Title

Dietary Intake of Nutrients, Index-Based Dietary Patterns,Genetic Predisposition with Stomach Cancer

Author

Zhu, Yuhui

Publication Date

2020

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

Dietary Intake of Nutrients, Index-Based Dietary Patterns, Genetic Predisposition with Stomach Cancer

A dissertation submitted in partial satisfaction of the

requirements for the degree Doctor of Philosophy in Epidemiology

by

Yuhui Zhu

2020

ABSTRACT OF THE DISSERTATION

Dietary Intake of Nutrients, Index-Based Dietary Patterns,

Genetic Predisposition with Stomach Cancer

by

Yuhui Zhu

Doctor of Philosophy in Epidemiology

University of California, Los Angeles, 2020

Professor Zuo-Feng Zhang, Chair

Background

Stomach cancer (SC) is the fifth most commonly diagnosed cancer and the third leading cause of cancer deaths worldwide. China is one of the countries with the highest incidence and mortality of stomach cancer. Different environmental factors are involved in the development of stomach cancer, including *Helicobacter (H.) pylori* infection, tobacco smoking, alcohol consumption, sodium intake, and dietary factors. The roles of various dietary factors on the development of stomach cancer are still an open question. Moreover, there is an increasing interest in studying gene-diet interactions that might explain variations in stomach cancer across different populations.

Methods

A population-based case-control study, Jiangsu Four Cancers (JFC) study, was conducted in four counties (Dafeng, Ganyu, Chuzhou, and Tongshan) in Jiangsu Province, China, from 2003 to 2010, to gather epidemiologic data to study both environmental and genetic factors on the development of four top cancers in a Chinese population, including stomach cancer. Epidemiologic data were collected by in-person interviews using a structured questionnaire. After the personal interview, blood samples were collected and separated in a local laboratory. *H. pylori* infection and genetic susceptibility markers were assayed. In specific aim 1, we evaluated the roles of total and subtypes of fatty acids, total cholesterol, and flavonoids on the development of stomach cancer. These nutrients were estimated based on the Food Frequency Questionnaire (FFQ) and China Food Composition (CFC) Tables. Missing data were imputed by multiple imputation methods. Adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) were estimated using multiple unconditional logistic regression models, energy-adjusted method, and semi-Bayes shrinkage method. Multiplicative and additive interactions between dietary factors and the known risk factors and their joint effects on the development of stomach cancer were assessed. Natural direct effect (NDE) and natural indirect effect (NIE) of mediation analysis were also estimated. In specific aim 2, we studied the impact of adherence to both modified Chinese Healthy Eating Index (mCHEI) and Healthy Eating Index-2015 (HEI-2015) in relation to stomach cancer. Multiple unconditional logistic regression analyses were applied to examine relationships between mCHEI, HEI-2015, and stomach cancer while adjusting for potential confounders. The possible interactions between mCHEI and HEI-2015 and established risk factors were investigated. In specific aim 3, we assessed the potential effects of genetic susceptibility markers, single nucleotide polymorphisms (SNPs) and their interplay with nutritional factors on stomach cancer. Adjusted odds ratios and their 95% CIs for candidate SNPs were estimated for stomach cancer using multiple unconditional logistic models and semi-Bayes shrinkage method. Log-additive, dominant, and recessive genetic models were employed for the evaluation of each SNP. Stratified analyses and gene-diet interaction analysis (multiplicative and additive scales) were performed by using dichotomous variables of total fatty acids, cholesterol, and flavonoids. Genetic risk scores (GRS) were applied to estimate the cumulative contributions of genetic factors on stomach cancer. All analyses were conducted using SAS, version 9.4.

Results

A total of 2,216 stomach cancer cases and 8,019 controls were recruited. In specific aim 1, 1,900 SC cases and 6,532 controls were included in the analyses, excluding individuals with incomplete data of FFQs. Dietary saturated fatty acids (SFAs), monounsaturated fatty acids (MUFAs), and total cholesterol were positively associated with the development of SC comparing the highest versus lowest quarters. Higher intakes of dietary SFAs (*p*-trend = 0.005; adjusted odds ratio (aOR), 1.11; 95% CI, 1.01-1.22 with a 7 g/day increase as a continuous variable) and total cholesterol (*p*-trend < 0.001; aOR, 1.13; 95% CI, 1.06-1.22 with a 250 mg/day increase as a continuous variable) were monotonically associated with elevated odds of developing SC. In specific aim 2, a higher score of sodium, reflecting less intake per day and better adherence to the guidelines, was inversely associated with stomach cancer (OR, 0.95; 95%CI, 0.91-0.99 for mCHEI; OR, 0.97; 95%CI, 0.94-0.99 for HEI-2015). There were null associations for total scores of HEI-2015 (*p*-trend = 0.98; OR, 0.98; 95% CI, 0.87-1.10 with a 10-point increase) and mCHEI (*p*-trend =0.22; OR, 1.05; 95% CI, 0.94-1.17 with a 10-point increase) in relation to stomach cancer. However, multiplicative interaction was identified between mCHEI and body mass index on stomach cancer (*p* for interaction=0.02). In specific aim 3, a total of 788 stomach cancer cases and 2,398 controls from Dafeng and Ganyu County were included because of the availability of SNP measurements. Associations with stomach cancer were observed for *miR-300* rs12894467, *IKBKAP* rs2230793, *PLCE1* rs2274223, *R267S* rs12934922, *TERT* rs2736100, *CHEK2* rs738722, *WWOX* rs12828, *E2F2* rs2075993, *HEY2* rs3734637, *WNT8A* rs4835761, *Gemin3* rs197412, *FTO* rs8050136, *SEMA5B* rs9868873. There was a dose-response relationship between increased genetic risk scores (polygenic risk score and weighted multi-genetic index) and stomach cancer. Potential interactions were observed between dietary fatty acids and *TERT* rs2736100, as well as *GKN2 -GKN1* rs4254535 on SC; and between dietary cholesterol and *R267S* rs12934922, *E2F2* rs2075993, and *Notch4* rs915894 on SC. Possible interaction was also observed between *IKBKAP* rs1538660 with dietary flavonoids on SC.

Conclusions

Our results confirm the associations between high intakes of dietary SFAs, MUFAs, total cholesterol, and the development of stomach cancer with a dose-response pattern. mCHEI is more sensitive to identify specific food components associated with stomach cancer compared with HEI-2015. Dietary total fatty acids, cholesterol, and flavonoids may modify the associations between some SNPs and stomach cancer. The findings might shed some light on the potential etiological roles of dietary factors on stomach cancer. A better understanding of genetic and dietary factors for stomach cancer would help to identify high-risk individuals in personalized risk prediction and dietary intervention.

The dissertation of Yuhui Zhu is approved.

Su Yon Jung

Jian Yu Rao

Frank J. Sorvillo

Zuo-Feng Zhang, Committee Chair

University of California, Los Angeles

2020

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ACKNOWLEDGMENTS

I want to express my sincere appreciation to my Ph.D. advisor, Professor Zuo-Feng Zhang, for all his academic support and guidance since the fall of 2015. I am also very grateful to the members of my Ph.D. committee, Drs. Frank J. Sorvillo, Jianyu Rao, Su Yon Jung, for their valuable comments for my dissertation. Thanks to Dr. Jin-Kou Zhao, the Principal Investigator and the research team of the Jiangsu Four Cancers study for allowing me to use the data to conduct my dissertation.

I thank all my peers in the Cancer Epidemiology group. Thanks to Drs. Esther Chang, Travis Meyers, Aileen Baecker, Shen-Chih Chang, Somee Jeong, and Yan Chai for their help and academic advice. Thanks to Ms. Kexin Jin, Ms. Gina Nam, Mr. Mingyan Zhang, Ms. Fang Fang for sharing ideas, and providing comments. Thanks to my friends, Drs. Yu Yu and Yanglu Zhao for their continuous support for my study and life.

I also want to express my sincere gratitude and appreciation to my family for encouraging and supporting me for my Ph.D. program. My parents always support my decisions for my professional career. My husband is the person who gave me the most significant encouragement for my courses and thesis. My daughter also gives me the courage to complete my dissertation.

The partial results of specific aim 1 of this dissertation have been published in the Nutrients[1]. Results of specific aims 2 and 3 are in preparation for publication. This project was supported by Jiangsu Provincial Health Department (RC 2003090); partially supported by the National Institutes of Health, National Institute of Environmental Health Sciences, National Cancer Institute, Department of Health and Human Services (ES06718, ES011667, CA90833, CA077954, CA96134, DA11386, and CA09142).

VITA

EDUCATION

2015 M.S. in Epidemiology and Biostatistics, Shandong University, China
2012 M.D. in Preventive Medicine, Shandong University, China

RESEARCH EXPERIENCE

2016 - 2020 Graduate Student Researcher, Integrated Substance Abuse Programs, UCLA
2014 Graduate Student Researcher, School of Life Science, Fudan University, China

PUBLICATIONS

Yue D, **Zhu Y**, Rasmussen PW, Godwin J, Ponce NA. Coverage, affordability, and care for low-income people with diabetes: 4 years after the Affordable Care Act's Medicaid expansions. J Gen Intern Med. 2020 Jan 2. doi: 10.1007/s11606-019-05614-2. Epub ahead of print. PMID: 31898136.

