current female drinkers was 31.4%, with an average ethanol intake of 6.28 g/day.
282 Both alcohol and smoking have been identified as risk factors for several types of cancer and
283 are included in cancer prevention guidelines. This significant disparity in alcohol and smoking
284 habits between men and women may have influenced our results.

285 Sodium is a crucial element for maintaining homeostasis and supporting various physiological
286 functions in the body, and it is typically acquired through salt consumption [45]. Both
287 insufficient and excessive sodium intake can lead to a range of clinical problems. Research
288 indicates that when sodium intake drops below 700 mg/day, it is associated with elevated total
289 cholesterol levels in the blood [46] and increased insulin resistance [47]. According to our data,
290 3.36% of men and 4.62% of women reported a sodium intake of less than 700 mg/day (data
291 not shown). Some studies have suggested a connection between a preference for salty food,

292 salt consumption, and stomach cancer [48, 49], but currently, there is no precise numerical
293 guideline for determining the appropriate sodium intake. The evidence linking low sodium
294 intake to cancer is both scarce and difficult to establish. Consequently, the current cancer
295 prevention recommendation aligns with the 2020 Dietary Reference Intakes for Koreans,
296 suggesting a sodium intake of less than 1500 mg/day. However, it is important to acknowledge
297 that these guidelines may need to be revised as more evidence becomes available in the future.

298 Our study has several limitations that should be taken into account. First, due to the absence of
299 data, 4 out of 10 Korean cancer prevention guidelines were not included. Further research in
300 Korea is required to incorporate these missing elements, namely: vaccination, sexual health,
301 safety and health, and cancer screening. Second, the cancer prevention guidelines used in our
302 study, including the Korean cancer prevention guidelines and the WCRF/AICR cancer
303 prevention recommendations, utilized a standardized scoring system for ease of comparison.
304 This system did not assign weights to the components, assuming all to be of equal importance.
305 Future studies should consider the relative weights of these components and their relevance to
306 different racial groups. Thirdly, despite adjusting for confounding factors, it is possible that
307 some residual and unmeasured confounding factors were not eliminated. Despite these
308 limitations, this study is significant as it is a large-scale investigation into the associations
309 between adherence to cancer prevention guidelines, including diet, and cancer risk, a topic that
310 has primarily been studied in the Western world. Another strength of this study is that the
311 accuracy of cancer diagnoses was ensured by linkage to the Korea Central Cancer Registry,
312 which contained an estimated 98.3% of data on cancer incidence in 2019 [50].

313 In conclusion, these cohort study's findings indicate that adherence to both the WCRF/AICR
314 cancer prevention recommendations and Korean cancer prevention guidelines can prevent

315 cancer in men. Additionally, we discovered that adherence to the WCRF/AICR cancer
316 prevention recommendations can aid in preventing breast cancer in Korean women. The
317 effectiveness of these guidelines may vary depending on the type of cancer and the individual's
318 sex. However, due to data limitations, we were unable to consider all aspects of the Korean
319 cancer prevention guidelines. Therefore, further research is required.

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320 **Author Contributions**

321 The authors' contributions were as follows: Lee J, Shin A, Shin WK, Choi JY and Kang D:
322 conceived and designed the analysis; Lee JK, Kang D, Choi JY and Shin A: collected the data; Lee
323 J and Shin A: contributed data or analysis tools; and Lee J and Shin A: performed the analysis

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465

Table 1. Baseline characteristics of the participants according to WCRF/AICR cancer prevention adherence score categories and sex.