Mooney LJ, Valdez J, Cousins SJ, Yoo C, **Zhu Y**, Hser YI. Patient decision aid for medication treatment for opioid use disorder (PtDA-MOUD): Rationale, methodology, and preliminary results. J Subst Abuse Treat. 2020 Jan;108:115-122. doi: 10.1016/j.jsat.2019.08.006. Epub 2019 Oct 24. PMID: 31668516.

Zhu Y, Jeong S, Wu M, Jin ZY, Zhou JY, Han RQ, Yang J, Zhang XF, Wang XS, Liu AM, Gu XP, Su M, Hu X, Sun Z, Li G, Li LM, Mu LN, Lu QY, Zhao JK, Zhang ZF. Dietary Intake of Fatty Acids, Total Cholesterol, and Stomach Cancer in a Chinese Population. Nutrients. 2019 Jul 26;11(8):1730. doi: 10.3390/nu11081730. PMID: 31357492; PMCID: PMC6723637.

Evans EA, **Zhu Y**, Yoo C, Huang D, Hser YI. Criminal justice outcomes over 5 years after randomization to buprenorphine-naloxone or methadone treatment for opioid use disorder. Addiction. 2019 Aug;114(8):1396-1404. doi: 10.1111/add.14620. Epub 2019 May 2. PMID: 30916463; PMCID: PMC6626574.

Liao JY, Mooney LJ, **Zhu Y**, Valdez J, Yoo C, Hser YI. Relationships between marijuana use, severity of marijuana-related problems, and health-related quality of life. Psychiatry Res. 2019 Sep;279:237-243. doi: 10.1016/j.psychres.2019.03.010. Epub 2019 Mar 13. PMID: 30876731; PMCID: PMC6713587.

Hser YI, Saxon AJ, Mooney LJ, Miotto K, **Zhu Y**, Yoo CK, Liang D, Huang D, Bell DS. Escalating Opioid Dose Is Associated With Mortality: A Comparison of Patients With and Without Opioid Use Disorder. J Addict Med. 2019 Jan/Feb;13(1):41-46. doi: 10.1097/ADM.0000000000000458. PMID: 30418260; PMCID: PMC6349485.

Mooney LJ, **Zhu Y**, Yoo C, Valdez J, Moino K, Liao JY, Hser YI. Reduction in Cannabis Use and

Functional Status in Physical Health, Mental Health, and Cognition. J Neuroimmune Pharmacol. 2018 Dec;13(4):479-487. doi: 10.1007/s11481-018-9813-6. Epub 2018 Oct 3. PMID: 30284156; PMCID: PMC6293461.

Zhu Y, Evans EA, Mooney LJ, Saxon AJ, Kelleghan A, Yoo C, Hser YI. Correlates of Long-Term Opioid Abstinence After Randomization to Methadone Versus Buprenorphine/Naloxone in a Multi-Site Trial. J Neuroimmune Pharmacol. 2018 Dec;13(4):488-497. doi: 10.1007/s11481-018-9801-x. Epub 2018 Aug 9. PMID: 30094695; PMCID: PMC6224303.

Hser YI, Mooney LJ, Huang D, **Zhu Y**, Tomko RL, McClure E, Chou CP, Gray KM. Reductions in cannabis use are associated with improvements in anxiety, depression, and sleep quality, but not quality of life. J Subst Abuse Treat. 2017 Oct;81:53-58. doi: 10.1016/j.jsat.2017.07.012. Epub 2017 Jul 29. PMID: 28847455; PMCID: PMC5607644.

Hser YI, Mooney LJ, Saxon AJ, Miotto K, Bell DS, **Zhu Y**, Liang D, Huang D. High Mortality Among Patients With Opioid Use Disorder in a Large Healthcare System. J Addict Med. 2017 Jul/Aug;11(4):315-319. doi: 10.1097/ADM.0000000000000312. PMID: 28426439; PMCID: PMC5930020.

Zhu Y, Yue D, Yuan B, Zhu L, Lu M. Reproductive factors are associated with oesophageal cancer risk: results from a meta-analysis of observational studies. Eur J Cancer Prev. 2017 Jan;26(1):1-9. doi: 10.1097/CEJ.0000000000000234. PMID: 26886236.

Chen H, Nie S, **Zhu Y**, Lu M. Teeth loss, teeth brushing and esophageal carcinoma: a systematic review and meta-analysis. Sci Rep. 2015 Oct 14;5:15203. doi: 10.1038/srep15203. PMID: 26462879; PMCID: PMC4604458.

Zhu Y, Xu Q, Lin H, Yue D, Song L, Wang C, Tian H, Wu X, Xu A, Li X. Spatiotemporal analysis of infant measles using population attributable risk in Shandong province, 1999-2008. PLoS One. 2013 Nov 19;8(11):e79334. doi: 10.1371/journal.pone.0079334. PMID: 24260199; PMCID: PMC3833981.

CHAPTER 1. BACKGROUND

1.1 Cancer Statistics

Stomach cancer (SC) is the fifth most commonly diagnosed cancer and the third leading cause of cancer deaths worldwide by GLOBOCAN 2018[2]. The incidence rates of stomach cancer in Eastern Asia are higher than the rates in Northern America, Northern Europe, and Africa. About 44% of the world's stomach cancer occurrence and almost half of the world’s total stomach cancer deaths (49.9%) occurred in China[2]. As the second most common and the second most deadly cancer in China[3], the age-adjusted 5-year survival rate of stomach cancer is relatively poor, in the range of 30.2-35.9%[4].

In general, the incidence rate of stomach cancer is two to three times more common in men than in women. Stomach cancer incidence varies widely across countries, ranging from about 3.1 per 100,000 men in Egypt to about 57.8 per 100,000 men in South Korea and from 2.4 per 100,000 women in Sweden to about 23.5 per 100,000 women in South Korea[5]. Although stomach cancer incidences have been declining over the past 50 years in most countries, adenocarcinoma of the stomach cardia (the part of the stomach attached to the esophagus) is increasing in the United States and many European countries, including Denmark and the United Kingdom, in recent decades[6,7].

1.2 Carcinogenesis and Biology

About 90% to 95% of cancers of the stomach are adenocarcinomas, which develop from the cells that form the mucosa. Based on the location of the tumor, we usually classify the stomach cancer into two groups: cardia and non-cardia subtypes. The distinction between stomach cancer of the proximal cardia region and those of the distal non-cardia region suggested that these two subtypes may have different etiologies[8]. Early SC and advanced SC (Borrmann classification) are classified differently according to the Japanese Gastric Cancer Association[9]. Lauren[10] demonstrated that histologic classification could be displayed two major distinct types: intestinal (with intercellular junctions) and diffuse (without intercellular junctions), representing two different oncologic entities.

Correa's cascade hypothesis is based on the development of the more common intestinal subtype of stomach cancer. This hypothesis, which was established in 1975, stems from a stepwise process, beginning with chronic atrophic gastritis and progressing to intestinal metaplasia and invasive cancer with the latency of 30 to 50 years[11]. In 1988, Correa furthered explored a detailed model on the phenotypic markers (e.g., nitroso compounds) in addition to his previously proposed SC development process, which is still well-accepted by research community[12]. However, his model has not included potential genetic factors. Therefore, more studies are necessary for knowledge on the role of genetic factors and potential interactions with dietary factors on the progression of stomach cancer.

1.3 Etiology

Different environmental and genetic factors are involved in the development of stomach cancer, although infection with *Helicobacter* (H.) *pylori* is regarded as the primary cause for distal stomach cancer. As we know, age and gender are common risk factors for different types of cancers. Stomach cancer mostly affects older people, which is regarded as a proxy of degenerative change and accumulation of DNA damages. Also, stomach cancer is more common in men than in women, which can be affected by some other factors, such as tobacco smoking, occupational exposures, alcohol consumption, and reproductive factors. The specific review of potential risk/ protective factors of stomach cancer is as follows.

Microorganism

Helicobacter Pylori

In 1994, the World Health Organization's International Agency for Research on Cancer (IARC) declared that there was sufficient evidence to classify *H. pylori* as a definite (group 1) carcinogen[13]. *H. pylori* is a primarily identified risk factor for peptic ulcer diseases, chronic gastritis, and stomach cancer, with more than 60% of new cases worldwide attributed to this bacteria[14]. It is further responsible for almost 90% of non-cardia SC cases worldwide, and approximately 5% of the total disease burden from all cancers globally[15]. *H. pylori* eradication might decrease the risk of SC by approximately 40% in studies of primary prevention and by 54% as a tertiary prevention strategy[16,17]. The pooled odds ratio (OR) for *H. pylori* and non-cardia SC from a pooled analysis of 12 prospective studies was 2.97 (95% CI 2.34-3.77), while the pooled OR was 0.99 (95% CI 0.40-1.77) for cardia SC[18]. The study[18] also reported that the odds ratio for *H. pylori* was not different between intestinal and diffuse histologic subtypes of SC, indicating that *H. pylori* infection might also be involved in the development of diffuse subtype of stomach cancer.

Environmental Factors

Dietary Factors

It has been hypothesized that dietary factors might play a role in stomach carcinogenesis. However, the roles of various dietary factors are still largely unknown. Possible high-risk food includes dietary intake of salt and N-nitroso compounds. A prospective study of the meta-analysis found that habitual intake of salt was associated with a high incidence of SC[19], especially in eastern Asians[20]. A high-salt diet has been shown to enhance the risk of *H. pylori* inflammation and promote the capability of *H. pylori* to SC by potentiating the carcinogenic effects of cagA expression[21]. N-nitroso compounds are regarded as another dietary risk factor that might play a role in stomach carcinogenesis. Dietary or endogenous exposure to N-nitroso compounds has been associated with increased risk of SC, especially with non-cardia cancer risk (HR=1.42; 95% CI, 1.14-1.78 for an increase of 40 μg/day), but not with cardia cancer (HR=0.96; 95% CI, 0.69-1.33)[22]. Cook et al. [23] found that intake of heme iron and total iron in red meat may increase the risk of non-cardia SC. Heme iron from the intake of red meat may catalyze the endogenous formation of endogenous N-nitroso compounds and enhance the risk of SC.

On the other hand, potential protective factors are non-starchy vegetables, fruits, green tea drinking, and certain micronutrients. The protective effects of vegetables and fruits have been reported in case-control studies, but weak and non-association in cohort studies. Recent studies have reported micronutrients, such as Selenium[24], Zinc[25], Vitamin C[26], Vitamin E, and carotenoids[27] may be associated with the development of SC.

Tobacco Smoking

Tobacco smoking is a well-established risk factor for many types of cancers. It was defined as a group 1 carcinogen by the International Agency for Research on Cancer (IARC)[28]. Compared with other tobacco-related cancers, tobacco smoking is associated with a moderately increased risk for SC. A pooled analysis including 23 epidemiological studies found that the ORs were 1.20 (95%

CI: 1.09-1.32) for ever-smokers, 1.12 (95% CI: 0.99-1.27) for former smokers, and 1.25 (95% CI: 1.11-1.40) for current cigarette smokers compared with never smokers[29]. This study and other meta-analyses have identified that the risk of SC increased with an increasing number of cigarettes per day, pack-years, or duration of smoking[30].

Alcohol Consumption

Association between alcohol consumption and stomach cancer has been observed among heavy alcohol consumers based on a systematic review[31]. A recent pooled analysis within the Stomach Cancer Pooling (StoP) project consortium including 20 observational studies reported that the pooled ORs were 1.26 (95%CI: 1.08-1.48) for heavy alcohol drinkers (> 4 to 6 drinks/day), 1.48 (95% CI: 1.29-1.70) for very heavy drinkers (> 6 drinks/day), and a higher risk for cardia than non-cardia SC with heavy alcohol consumption[32]. Also, Moy et al. [33] found that different types of alcohol drinking had different risks for SC, e.g., spirits had a higher risk compared with the beer in a Chinese population.

Obesity and Physical Activity

Obesity is associated with the increased risks of various types of gastrointestinal cancer, such as colon, esophageal, and cardia adenocarcinoma. However, the studies addressing the influence of obesity on non-cardia SC are still conflicting. In a previous meta-analysis, obesity had a positive association with cardia SC, but the effect was not observed in non-cardia SC[34]. Although several reviews with different degrees of rigor have discussed the possible role of habitual physical activity in reducing the risk of SC, approximately 20% to 30%[35,36], and occupational physical activity might offer some protection[37]. Future studies are needed to evaluate the role of physical activity on SC.

Socioeconomic Status

Low socioeconomic status (SES) has been associated with the increased risks of incidence and mortality of many diseases. A meta-analysis observed that an increased risk of SC among the lowest socioeconomic position (SEP) categories compared with the highest SEP categories: Relative Indexes of Inequality (RIIs) were 2.97 (95% CI 1.92-4.58) for education, 4.33 (95% CI 2.57-7.29) for occupation, and 2.64 (95% CI 1.05-6.63) for combined SEP[38]. Although the pathway of low SES associated with stomach cancer has not been established, lower educational attainment could be associated with less income, more unsatisfactory working conditions, and thus a less healthy lifestyle and less access to good healthcare[39]. Risk factors associated with SC, such as *H. pylori* infection, dietary habits, obesity, and cigarette smoking, are related to low SES[40–42]. The increased risk of SC among people with lower educational attainment and lower income may, therefore, be mediated partly through these factors[38]. In a U.S. study, a higher rate of *H. pylori*, particularly CagA-positive strains, was found among low-income African-Americans and may contribute to the higher risk of SC in this group[43]. Strategies for dealing with socioeconomic inequality in the risk of SC are needed.

Familial Aggregations

Individuals with first-degree relatives (parents, siblings, or children) who have had stomach cancer are more likely to develop this cancer. Having first-degree relatives with SC increased the odds of SC by almost 3-fold (OR=2.85; 95% CI: 1.83-4.46). Hereditary diffuse stomach cancer (HDSC) is the most famous familial SC, but the inherited condition (*CDH1* deletion) is rare[44]. Other known cancer syndromes, such as hereditary non-polyposis colorectal cancer (HNPCC) and Familial adenomatous polyposis (FAP), do not account for a large proportion of the family aggregation[45]. Family aggregation is regarded as a mixture of various factors shared by family members, including environmental factors, bacterial virulence, and genetic susceptibility[46].

Host Genetic Polymorphisms

The polymorphisms of the gene in the normal population is linked with individual variations in the risk of specific cancer. Genes involved in the inflammatory genes (IL-1β, IL8, IL10, TNF- β), tumor-suppressor genes (TP53) and prostate stem cell antigen (PSCA) were associated with stomach cancer that confirmed by several meta-analyses[47–49]. The associations between genetic variation at different genes, such as XPG, Mucin 1, PLCE1, HFE, ERCC5, EZH2, DOC2, CYP19A1, ALDH2, CDH1, and stomach cancer were also reported in observational studies[50]. However, these results of genome-wide association studies are not consistent across Asian and non-Asian populations, and the biological mechanisms involved in these polymorphisms are still not completely understood.

MicroRNAs

MicroRNAs (miRNAs) are a group of small non-coding RNAs (18-25 nt) that have been associated with a variety of diseases, including cancer. The role in stomach carcinogenesis complements and enriches the mechanism of tumorigenesis by targeting oncogene and tumor suppressor genes. A profile of several miRNAs (miRNA let-7b, hsa-miRNA-103, hsa-miR-375, and hsa-miR-200a) was associated with reductions of all inflammatory cytokines, suggesting a common mechanism for the control of the expression of these inflammatory mediators [51]. The role played by miRNA in SC is the result of a delicate balance between pro- and anti-cancer miRNA, and this balance is modified by the interaction of many factors, containing dietary factors. Therefore, more comprehensive studies on miRNAs and SC are required.

Stem Cells

Cancer stem cells (CSCs) are defined as a small group of cells in the tumor that could self-renewal and generation of differentiated progeny[52]. The main difference between normal stem cells and CSCs is that self-renewal pathways are strictly regulated in normal, while significantly dysregulated in CSCs[53]. Stomach cancer stem cells (SCSCs), which was identified by Takaishi et al. in *vitro*[54], is associated with metastasis, drug resistance, recurrence, and survival. In the regulation of SCSC self-renewal, several factors and critical signaling pathways (e.g., Wnt, Sonic hedgehog, Nuclear factor-kappa B, Notch signaling pathway) are utilized.

Nuclear factor-kappa B (NF-κB) refers to a group of transcription factors that form homo- and heterodimers and upregulate or suppress the expression of many genes[55]. NF-κB-driven gene products include cytokines/chemokines, growth factors, anti-apoptotic factors, angiogenesis regulators, and metalloproteinases[56], which are related to stomach carcinogenesis. There was evidence that the NF-κB system could be deregulated in SC[57,58] in the early-2000s, but the relationship between NF-κB activity and the specific mechanism is still not clear. Recent research has reported that contact of *H. pylori* with epithelial cells leads to the expression of interleukin (IL)-8 via activation of the nuclear factor (NF)-kB pathway[59]. Endo et al. [60] have also found that chemotherapy-caused cellular stress could elicit activation of the survival factor NF-κB in stomach cancer cell lines, which suggested a way of therapeutic targeting.

GWAS

Genome-wide association studies (GWAS) of stomach cancer have reported differences in single-nucleotide polymorphism (SNP) associations for tumor subtypes. Recently, several GWAS related to SC in East Asia have been published. A GWAS from Japan reported significant associations for PSCA rs2976392 and rs2294008 at 8q24 with diffuse-type SC[61]. The associations for PSCA rs2976394 and rs2294008 at 8q24 with the risk of SC were also found in a Korean population[62]. Abnet et al[63] reported the genome-wide significant association between PLCE1 rs2274223 at 10q23, MUC1 rs4072037 at 1q22, and mixed types of SC in ethnic Chinese subjects. This study group further found PRKAA1 rs10074991 at 5p13.1 was associated with the risk of the cardia and non-cardia SC, and rs2294693 near UNC5CL at 6p21.1 was genome-wide significant for the risk of non-cardia SC[64]. Other groups from China reported significant genome-wide associations for PRKAA1 rs10074991 at 5p13.1, ZBTB20 rs9841504 at 3q13, SLC52A3 rs13042395 at 20p13, LRFN2 rs2494938 at 6p21.1, DNAH11 rs2285947 at 7p15.3 with SC in Han Chinese population[65–67].

BCMO1

SNPs of the human β-carotene-15,15'-monooxygenase 1 (BCMO1) gene, which is located on chromosome 16, have shown to affect the concentrations of circulating carotenoids and β-carotene conversion efficiency[68]. Leung et al.[69] showed that two common nonsynonymous SNPs (rs12934922 and rs7501331) reduced BCMO1 catalytic activity by 57% (P<0.001) in *vitro* biochemical characterization of the recombinant SNPs double mutant. A *vivo* study on adult female human volunteers found the homozygous rs6564851 genotype of BCMO1 decreased the catalytic activity of BCMO1 by 48%[70].