	WCRF/AICR adherence score								
	Men (n=36,266)				P-value*	Women (n=68,130)			P-value*
	Tertile 1	Tertile 2	Tertile 3	Tertile 1		Tertile 2	Tertile 3		
Score range	0≤score<3.25	3.25≤score<4.25	score≥4.25		0≤score<4.50	4.50≤score<5.50	score≥5.50		
No. of participants	10947 (30.2)	13091 (36.1)	12228 (33.7)	<.001	19732 (29.0)	24186 (35.5)	24212 (35.5)	<.001	
Age (years)	50.9±8.2	53.4±8.3	56.0±7.9	<.001	49.3±7.5	52.5±7.7	54.5±7.2	<.001	
Body mass index (kg/m ²)	25.5±2.9	24.4±2.7	23.5±2.2	<.001	24.2±3.3	23.7±3.0	23.0±2.5	<.001	
Education				<.001				<.001	
≤Middle school	1973 (18.0)	2799 (21.4)	2554 (20.9)		4977 (25.2)	9003 (37.2)	10145 (41.9)		
High school	4579 (41.8)	5301 (40.5)	4928 (40.3)		9018 (45.7)	10233 (42.3)	10336 (42.7)		
≥College	4309 (39.4)	4881 (37.3)	4623 (37.8)		5614 (28.5)	4784 (19.8)	3552 (14.7)		
missing	86 (0.8)	110 (0.8)	123 (1.0)		123 (0.6)	166 (0.7)	179 (0.7)		
Income (¥10,000)				<.001				<.001	
<200	2168 (19.8)	3172 (24.2)	3274 (26.8)		5003 (25.3)	7475 (30.9)	7786 (32.2)		
200-400	5038 (46.0)	5631 (43.0)	5042 (41.2)		8257 (41.9)	9341 (38.6)	9231 (38.1)		
≥400	3250 (29.7)	3548 (27.1)	3180 (26.0)		5320 (27.0)	5707 (23.6)	5275 (21.8)		
missing	491 (4.5)	740 (5.7)	732 (6.0)		1152 (5.8)	1663 (6.9)	1920 (7.9)		
Smoking status				<.001				<.001	
Never	2366 (21.6)	3485 (26.6)	3940 (32.3)		18505 (93.8)	23428 (96.9)	23755 (98.1)		
Former	4074 (37.2)	5291 (40.4)	5446 (44.5)		409 (2.0)	269 (1.1)	180 (0.8)		
Current	4507 (41.2)	4315 (33.0)	2842 (23.2)		818 (4.2)	489 (2.0)	277 (1.1)		
Missing									
Alcohol intake, (g of ethanol/d)	23.9±44.5	14.7±26.4	8.6±19.2	<.001	3.8±13.5	1.7±26.1	0.7±4.1	<.001	
Physical activity				<.001				<.001	
<75	8170(74.6)	6635(50.7)	2438(19.9)		15863(80.3)	14565(60.2)	6016(24.9)		
75-149 min/wk	891 (8.2)	1414 (10.8)	1060 (8.7)		1410 (7.2)	2457 (10.2)	2332 (9.6)		
≥150 min/wk	1886 (17.2)	5042 (38.5)	8730 (71.4)		2459 (12.5)	7164 (29.6)	15864 (65.5)		
Family history of cancer				0.618				0.615	
No	8049 (73.5)	9521 (72.7)	8967 (73.3)		13878 (70.3)	16951 (70.1)	17081 (70.5)		
Yes	2877 (26.3)	3539 (27.1)	3233 (26.5)		5803 (29.4)	7178 (29.7)	7082 (29.3)		
Missing	21 (0.2)	31 (0.2)	28 (0.2)		51 (0.3)	57 (0.2)	49 (0.2)		
Breastfeeding									
None					7987 (40.5)	3629 (15.0)	1083 (4.4)		
Less than 6 months					2628 (13.3)	2181 (9.0)	1151 (4.8)		
More than 6 months					9117 (46.2)	18376 (76.0)	21978 (90.8)		