Gene-Diet Interactions

Stomach cancer is thought to be stemmed from a combination of environmental factors and the accumulation of acquired somatic alterations. Common dietary factors could act on the human genome, either directly or indirectly, to alter gene expression or structure, which may, in turn, affect the risk of stomach cancer[71]. Gene-diet interactions may explain variations in SC incidence in different populations and the inconsistent findings of the gene or dietary studies[72]. In previous studies on gene-diet interactions for SC[73], they examined various dietary factors (e.g., fresh fruits and vegetables, meat, salted and preserved foods, and alcohol) and polymorphisms in genes. For instance, some studies found the interaction between DNA synthesis and repair-related genetic polymorphisms (e.g., MTHFR) and dietary folate on SC[74,75]. The effect of dietary factors on SC according to the carcinogen metabolism-related genetic polymorphisms (e.g., GSTT1/GSTM1 and tea, ALDH2, and alcohol) was also reported in different populations[45]. Also, inflammation-related polymorphisms were contributed to the variation of SC. Ko et al. [76] found that IL-10 genetic variants and low intake of soybean products increased SC risk compared with the same variants combined with high consumption of soybean products.

Other Miscellaneous Factors

Some research also found EB virus, HIV-infected, occupational exposures, reproductive factors, radiation, previous stomach surgery, pernicious anemia, menetrier disease, type A blood, and common variable immune deficiency (CVID) increase the risk of developing SC.

1.4 Diagnosis, Treatment, and Survival

The patterns of mortality of SC generally follows the patterns of incidence of stomach cancer because an average 5-year survival rate of stomach cancer is low, in the range 20-40%[4], because stomach cancer patients are more likely to be diagnosed at an advanced stage of SC. Early detection of SC is an essential strategy for better survival. The 5-year age-adjusted survival rate was increasing in Japan and South Korea because of early detection. The 5-year survival rate for all stages of SC combined is 68.9% in South Korea and 60.3% in Japan, while 33.1% in the United States and about 20-30% in European countries[4]. In developing countries, relative survival rates are generally below 20%[4].

1.5 Dietary Fatty Acids and Stomach Cancer

"Western diet" is widespread all over the world, with this progression comes an urban lifestyle. High intakes of refined sugar, fat, and animal protein and low intakes of fiber are the main characteristics of the "Western diet". Fats and oils are the most energy-rich constituents of this diet.

Three fatty acid molecules reacting with a glycerol molecule and three water molecules are the constituents of fat (or oil). Fatty acids are composed of carbon, hydrogen, and oxygen set up as a linear carbon chain skeleton with a carboxyl group at one end[77]. Fatty acids (FAs) can be separated into three categories: saturated (SFA), monounsaturated (MUFA), and polyunsaturated (PUFA) based on the number of double bonds. Saturated fatty acids such as stearic acids are common ingredients of foods and possess no double bond in their structure. Some FAs such as oleic acid have one double bond and, hence, are called monounsaturated. Polyunsaturated fatty acids have more than one double bond. There are other classifications for fatty acids. Based on the number of carbons, there are a short-chain (2 to 6 carbons), medium-chain (8 to 14 carbons), and long-chain (16 carbons and up). In terms of the position of the double bond relative to the last carbon of the chain, omega 3 (n-3) means the double bond nearest the last carbon of the chain (Cω) is three carbons apart from the end of the chain, while omega 6 (n-6) means the double bond nearest to the last carbon of the chain is six carbons apart[77]. More than 20 types of fatty acids are found in foods. Linoleic acid (LA) is a representative of n-6 PUFA, serving as a substrate to be converted into arachidonic acid (AA). α-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are the main n-3 PUFAs stored in human beings.

Evidence is accumulating that many changes of fat and fatty acids have led to detrimental increases in obesity and gene-diet interactions that are responsible for an elevation in localized and systemic inflammation[78]. This inflammation then contributes to a variety of human diseases, including cardiovascular disease, diabetes, cancer, asthma, allergies, chronic joint disease, skin, and digestive disorders, dementia, and Alzheimer's disease[79]. For this reason, the World Health Organization (WHO) recommends limiting the total fat intake for humans, between 15% and 30% of daily energy intake[80].

Measurements of Fatty Acids

Precise assessment of nutrients intake is essential for nutritional epidemiologic studies. However, fat is one of the most difficult dietary components to measure[81]. Food frequency questionnaires

(FFQs) are commonly used to estimate usual dietary intakes because of relatively inexpensive administration and lower respondent burden compared to other methods. Furthermore, we could identify the fat sources to explore the different long-term dietary patterns of nutrients. FFQs are better suited for ranking individuals than for precise numeric estimation. The limitations of FFQ include errors in the estimation of portion size and incomplete food items. Also, biomarkers of dietary fatty acids are used to explore the associations between exogenously and endogenously produced fatty acids and diseases. However, various biological samples reflect some extent of dietary fatty acids, but no biomarkers reflect absolute fat intake. The biomarkers are also subject to measurement error that results from absorption, metabolism, and all the factors that have an impact on metabolic efficiency[81].

For instance, plasma saturated fat is not likely to be associated with dietary saturated fat, as saturated fatty acids can be synthesized endogenously. PUFAs are largely exogenous, and diet is the primary source. FAs in adipose tissue may best reflect the long-term fatty acid composition of the diet but are rarely used as biomarkers because sample collection may not be acceptable to study participants[82]. Plasma phospholipid (PL) and cholesterol ester (CE) fatty acids only reflect the intake of fatty acids over the past few days or more[82]. The exogenously produced fatty acids (e.g., EPA and DHA) are more closely related to FFQ than kinds of endogenously synthesized fatty acids (e.g., SFAs).

Biologic Mechanisms

More than two decades ago, an experimental study *in vitro* hypothesized that dietary fats might be risk factors for stomach cancer[83]. Since *H. pylori* infection is the primary carcinogenic agent for distal SC, dietary factors that contain chemicals that naturally inhibit/promote this infection are, therefore, potential effects on SC. *In vitro* studies have shown that *H. pylori* extract lipids from plasma membranes of epithelial cells for subsequent glycosylation[84]. A hypothesis was put forward that increased intake of vegetable oils over animal fats contributed to the decline of peptic ulcer disease in both the United States and in England and Wales[85]. Olive oil (rich MUFAs) intake has been inversely associated with the risk of SC by inhibiting *H. pylori*[86].

PUFAs, which are involved in many critical biological functions, are essential nutrients for life and cannot be produced endogenously[87]. PUFAs play a crucial role in cell membranes by influencing membrane composition and function; besides, some of PUFAs are mediators of cellular signaling and regulation of gene expression. Arachidonic acid (AA) is a precursor of n-6 PUFAs, which is released from membranes by phospholipase A2 and converted into various lipid mediators that involved in many homeostatic biological functions and inflammation[88]. In contrast, the health benefits of n-3 PUFA have been known for a long time. There is accumulating evidence that higher consumption of dietary n-3 PUFAs is associated with a lower risk of *H. pylori*-associated stomach diseases and even stomach cancer risk by influencing multiple targets, including proliferation, survival, angiogenesis, inflammation, and metastasis[89].

Epidemiologic Evidence

Except for experimental studies, observational studies also have examined the relationships between various dietary fatty acids consumption and stomach cancer. In a meta-analysis with one cohort and 21 case-control studies, dietary intake of total fat was potentially associated with SC (highest vs. lowest OR, 1.18; 95% CI, 0.999-1.39)[90]. When separated into subtypes of fatty acids, some case-control studies found the development of SC has been positively linked to saturated fatty acids (SFAs) [91–95] and monounsaturated fatty acids (MUFAs) diet [91,93]. However, other case-control studies found no significant associations between dietary SFAs[96–100], MUFAs[92,97,99,100], PUFAs[92–94,97,99], and SC. A cohort study among elderly persons in U.S.[101] investigated that total fat and selected fat subtypes (SFAs, MUFAs, PUFAs, trans-fat, and n-3 PUFAs) were not related to the risk of SC. Furthermore, some previous case-control studies even found inverse associations with dietary MUFAs[96] and PUFAs[91,96,102,103].

Other observational studies investigated the associations between serum fatty acids and stomach cancer. A hospital-based case-control study of 179 stomach cancer cases in Japan[104] found that the erythrocyte composition of docosahexaenoic acid (DHA) was inversely linked to stomach cancer (highest vs. lowest tertile OR, 0.47; 95% CI, 0.28-0.79), especially well-differentiated adenocarcinoma. A nested case-control study including 238 stomach cancer cases and matched to 626 controls observed positive associations between plasma oleic acid (OR, 1.72; 95% CI, 1.01-2.94), di-homo-γ-linolenic acid (OR, 1.92; 95% CI, 1.10-3.35), α-linolenic acid (OR, 3.20; 95% CI, 1.70-6.06), the ratio of MUFAs to SFAs (OR, 1.40; 95% CI, 0.81-2.43) and SC risk[105]. In the same study, they also found that the ratio of linoleic to α-linolenic acid was inversely associated with SC risk (OR, 0.37; 95% CI, 0.20-0.66)[105].

1.6 Dietary Cholesterol and Stomach Cancer

Cholesterol is a type of lipid, which serves as a precursor for the biosynthesis of steroid hormones, bile acid, and vitamin D[106]. Cholesterol is also a major structural component of all cell membranes. There is only one type of cholesterol, but it travels through the blood on proteins: LDL (low-density lipoprotein) and HDL (high-density lipoprotein). So, cholesterol plays an essential role in the function of keeping human health.

Biologic Mechanisms

The mechanisms on the relationship between total dietary cholesterol and stomach cancer have been hypothesized. Controlled experiments in mice suggest an association between dietary cholesterol and cancer[107–110]. It has been reported that cholesterol metabolism may play an important role in *H. pylori* eradication[111].

Epidemiologic Evidence

There are inconsistent results on dietary cholesterol with the development of stomach cancer in observational studies. A population-based case-control study in Canada reported that dietary cholesterol was associated with SC (Highest vs. Lowest quartile OR, 1.75; 95%CI, 1.36-2.25)[92]. Another population-based case-control study in the U.S. found a positive association between dietary cholesterol and SC (75th vs. 25th percentile OR, 1.50; 95%CI, 1.19-1.90)[94]. The increased odds of SC were observed in a hospital-based case-control study in Spain for high consumption of cholesterol (Highest vs. Lowest quartile OR, 1.78; p-trend = 0.03)[112]. However, no significant association between dietary cholesterol and SC in a hospital-based case-control study in Italy (OR,1.11; 95%CI, 0.94-1.32 for one standard deviation of controls increase)[102] and a population-based case-control study in Poland (Highest vs. Lowest quartile OR, 0.90; 95%CI, 0.58-1.38)[113].

Except for the dietary cholesterol, the role of serum cholesterol in the development of stomach cancer is also uncertain in observational studies. The Swedish Apolipoprotein Mortality Risk

(AMORIS) study found no association between serum total cholesterol and SC[114]. The metabolic syndrome and cancer project (Me-Can), including cohorts from Norway, Austria, and Sweden, also found no association between serum triglycerides and SC[115]. The other two cohorts in Japan and Korea investigated that serum total cholesterol levels were inversely associated with the risk of SC[116,117]. However, these cohorts did not adjust for *H. pylori* infection because the outcomes of these studies were the incidence of various cancers or all-cancer.

1.7 Dietary Flavonoids and Stomach Cancer

The World Health Organization (WHO) has ranked low consumption of fruits and vegetables among the top 10 risk factors leading to mortality[118]. High fruit and vegetable intakes are associated with beneficial health effects, which is partly attributed to flavonoids in addition to many potentially bioactive components such as fiber, folate, antioxidant vitamins, and potassium. Flavonoids are a group of polyphenolic compounds, which occur ubiquitously in plant foods. There are several significant subclasses of flavonoids, including flavonols, flavones, flavanols, flavanones, anthocyanidins, and isoflavones, based on their chemical structures[119]. Within the subclass of flavonoids, there are still more subgroups.

The source of flavonoids in the Asian diet has its distinct characteristics compared with the western diet. In the U.S., Chun et al. [120] found that the primary dietary sources for the total flavonoids were tea, citrus fruit juices, wine, and citrus fruits by analyzing the NHANES data. A study on the Mediterranean diet among young adults in Spain[121] showed that fruits (including apples, oranges, and fruit juices), vegetables (particularly spinach, onions, artichokes, and lettuce), and chocolate products were the primary sources of total flavonoids. However, Li et al. [122] identified that the richest sources of flavonoids were the fruit group (e.g., apple, plum, pear, and peach) and the vegetable group (e.g., lotus root, taro) for Chinese diet. Another research in China has found that nearly 50% of dietary flavonoids come from tea consumption[123], which was relatively lower in western countries[124].

Measurements of Flavonoids

Self-reported questionnaires and nutritional biomarkers are the two main methods used for estimating dietary flavonoids. The limitations of self-reported questionnaires (especially FFQs) are mentioned above. However, FFQs are still the most common method used in large observational studies. As biomarkers, there are only a few validated concentration markers of dietary flavonoids, because it is challenging to find markers that meet all the following criteria: 1) to be specific; 2) to have an adequate half-life, and 3) to provide a good correlation between the biomarker and the intake[125].

Biologic Mechanisms

The biological effects of flavonoids for cancer prevention include the regulation of cell signaling and the cell cycle, anti-mutagenic and anti-proliferative properties, free radical scavenging, and inhibition of angiogenesis[126]. *In vitro* and animal studies have shown the chemopreventive effect of flavonoids on the development of stomach cancer. A study on flavonoid compounds isolated from Chrysosplenium nudicaule has investigated that flavonoid compounds could inhibit the growth and inducement of apoptosis in the human stomach cancer cell line[127]. Skiba et al. also noted that flavonoids might limit the inflammatory process via the inhibition of IL-8 release in *H. pylori*-induced activation of human stomach adenocarcinoma cells[128]. Moreover, Shen et al.

observed that quercetin triggered mitochondrial apoptotic dependent growth inhibition via the blockade of phosphoinositide 3-kinase (PI3K)-Akt signaling in the human stomach cancer stem cells[129]. Another study by Ohno et al. found that green tea catechins might play a protective role in the development of gastritis and pre-malignant lesions via an IFN-γ, gastrin, and mucosal cell proliferation-dependent mechanism using a rodent model[130].

Epidemiologic Evidence

In recent years, there is growing evidence of dietary intake of flavonoids and cancer. However, it is difficult to assess the effects of dietary flavonoids on the development of stomach cancer. Hot beverages, wine, and beer are relevant sources of dietary flavonoids in western country diets, yet hot beverages and alcohol intake are risk factors for SC. Among epidemiological investigations conducted in the United States, European and Asian countries, few studies did find significant associations with specific classes of flavonoids. For example, dietary flavone intake was inversely associated with SC in a Spain case-control study described by Garcia-Closas et al. (Highest vs. lowest quartile OR, 0.44; 95%CI, 0.25-0.78)[131]. Another case-control study in Greece[132], the OR of SC per one standard deviation increase in intake of one class of flavanones was 0.55 (95% CI, 0.31-0.96). In a U.S.-based study[133], no association was found between total flavonoid intake and incidence or survival for SC, but anthocyanidins were associated with decreased risk of mortality for SC (HR, 0.63; 95% CI, 0.42-0.95) with small sample size (n=248 cases). In a Korean case-control study[134], significant associations were observed in total flavonoids intake and SC (Highest vs. lowest tertile OR, 0.49; 95% CI, 0.31-0.76). A cohort from the European Prospective Investigation into Cancer and Nutrition study[135] examined the association between total flavonoid intake and SC risk and observed a significant inverse association in women (HR, 0.81; 95% CI, 0.70-0.94), but not in men (HR, 0.97; 95% CI, 0.85-1.09).

1.8 Index-Based Dietary Patterns and Stomach Cancer

The effect of various dietary factors on the development of stomach cancer has been suggested. Epidemiological studies have shown that fruit and vegetables with rich folates, vitamins, and fiber appear to lower the risk of stomach cancer, while dietary intake of salt is associated with increased risk of stomach cancer[19,136,137]. Other foods, such as meats, are associated with a high risk of stomach cancer in some populations, but the results have been inconsistent[136,138]. It is difficult to distinguish the individual effect of specific food or nutrients as a result of the combination of food consumption and the interaction of various food or nutrients in daily life[139]. Index-based dietary patterns may provide reasonable insight into the association between dietary factors and stomach cancer.

Index-based dietary pattern has been associated with a lower risk of several cancers, such as breast cancer[140,141], colorectal cancer[142,143], esophageal cancer[144], liver cancer[145], and lung cancer[146]. However, to the best of our knowledge, few studies have investigated the association of index-based dietary patterns with stomach cancer in a Chinese population. Most recent research has focused on the relationships between Mediterranean diet (MED) and stomach cancer, which is different from Chinese dietary pattern[144,147–151].

1.9 Evidence Gaps in the Literature

In the literature to date, the relationships between the dietary intakes of fatty acids, total cholesterol as well as flavonoids and stomach cancer have been considered in several epidemiologic studies, but the results are still conflicting. This study is the first to look at the associations between dietary intake of fatty acids, total cholesterol, and flavonoid and SC, and the potential interaction or mediation with major risk factors in a high-risk population in China, and it is the largest study to assess whether dietary intakes of fatty acids, total cholesterol, and flavonoid are associated with SC in a Chinese population.

Additionally, few studies have investigated the association between index-based dietary patterns and stomach cancer, and the potential interaction with established risk factors. The high-quality dietary data and large sample size of this population-based study enable us to examine the associations of index-based dietary patterns on stomach cancer in China.

Lastly, this study further assessed the potential interactions between dietary factors and SNPs associated with miRNAs, stem cells, GWAS, and beta-carotene metabolism. No published study has assessed the interactions of candidate SNPs with diet on SC. It is the first study to evaluate how dietary fatty acids, total cholesterol, and flavonoid modify the associations between established and novel SNPs on SC susceptibility.

CHAPTER 2. STUDY AIMS AND METHODS

2.1 Research Objectives

This study examines the associations between dietary factors and stomach cancer, which might provide a potential intervention strategy that could be implemented to reduce the disease burden associated with stomach cancer. Specific aims are as follows.

2.2 Specific Aims and Hypotheses

Specific Aim 1:

To estimate nutrients from dietary history for each study participants, and to estimate the associations of dietary fatty acids, total cholesterol, and flavonoids with the development of stomach cancer.

Hypothesis 1:

We hypothesized that an increase in dietary intake of specific dietary fatty acids (FAs, SFAs, n-6 PUFAs) and total cholesterol might be associated with stomach cancer, while higher intake of n-3 PUFAs and dietary flavonoids might be inversely associated with stomach cancer.