Energy intake, kcal/d	2012.2±533.7	1823.4±489.9	1718.4±420.9	<.001	1809.5±544.4	1667.2±503.6	1613.2±454.8	<.001
Vegetable and fruits intake, g/d	244.5±163.1	260.5±178.4	299.3±191.7	<.001	226.4±153	247±168.9	300.6±197.1	<.001
Fast food intake, g/d	61.7±51.7	40.8±44.5	21.9±29.8	<.001	57.8±54.6	35.0±43.6	18.1±29.4	<.001
Red meat intake, g/d	78.5±58.3	49.8±48.2	33.6±31.9	<.001	57.1±55.2	35.1±39.3	25.8±27.4	<.001
Sugar-sweetened drinks, g/d	75.0±104.7	54.8±78.3	47.2±62.1	<.001	64.8±93.0	54.8±75.5	51.3±66.7	<.001
Sodium intake, g/d	2637.7±1371.2	2587.4±1432.0	2717.5±1450.8	<.001	2296.3±1226.6	2298.3±1301.1	2559.2±1412.6	<.001

The distribution of variables was reported as n (%) and means ± SD.*p-values were obtained using the chi-square test (for categorical variables) and generalized linear model (for continuous variables)

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Table 2. Hazard ratios (HRs) and 95% confidence intervals (CI) for cancer risk according to WCRF/AICR cancer prevention guideline adherence score categories.

	Men (n=36,266)				Women (n=68,130)					
	Tertile 1	Tertile 2	Tertile 3	p for trend	Continuous (per 1-point increase in score)	Tertile 1	Tertile 2	Tertile 3	p for trend	Continuous (per 1-point increase in score)
Score range	0≤score<3.25	3.25≤score<4.25	score≥4.25			0≤score<4.50	4.50≤score<5.50	score≥5.50		
Person-years	96520.70	115445.60	107406.40			172867.90	214532.00	215386.00		
Total cancer										
no. of cases/total subjects	724/10947	1000/13091	1034/12228			1173/19732	1510/24186	1546/24212		
Crude HR (95% CI)	1.00	0.95 (0.86-1.05)	0.89 (0.80-0.98)	0.013	0.97 (0.93-1.00)	1.00	0.98 (0.91-1.06)	0.97 (0.89-1.05)	0.394	0.99 (0.96-1.02)
Multivariable-adjusted HR (95% CI)	1.00	0.96 (0.87-1.05)	0.91 (0.82-1.00)	0.053	0.98 (0.94-1.02)	1.00	0.99 (0.91-1.07)	0.98 (0.90-1.06)	0.553	0.99 (0.96-1.02)
Stomach cancer										
no. of cases/total subjects	134/10947	183/13091	181/12228			87/19732	137/24186	178/24212		
Crude HR (95% CI)	1.00	0.97 (0.77-1.21)	0.89 (0.71-1.12)	0.314	0.95 (0.87-1.04)	1.00	1.09 (0.83-1.43)	1.29 (0.99-1.69)	0.050	1.14 (1.04-1.26)
Multivariable-adjusted HR (95% CI)	1.00	1.00 (0.79-1.25)	0.95 (0.75-1.21)	0.651	0.98 (0.89-1.08)	1.00	1.07 (0.81-1.41)	1.26 (0.96-1.65)	0.080	1.13 (1.02-1.25)
Colorectal cancer										
no. of cases/total subjects	111/10947	143/13091	143/12228			89/19732	152/24186	147/24212		
Crude HR (95% CI)	1.00	0.92 (0.72-1.18)	0.87 (0.67-1.11)	0.260	0.93 (0.84-1.03)	1.00	1.12 (0.86-1.46)	0.97 (0.74-1.27)	0.742	0.97 (0.88-1.07)
Multivariable-adjusted HR (95% CI)	1.00	0.90 (0.70-1.16)	0.83 (0.64-1.08)	0.161	0.91 (0.82-1.02)	1.00	1.14 (0.87-1.49)	0.99 (0.76-1.31)	0.864	0.98 (0.89-1.08)
Lung cancer										
no. of cases/total subjects	76/10947	114/13091	101/12228			62/19732	93/24186	88/24212		