Specific Aim 2:

To assess the index-based dietary pattern associated with stomach cancer and investigate the interaction with established risk factors on stomach cancer.

Hypothesis 2:

We hypothesized that index-based dietary patterns and their components might reduce the odds of stomach cancer.

Specific Aim 3:

To examine the specific genetic polymorphisms associated with stomach cancer and explore potential gene-diet interactions with dietary intake of fatty acids, total cholesterol, and flavonoids on stomach cancer.

Hypothesis 3:

We hypothesized that dietary intake of fatty acids, total cholesterol, and flavonoids might modify the associations between candidates SNPs in selected genetic pathways with the stomach cancer susceptibility.

2.3 Study Design and Population

Study Area

Jiangsu province is one of the highest risk areas for stomach cancer in China. From 2003-2012 cancer register data in Jiangsu province, the average incidence rate of SC alone was 48.2/100,000, and the average mortality rate was 35.1/100,000[152]. Jiangsu province is an eastern-central coastal province located in north latitude 30.45 N to 35.20 N and east longitude 116.18E to 121.57E, covering an area of 107,200 km^2. According to the 2016 census data reported, the thirteen prefecture-level divisions of Jiangsu are subdivided into 96 county-level divisions (55 districts, 21 county-level cities, and 20 counties) with a population of around 80 million, which is a blend of the population from northern and southern of China. Along two famous rivers - the Yangtze River and the Yellow Sea, Jiangsu is endowed with flat land and connected to Shanghai. Therefore, this province owes considerably beneficial geographical location, abundant resources, and stable economic status.

To collect consistent and high-quality data to reduce the methodological limitations, the Jiangsu Four Cancers (JFC) Study[153] was implemented to gather enough data containing related study factors from both environmental and genetic fields for essential cancers including stomach cancer in four counties (Dafeng, Ganyu, Chuzhou, and Tongshan) in Jiangsu province, China. The reason to choose these four counties is that Dafeng and Chuzhou counties have a higher SC incidence and mortality, while Ganyu and Tongshan counties have a lower SC incidence and mortality based on investigations of the Centers for Disease Control and Prevention (CDC) in Jiangsu Province.

Case Recruitment

This JFC study identified newly diagnosed primary stomach cancer cases from a local population-based cancer registry from January 2003 to December 2010. Diagnostic methods included medical imaging (19%), pathology (46.7%), endoscopy (29.1%), biochemistry (1.4%) and clinical diagnosis (3.7%)[153]. Cases were recruited to be at least 18 years old, indigenous residents of the respective county for at least five years before diagnosis date for SC patients, and in a stable medical condition as determined by their physicians. The number of the available questionnaire of SC cases for the JFC study is 2,216. 712 of 2,216 cases (32.1%) were too ill to be interviewed, so family members served as a proxy respondent. 1,710 of 2,216 cases (77.2%) had blood samples drawn. The participation rate of SC cases was 40%.

Control Selection

The control group was randomly chosen from the populace registry list of each county and matched to the corresponding cases for age (± five years) and gender with a case/control ratio of about 1 to 1 initially. Controls participants were also refined to indigenous residents who were at least 18 years old, have dwelled in the same county for more than five years before the interview date, without any history of cancer, and in a stable medical condition. If a control did not fulfill the criteria or refused to participate in, basic demographic data were recorded, and the same selection process was used to choose another control. Then, considering various exposure-cancer associations and gene-environmental interactions, we pooled together all controls for all four cancer sites to increase the power. A total of 8,019 completed questionnaires and 6,650 (82.9%) had blood samples drawn. The participation rate of the controls was 87%.

Questionnaire Data

Face-to-face interviews of participants were conducted using a structured questionnaire with detailed information on (1) demographic features (e.g., age, gender, education, family income per year, and home address); (2) residence environment factors; (3) health behaviors (dietary history, life-long history of tobacco smoking, alcohol consumption, green tea drinking, and physical activity); (4) medical history; (5) occupational exposures; (6) family history of cancer; and (7) reproductive factors among women. The interviews of the cases took place at their hospital ward or home after they were reported to the county cancer registry, and those of the controls took place at their home.

Participants were asked to report their general dietary history one year before the diagnosis or the interview date to capture dietary patterns by using a 90-item food frequency questionnaire (FFQ). For each food item, participants were asked whether they ever consumed the food or not in the year before the diagnosis or the interview date. For each food item they consumed, the frequency and the portion size were asked, according to five predefined frequency categories (never, times per year, times per month, times per week, and times per day) and one predefined portion size (1 Liang = 50 g).

Blood Sample Collection

Nonfasting peripheral blood samples (5-8ml) were collected after the time of the interview. Blood samples were collected in EDTA or heparin-coated tubes and assigned an identification number. They were then separated into serum, red blood cells, and white blood cells and stored below -20°C at the local CDCs. All samples were transported to the Jiangsu CDC, where they are currently stored below -70°C for further process. DNA samples were then extracted in a molecular epidemiology lab at the department of non-communicable disease (NCD) at the Jiangsu CDC. One thousand six hundred twenty-four cases and 6,666 controls had data of serological tests for *H. pylori*. Anti-*H. pylori* antibody immunoglobulin G (anti-*H. pylori* Ab IgG) was measured by enzyme-linked immunosorbent assays (ELISA) using kits from Beier Bioengineering (Beijing, China). Serology tests are relatively cheap and readily available as non-invasive procedures for population screening of *H. pylori*. The sensitivity and specificity of commercial enzyme immunoassay tests range from 60% to 100%[154]. According to the manufacturer's instruction, levels of IgG were categorized as seropositive and seronegative for *H. pylori* according to a particular cutoff value. Moreover, 1,169 SC cases and 2,470 controls had data of SNPs. SNPs were genotyped with a Fluidigm Dynamic 96.96 Array™ Assay (Fluidigm, South San Francisco, CA) at the UCLA Genotyping and Sequencing Core.

Quality Control

Quality control is an essential process in this study for data collection and management. Under the guidance of the Jiangsu CDC and UCLA staff, all interviewers have received a 2-day training session and field practice. Refresh training took place during annual reviews. Any new interviewers were trained and supervised by an experienced interviewer. The questionnaire data collected from the first interview was reviewed by research staff at the county level and then by an epidemiologist at the Jiangsu Provincial CDC. Ten percent of the face-to-face interviews were randomly selected and conducted again to verify the quality of the data - an overall accuracy of 96% for the cases and 97% for the controls. Data were double entered into a database designed using EpiData (Odense, Denmark) at each county CDC and then cleaned and managed at Jiangsu Provincial CDC.

The JFC study was approved by both Jiangsu CDC and UCLA institutional review boards. Written informed consent was obtained from all participants before the epidemiologic data and biological specimen collections.

2.4 Statistical Analyses

Specific Aim 1

Dietary Assessment

For each food item in FFQ, a matched food item or list of food items were found in the China Food Composition (CFC) Tables 2010, released by the China CDC (Institute of Nutrition and Food Safety 2010). For two food items in FFQ that could not be matched with the CFC tables, frog and sugar cane, we employed the Japanese Food Composition Tables for frog and the U.S. Department of Agriculture (USDA) database for sugar cane. An average daily intake of each food item was calculated by multiplying the portion size and frequency of consumption per day obtained from the FFQ. The average daily intake of calories for each food item was estimated by multiplying the average daily intake of each food by the corresponding calorie value obtained from the CFC Tables. Then, the total intake of calories per day was calculated by summing up the calories from all the food items the participants consumed.

We multiplied the average daily intake of each food by the corresponding contents of fatty acids obtained from the CFC Tables and summed up the values for each participant. Intakes of total fatty acids (FAs), saturated fatty acids (SFAs), monounsaturated fatty acids (MUFAs), and polyunsaturated fatty acids (PUFAs) were estimated. For PUFAs, n-3 fatty acids, including alpha-linolenic acid (ALA), docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), and n-6 fatty acids, including linoleic acid (LA) and arachidonic acid (AA) were estimated. We also included total fat and total cholesterol in data analyses.

For dietary flavonoids, a database listing the flavonoid values (mg/ 100g food) for common Chinese foods was constructed in our lab by other study researchers[155]. In short, there are 50 fruit, vegetables, legume, and nut food items matched to the FFQ based on Chinese articles, articles reporting Chinese foods, USDA flavonoids, and isoflavone database. Pumpkin seeds, wood ear, sugar cane, and wheat gluten, which was not covered, are not the primary source of flavonoids in this population. The wine was also excluded from the analysis as wine consumption was deficient in this population. Tea consumption was asked as grams of dry black, green, flower, or oolong tea intake per month in the questionnaire. Hence, we also converted the unit into milligram flavonoids per gram of dry tea. After linking the amount of each food item or tea with its flavonoid value, we estimated six subclasses of flavonoids including flavonols (isorhamnetin, kaempferol, myricetin, quercetin), flavones (apigenin, luteolin), flavanones (eriodictyol, hesperetin, naringenin), flavan_3_ols (catechin, catechin-3-gallate, epicatechin, epicatechin-3-gallate, epigallocatechin, epigallocatechin-3-gallate, gallocatechin, gallocatechin-3-gallate, theaflavins, thearubigins), anthocyanidins (cyanidin, delphinidin, malvidin, pelargonidin, peonidin, petunidin) and isoflavones (daidzein, genistein) for each participant. Then we summed these six subclasses to calculate total flavonoids intake (mg/day). Also, we separated the total flavonoids based on the different sources from vegetables, fruit, and tea.

In the JFC study population, the median of total intake of calories from food among controls was 1,855.0 calories per day. We excluded individuals who consumed less than 500 or more than 5,000 calories per day, and those who ate only less than four food items (cases = 316, controls = 1,487) because their FFQs were considered incomplete. Finally, 1,900 SC cases and 6,532 controls remained in our analyses of specific aim 1 (Figure 2.1). Chi-square tests or t-tests were used to compare the distribution of potential risk and protective factors between SC cases and the controls.

We estimated cumulative exposures to each kind of fatty acids, total cholesterol, and flavonoids for each study participant based on data collected. Exploring the associations between dietary fatty acids, total cholesterol, flavonoids, and SC, adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) were estimated by multiple unconditional logistic regressions. Potential confounding factors included age (years), gender (male vs. female), county (Dafeng, Ganyu, Chuzhou, and Tongshan), education (illiterate, primary, middle, and high school or above), income 10 years ago (<1,000, 1,000 to <1,500, 1,500 to <2,500, ≥2,500 yuan/year), family history of stomach cancer (yes vs. no), tobacco smoking (pack-years), alcohol consumption (ethanol, g/day), total energy intake (kcal/day), dietary sodium intake (<0.55, 0.55 to <1.04, 1.04 to <1.96, ≥1.96 g/day), *H. pylori* infection (yes vs. no), physical activity 10 years ago (yes vs. no), and body mass index (BMI) (<18.5, 18.5 to <24, 24 to <28, ≥28 kg/m^2). Dietary intakes of fatty acids, total cholesterol, and flavonoids were examined as both categorical variables and continuous variables. Dietary intakes of these nutrients were categorized as quartiles, according to their distributions among controls. Trend analyses were performed by scoring the ordinal level of dietary exposures (0, 1, 2, 3) and treating them as a continuous variable in the models. For continuous variables, the rescaling units were chosen based on the interquartile range (IQR) of controls as well as on the availability of intervention ranges. The 2016 Chinese Dietary Guidelines[156] recommended no more than 25 g ethanol/day for men and 15 g ethanol/day for women. Three groups of alcohol consumption were created according to this recommendation: never (0 g ethanol/day), low-risk (≤ 25 g ethanol/day for men and ≤15 g ethanol/day for women), and high-risk (> 25 g ethanol/day for men and >15 g ethanol/day for women). Covariates considered as potential confounders or effect measure modifiers for this analysis were chosen using a priori knowledge of the relationships between the dietary exposures, outcome, and potential confounders using a Directed Acyclic Graph (DAG).

Multiple Imputations for Missing Data

Missing data is a common problem in FFQ, especially when the questionnaires are relatively long. We have used multiple imputations to impute the values of each dietary exposure and covariates in the full dataset to maximize the use of available information. The procedures for conducting multiple imputations are as follows:

Firstly, we checked the number and proportion of missing values for exposures of interest (continuous/category) and covariates, which were the same as the logistic model we mentioned above. In this study, the number of missing values for dietary factors were the same as the number of individuals who were excluded because their total energy expenditures were outliners, indicating those individuals either e under- or over-reported their dietary history. Missing values were less than 10% for all variables except for *H. pylori* infection (19% of missing), so the proportion of individuals with at least one missing variable is more than 20% of entire observations. The missing scenario of covariates is shown in Table 2.2. Then, we checked the missing data patterns among all these variables. The choice of method to use was relied on whether the missing pattern was monotone or not. The missing patterns of categorical variables may not be monotone, so we considered the arbitrary missing pattern. Markov Chain Monte Carlo (MCMC) method was used for partial imputation of non-monotone missing records while treating categorical variables as if they were continuous and modeling them with a multivariate normal distribution. This method was not the best option, but it was acceptable. We also conducted the fully conditional specification (FCS) method for use with an arbitrary missing data pattern and continuous or categorical variables. The interaction term was added into imputed models if the interaction terms existed in the logistic models. The results from complete case analysis were consistent with that of multiple imputations using MCMC or FCS. We presented the results of both complete analysis and multiple imputations using MCMC.

Multiple Comparisons and Semi-Bayes Shrinkage

For epidemiologic studies, analyses of multiple exposures and outcomes face issues of multiple comparisons, leading to false-positive or inflated coefficient estimates. Therefore, we performed the semi-Bayes shrinkage approach with prior distributions on the main effect or product terms in order to reduce the impact of multiple comparisons and sparse data[157]. The data augmentation approach of semi-Bayes shrinkage was applied with null-effect prior (OR=1.00, 95% CI 0.25-4.00). This process usually improves the overall accuracy of estimation and prediction.

Adjustment for Energy Intake

Intakes of most specific nutrients are correlated with total energy intake, so the relationships between specific nutrients and disease risks are usually confounded by total energy intake. Additionally, individuals tend to under-report or over-report food items in the same direction in FFQ. Measurement errors in nutrients intakes are correlated with measurement errors of total energy intake, controlling for total energy intake will also reduce extraneous variation[158].

In this study, dietary nutrients were adjusted for total energy intake using the residual method[158]. This method computes residuals of nutrient intake by building a regression model with dietary nutrients as the dependent variable and total energy intake as the independent variable[158]. The nutrient residuals from the regression were extracted to represent the differences in the individual's actual intake and the intake predicted by total energy intake. So, the nutrient residual is uncorrelated with total energy intake, and the variation from the nutrient composition of the diet could be evaluated directly.

Sensitivity Analyses

The exposures of interest (dietary fatty acids, total cholesterol, and flavonoids) were estimated from FFQ in this study, and some degrees of bias was expected. An analysis restricting the data to participants who were interviewed directly (excluding the data obtained in proxy interviews) would be conducted. Besides, another empirical approach of excluding individuals with reported total energy intake in the upper and lower 2.5%[159] (cases=309, controls=1,421) was also conducted for this study.

Interaction Analysis

For many studies, it is impossible to assume that the exposure and mediator do not interact in their effects on the outcome. Conducting the mediation analysis incorrectly assuming no interactions may result in invalid inferences. Therefore, we assessed both multiplicative and additive interactions[160] between dietary factors (fatty acids, total cholesterol, flavonoids) and major risk factors (tobacco smoking, alcohol consumption, *H. pylori* infection, dietary sodium intake, and family history of stomach cancer) and their joint effects on the development of SC.

To conduct this analysis, we applied multiple unconditional logistic regression models with adjustment for covariates listed above. For example, we added a product term of two main factors, e.g., SFAs × *H. pylori*, in the model with both main factors plus potential confounding factors, to assess the interaction between SFAs and *H. pylori* infection on the multiplicative scale. Also, we calculated the relative excess risk for interaction (RERI) as a measure of additive interaction: OR_{11}- OR_{10}- OR_{01} + 1, where OR_{11}, OR_{10}, and OR_{01} respectively represented the joint effect of SFAs and *H. pylori* infection, the main effect of dietary SFAs, and the main effect of *H. pylori* infection.

Mediation Analysis: 2-Way Natural Decomposition

We assumed that dietary intakes of fatty acids, cholesterol, and flavonoids influence the effects of the modifiable risk factors (tobacco smoking, alcohol drinking, *H. pylori* infection, and dietary sodium intake) on stomach cancer in this population-based case-control study. Stomach cancer can be attributed to the dietary exposures and the modifiable risk factors considering the associations observed. We also invoked the stable unit treatment value assumption and assumptions of consistency, positivity, conditional exchangeability (no-uncontrolled confounding), and no selection bias and measurement errors[161].

Taking SFAs and *H. pylori* infection as an example in Figure 2.2, natural direct effect (NDE) is defined as the odds ratio for SC comparing high to low intake of SFAs while allowing *H. pylori* infection to attain the natural value under the low intake of SFAs level. Natural indirect effect (NIE) is defined as the odds ratio for SC comparing *H. pylori* infection (Positive vs. Negative) – the natural *H. pylori* infection under high SFAs versus the natural *H. pylori* infection under low SFAs intake– while setting SFAs level to be high. The total effect is equal to the product of NIE and NDE.

Binary Outcome, Binary Mediator, and Case-Control Study

Because stomach cancer is a rare disease, the odds ratio approximates the risk ratio. Therefore, the causal effects previously defined would not be biased if logistic regression is used to model the outcome. Notation: exposure A, mediator M, and outcome Y, and confounders C.

$$\text{logit}\{P(Y = 1|\, a, m, c)\} = \theta_0 + \theta_1 a + \theta_2 m + \theta_3 am + \theta'_4 c$$

We also extended the previous results to the cases in which the mediator is a dichotomous variable. The identifiability assumptions do not change, but we used a logistic model for the mediator.

$$\text{logit}\{P(M = 1|\, a, c)\} = \beta_0 + \beta_1 a + \beta_2' c$$

Additionally, the direct and indirect effects can be estimated even in case-control designs. The formulas for the effects remain the same; however, the mediator regression is run only for controls, to consider the case-control design[162]. This approach works in terms of a rare outcome Y; the distribution of M among the controls approximates the distribution in the population.

$$OR^{NDE} = exp[log\{\frac{P(Y_{aM_{a*}}=1|c)/(1-P(Y_{aM_{a*}}=1|c))}{P(Y_{a^*M_{a*}}=1|c)/(1-P(Y_{a^*M_{a*}}=1|c))}\}]$$
$$= exp[logit\{P(Y_{aM_{a^*}} = 1|c)\} - logit\{P(Y_{a^*M_{a^*}} = 1|c)\}]$$

$$OR^{NIE} = exp[log\{\frac{P(Y_{aM_a}=1|c)/(1-P(Y_{aM_a}=1|c))}{P(Y_{aM_{a*}}=1|c)/(1-P(Y_{aM_{a*}}=1|c))}\}]$$
$$= exp[logit\{P(Y_{aM_a} = 1|c)\} - logit\{P(Y_{aM_{a^*}} = 1|c)\}]$$

PROC CAUSALMED in SAS is designed to enable the investigator to easily implement mediation analysis in the presence of exposure-mediator interaction accounting for binary outcomes and binary mediators of interest[163]. The adjusted covariates for mediation analysis were the same as the covariates above.