Crude HR (95% CI)	1.00	0.95 (0.71-1.27)	0.70 (0.52-0.95)	0.015	0.90 (0.81-1.00)	1.00	0.89 (0.65-1.23)	0.73 (0.53-1.01)	0.047	0.91 (0.80-1.03)
Multivariable-adjusted HR (95% CI)	1.00	1.02 (0.76-1.37)	0.86 (0.63-1.18)	0.333	0.99 (0.88-1.11)	1.00	0.94 (0.68-1.30)	0.77 (0.55-1.07)	0.102	0.93 (0.82-1.06)
Prostate cancer/ Breast cancer										
no. of cases/total subjects	103/10947	153/13091	193/12228			294/19732	295/24186	273/24212		
Crude HR (95% CI)	1.00	0.89 (0.70-1.14)	0.91 (0.72-1.16)	0.507	0.97 (0.88-1.07)	1.00	0.84 (0.71-0.98)	0.79 (0.66-0.94)	0.006	0.91 (0.85-0.97)
Multivariable-adjusted HR (95% CI)	1.00	0.89 (0.69-1.14)	0.89 (0.70-1.13)	0.367	0.95 (0.87-1.05)	1.00	0.84 (0.71-1.00)	0.80 (0.67-0.95)	0.010	0.91 (0.85-0.97)

Adjusted for education level (less than high school, high school, college or above, and missing), smoking status (non-smoker, ex-smoker, current smoker, and missing), total energy intake (tertiles), and family history of cancer (yes, no, and missing). The test for trend was calculated with the median score for each category of the cancer prevention guideline as a continuous variable.

Table 3. Hazard ratios (HRs) and 95% confidence intervals (CI) for cancer risk according to Korean cancer prevention guideline adherence score categories.

	Men (n=36,266)					Women (n=68,130)				
	Tertile 1	Tertile 2	Tertile 3	p for trend	Continuous (per 1-unit increase in score)	Tertile 1	Tertile 2	Tertile 3	p for trend	Continuous (per 1-unit increase in score)
Score range	0≤score<2.50	2.50≤score<3.25	score≥3.25			0≤score<3.50	3.50≤score<4.00	score≥4.00		
Person-years	101000.20	106238.80	112133.70			194374.80	151862.50	256548.60		
Total cancer no. of cases/total subjects	827/11402	975/12139	956/12725			1396/21979	1031/17065	1802/29086		
Crude HR (95% CI)	1.00	0.97 (0.88-1.06)	0.80 (0.73-0.88)	<.001	0.90 (0.86-0.94)	1.00	0.95 (0.88-1.03)	0.97 (0.91-1.05)	0.587	0.98 (0.95-1.02)
Multivariable-adjusted HR (95% CI)	1.00	0.97 (0.88-1.06)	0.80 (0.73-0.88)	<.001	0.90 (0.86-0.94)	1.00	0.94 (0.87-1.02)	0.96 (0.90-1.03)	0.407	0.98 (0.94-1.02)
Stomach cancer no. of cases/total subjects	168/11402	171/12139	159/12725			132/21979	80/17065	190/29086		
Crude HR (95% CI)	1.00	0.85 (0.69-1.06)	0.68 (0.55-0.85)	<.001	0.83 (0.75-0.92)	1.00	0.79 (0.60-1.04)	1.09 (0.88-1.36)	0.253	1.07 (0.94-1.22)
Multivariable-adjusted HR (95% CI)	1.00	0.85 (0.69-1.05)	0.68 (0.54-0.84)	<.001	0.83 (0.75-0.92)	1.00	0.79 (0.59-1.04)	1.09 (0.87-1.36)	0.276	1.07 (0.94-1.22)
Colorectal cancer no. of cases/total subjects	134/11402	128/12139	135/12725			132/21979	98/17065	158/29086		
Crude HR (95% CI)	1.00	0.81 (0.64-1.04)	0.74 (0.58-0.94)	0.021	0.90 (0.81-1.01)	1.00	0.97 (0.74-1.25)	0.89 (0.71-1.13)	0.328	0.93 (0.81-1.06)
Multivariable-adjusted HR (95% CI)	1.00	0.81 (0.64-1.04)	0.74 (0.58-0.95)	0.047	0.90 (0.81-1.01)	1.00	0.95 (0.73-1.24)	0.88 (0.69-1.11)	0.254	0.92 (0.80-1.05)
Lung cancer no. of cases/total subjects	111/11402	114/12139	66/12725			89/21979	48/17065	106/29086		

Crude HR (95% CI)	1.00	0.79 (0.60-1.02)	0.36 (0.27-0.49)	<.001	0.68 (0.60-0.76)	1.00	0.72 (0.50-1.02)	0.92 (0.69-1.21)	0.744	1.03 (0.86-1.23)
Multivariable-adjusted HR (95% CI)	1.00	0.80 (0.61-1.04)	0.37 (0.27-0.51)	<.001	0.69 (0.61-0.78)	1.00	0.70 (0.49-0.99)	0.88 (0.66-1.17)	0.554	1.01 (0.84-1.20)
Prostate cancer no. of cases/total subjects	95/11402	154/12139	200/12725			289/21979	218/17065	355/29086		
Crude HR (95% CI)	1.00	1.20 (0.93-1.56)	1.22 (0.96-1.56)	0.154	1.07 (0.96-1.19)	1.00	0.96 (0.81-1.15)	0.93 (0.80-1.09)	0.389	0.95 (0.87-1.04)
Multivariable-adjusted HR (95% CI)	1.00	1.18 (0.92-1.53)	1.18 (0.92-1.51)	0.260	1.05 (0.95-1.17)	1.00	0.93 (0.78-1.11)	0.88 (0.75-1.04)	0.132	0.92 (0.84-1.01)

Adjusted for education level (less than high school, high school, college or above, and missing), total energy intake (tertiles), and family history of cancer (yes, no, and missing). The test for trend was calculated with the median score for each category of the cancer prevention guideline as a continuous variable.

Table 4. Associations between adherence to individual components of the 2 cancer prevention guideline scores and total cancer risk.

Components of the cancer prevention guideline score	Men (n=36,266)				Women (n=68,130)			
	No. of cases/total participants	Person year	Crude HR (95% CI)	Multivariable-adjusted HR (95% CI)	No. of cases/total participants	Person year	Crude HR (95% CI)	Multivariable-adjusted HR (95% CI)
Maintain a healthy weight (BMI) ^{#§}								
0	1198/15038	132232.10	1.00	1.00	1369/20481	180210.80	1.00	1.00
0.25	792/10966	96903.70	0.86 (0.79-0.94)	0.86 (0.79-0.94)	1147/18088	161030.00	0.95 (0.88-1.03)	0.95 (0.88-1.03)
0.5	768/10262	90236.90	0.89 (0.82-0.98)	0.88 (0.81-0.97)	1713/29561	261545.10	0.91 (0.85-0.98)	0.90 (0.83-0.96)
Maintain a healthy weight (Waist circumference) ^{#§}								
0	921/10506	92990.00	1.00	1.00	1003/13984	124309.40	1.00	1.00
0.5	1837/25760	226382.70	0.87 (0.81-0.94)	0.87 (0.81-0.95)	3226/54146	478476.50	0.89 (0.83-0.96)	0.88 (0.81-0.94)
Be physically active ^{#§}								
0	1293/17243	153028.70	1.00	1.00	2232/36444	324485.80	1.00	1.00
0.5	229/3365	30058.30	0.97 (0.85-1.12)	1.01 (0.87-1.16)	386/6199	55514.50	1.01 (0.91-1.13)	1.00 (0.90-1.12)
1	1236/15658	136285.80	0.94 (0.87-1.02)	0.98 (0.90-1.06)	1611/25487	222785.50	1.04 (0.97-1.11)	1.03 (0.97-1.10)
Eat a better diet ^{#§}								
0	1115/14175	124235.30	1.00	1.00	1762/28614	250984.80	1.00	1.00
0.5	1203/16220	142456.70	0.96 (0.88-1.04)	0.96 (0.88-1.04)	1849/29557	260334.70	1.01 (0.95-1.08)	1.01 (0.94-1.08)
1	440/5871	52680.80	0.96 (0.86-1.08)	0.97 (0.87-1.10)	618/9959	91466.30	0.96 (0.88-1.05)	0.95 (0.87-1.05)
Limit fast foods [#]								
0	719/12078	106275.40	1.00	1.00	1329/22675	200205.80	1.00	1.00
0.5	927/12158	106979.00	1.09 (0.99-1.20)	1.08 (0.98-1.20)	1400/22808	201475.80	1.00 (0.93-1.08)	1.01 (0.94-1.10)
1	1112/12030	106118.40	1.05 (0.95-1.15)	1.04 (0.94-1.16)	1500/22647	201104.30	1.01 (0.94-1.09)	1.04 (0.96-1.13)
Limit red and processed meat [#]								
0	580/8857	78183.60	1.00	1.00	587/9901	86949.20	1.00	1.00
0.5	83/1975	17114.30	0.85 (0.68-1.07)	0.85 (0.67-1.07)	194/3643	31001.70	0.99 (0.84-1.17)	0.99 (0.84-1.16)

1	2095/25434	224074.90	1.04 (0.95-1.14)	1.05 (0.95-1.16)	3448/54586	484835.00	1.01 (0.92-1.10)	1.01 (0.92-1.11)
Cut down on sugary drinks #								
0	97/1393	12506.20	1.00	1.00	137/2303	21171.20	1.00	1.00
0.5	2601/34352	302363.00	0.92 (0.75-1.13)	0.90 (0.73-1.11)	4043/64961	573944.50	1.07 (0.90-1.27)	1.08 (0.91-1.29)
1	60/521	4503.50	1.22 (0.88-1.69)	1.18 (0.85-1.64)	49/866	7670.20	0.93 (0.67-1.29)	0.96 (0.69-1.33)
Limit alcohol consumption#§								
0	469/6442	56408.00	1.00	1.00	120/2224	19311.50		1.00
0.5	1405/19788	174640.80	0.88 (0.79-0.97)	0.91 (0.81-1.01)	1063/18455	162073.20	1.04 (0.86-1.26)	1.04 (0.86-1.26)
1	884/10036	88323.90	0.93 (0.83-1.04)	0.99 (0.88-1.11)	3046/47451	421401.20	1.07 (0.89-1.29)	1.07 (0.89-1.30)
For mothers: breastfeed your baby#								
0					762/12699	110432.50	1.00	1.00
0.5					319/5960	52663.30	0.90 (0.79-1.03)	0.90 (0.79-1.02)
1					3148/49471	439690.10	0.96 (0.88-1.04)	0.98 (0.90-1.07)
Limit smoking§*								
0	864/11664	102415.50	1.00	1.00	94/1584	13646.70	1.00	1.00
0.5	1191/14811	129113.40	0.81 (0.74-0.89)	0.81 (0.74-0.89)	53/858	7503.90	1.01 (0.72-1.41)	1.00 (0.71-1.39)
1	703/9791	87843.80	0.73 (0.66-0.80)	0.73 (0.66-0.81)	4082/65688	581635.30	0.97 (0.79-1.19)	0.96 (0.78-1.18)
Eat food without salty (sodium intake)§								
0	1470/20060	178067.60	1.00	1.00	2010/31956		1.00	1.00
0.5	675/8784	76092.30	1.03 (0.94-1.13)	1.03 (0.94-1.13)	1090/18236	286165.80	0.98 (0.91-1.05)	0.98 (0.91-1.06)
1	613/7422	65212.80	1.04 (0.95-1.14)	1.04 (0.94-1.16)	1129/17938	158697.80	1.01 (0.94-1.08)	1.01 (0.94-1.10)

Adjusted for education level (less than high school, high school, college or above, and missing), smoking status (non-smoker, ex-smoker, current smoker, and missing), total energy intake (tertiles), and family history of cancer (yes, no, and missing). *Adjusted for education level (less than high school, high school, college or above, and missing), total energy intake (tertiles), and family history of cancer (yes, no, and missing). # Components of the WCRF/AICR score. § Components of the Korean Cancer Prevention Guidelines score