Specific Aim 2

Dietary Recommendation Adherence Score

The dietary assessment was described in the specific aim 1 in detail. The original Chinese Healthy Eating Index (CHEI) was designed to assess the adherence to the 2016 Dietary Guidelines for the Chinese[156]. Daily food and nutrients intakes were transformed into standard portions (SP) on a density basis (per 1,000 kcal) except for added sugars, cooking oil, and alcohol[164]. Given that the amount of cooking oil was not collected in our questionnaire, we modified CHEI by including dietary fat instead of cooking oil. The original components of CHEI include 1) adequacy components (total grains, whole grains and mixed beans, tubers, total vegetables, dark vegetables, fruits, dairy, soybeans, fish and seafood, poultry, eggs, seeds and nuts), with a higher intake indicating a higher score and 2) limitation components (Red meat, sodium, added sugars, alcohol), with a higher intake representing a lower score. For each component, there were standards for the minimum point as zero and maximum points (5 or 10) in the mCHEI. Intermediate intakes were scored proportionately between zero and maximum. The total score of mCHEI with all 17 components ranged from 0 to 100, which a higher score indicated better adherence to the dietary guideline for the Chinese. Details of scoring were shown in Table 4.6.

The United States Healthy Eating Index (HEI)-2015 was designed to align with the 2015-2020

Dietary Guidelines for Americans[165]. HEI-2015 includes 13 components. The nine components, including whole grains, greens and beans, total vegetables, total fruit, whole fruit, total protein foods, seafood and plant proteins, dairy, and fatty acids, were adequacy components, and four components including refined grains, sodium, added sugars, and saturated fats were limitation components. Each of the components was scored on a density basis out of 1,000 kcal, except for fatty acids (a ratio of unsaturated to saturated fatty acids), added sugars (percentage of energy), and saturated fats (percentage of energy). The total score was between 0 (nonadherence) and 100 (optimal adherence). Details of components and scoring were listed in Table 4.7.

Statistical Analysis

First, we performed t-tests for continuous variables and chi-square tests for categorical variables, respectively. Then, the association of daily intake of each food component in mCHEI with stomach cancer was estimated. The scale was one interquartile range (IQR) based on the distribution in the controls. The association between the corresponding score of each component in HEI-2015 and stomach cancer was also added to compare with those in mCHEI. Multiple unconditional logistic regression was applied to calculate odds ratios (ORs) and their 95% confidence intervals (CIs), adjusting for potential confounding factors, including age (years), gender (male vs. female), county site, total energy intake (kcal/day) in model 1, and additionally for educational attainment (illiterate, primary, middle, high school or above), income ten years ago (yuan/year), *H. pylori* infection (yes vs. no), family history of stomach cancer (yes vs. no), tobacco smoking (yes or no and pack-years), and BMI (kg/m^2) in model 2. Furthermore, the categorical (quartiles) and continuous (per 10-point increase) analyses were carried out to estimate the associations of total scores in mCHEI and HEI-2015 with stomach cancer. Analyses were performed stratified by gender, tobacco smoking, *H.*

pylori infection, family history of stomach cancer, and BMI. Interaction effects were assessed by including terms of each binary variable and the scores of either dietary indexes (per 10-point increase), two main factors and potential confounding factors in the model 2 to explore the potential effect modification on stomach cancer.

Specific Aim 3

SNPs Selection

Fifty-seven candidate SNPs (18 SNPs from the microRNA pathway, 2 SNPs from beta-carotene metabolism pathway,19 SNPs from the stem cell pathway, and 18 SNPs from GWAS) in the JFC study was selected in Table 2.3 using the following criteria: 1) The minor allele frequencies (MAF) were at least 5% among Han Chinese; 2) The call rate was larger than 90%. 3) Hardy-Weinberg Equilibrium (HWE). For HWE, a Bonferroni-corrected p-value of 0.000521 (0.05/96 SNPs) was used as the cutoff among the control group. We also checked the linkage disequilibrium between all SNPs, and we only listed the results of rs3204145 because there was a non-random association of rs1538660 and rs3204145.

Statistical Analysis

The demographic characteristics and other risk factors between the cases and controls were analyzed using Chi-square tests for categorical variables or t-tests for continuous variables. The odds ratios and 95% CIs according to candidate SNPs were estimated using multiple unconditional logistic models when adjusting for potential confounding factors. Confounding variables in these analyses were age (years), gender (male vs. female), county (Dafeng, Ganyu), education (illiterate, primary, middle, high school or above), income 10 years ago (<1,000, 1,000-1499, 1,500-2,499,

≥2,500 yuan/year), family history of stomach cancer (yes vs. no), tobacco smoking (pack-years), alcohol intake (g ethanol/day), *H. pylori* infection (yes vs. no), and BMI (<18.5, 18.5- <24, 24- <28, ≥28 kg/m^2). Log-additive, dominant, and recessive genetic models for each SNP were performed. We implemented stratified analyses and gene-diet interaction tests (multiplicative and additive scales) by using dichotomous variables of total dietary intake of fatty acids, cholesterol, and flavonoids. For gene-diet interaction analysis, the reference group was recorded if the variant allele was preventive. Chosen dietary exposures were dichotomized by using the median values among controls as cutoff points for stratification and interaction analyses. For molecular epidemiology studies, we often suffer false positive or inflated findings from multiple comparisons or sparse data. In this study, the data augmentation approach of semi-Bayes shrinkage was applied in all analyses with null-effect prior (OR=1.00, 95% CI 0.25-4.00)[157].

One thousand one hundred sixty-nine cases and 2,470 controls have SNPs data. The only part of cases in Dafeng, Ganyu, and Chuzhou county or controls in Dafeng and Ganyu have SNPs data. We compared SC cases and the controls who had SNPs with those who did not have SNPs to see whether samples were representative of the total population being studied.

Population Stratification

Case-control studies are susceptible to potential confounding by population stratification (or admixture). A population may comprise two or more groups with distinct genetic ancestry, such as ethnic groups in the US. Therefore, population stratification may distort the relationship between a genotype of interest and specific disease because of an actual risk factor that is related to the genotype. In population stratification, race/ethnicity acts as a surrogate for the actual risk factor, which may be environmental or genetic; as such, controlling for ethnicity can reduce the confounding bias. However, the JFC study is not a multiracial population because it is composed of approximately 99.7% of Han Chinese. The bias by population stratification is not the primary consideration in our analyses.

Genetic Risk Scores

Genetic risk scores (GRS) are estimates of the cumulative contribution of genetic factors with small effects on specific diseases in individuals. GRS allows for the evaluation of contribution by multiple factors, including genetic data, environmental, and demographic information. Many methods are available to generate GRS. One method of GRS is polygenic risk scores (PRS). PRS[166] is the sum of genetic loci, typically weighted by log odds ratios using the log-additive models. All SNPs up to *p*-value threshold (0.05) in the main effect analysis were selected to compute the PRS. Another GRS is a weighted multi-genetic index (MGI)[167], which is based on the number of risk genotypes for individuals, weighted by log odds ratios from dominant models. The *p*-value threshold of all included SNPs was the same as PRS, which was less than 0.05. If the variant allele was preventive, we recoded the variant allele as the reference group to calculate the GRS. GRS was classified into low GRS (less than the median in controls) and high GRS (greater than or equal to the median in controls). Possible interactions (additive and multiplicative scales) were explored between dietary factors and GRS when adjusting for potential confounders.

All analyses were conducted using SAS, version 9.4. Differences were considered statistically significant at $p < 0.5$ unless specific indications were mentioned.

CHAPTER 3. RESULTS FOR DIETARY EXPOSURES

3.1 Demographic Characteristics

The distributions of selected demographic characteristics, behavioral variables, total energy intake, and *H. pylori* infection among stomach cancer cases (n=1,900) and controls (n=6,532) are summarized in Table 3.1. In brief, the cases and controls had similar distributions of gender, age, physical activity ten years ago and total energy intake, but differences were observed regarding the county of residence, education level, income ten years ago, body mass index (BMI), dietary sodium intake, tobacco smoking, alcohol consumption, family history of stomach cancer and *H. pylori* infection. Compared to the control group, the cases were more likely to have a lower education level, lower-income ten years ago, and lower BMI levels. The cases had a higher intake of dietary sodium and pack-year of tobacco smoking. Also, the proportion of high-risk drinking status, *H. pylori* infection, and having a family history of SC among the cases were higher than the controls.

3.2 Dietary Fatty Acids, Total Cholesterol, and Flavonoids

Table 3.2 shows the median values of dietary fatty acids, total cholesterol, and flavonoids intake among controls in this population using non-energy adjusted and energy-adjusted methods. The median intake of total fatty acids was 24.75g/day for non-energy adjusted and 36.66 g/day for energy-adjusted methods. SFAs (median, 7.14 g/day for non-adjusted vs. 10.19 g/day for energy-adjusted), MUFAs (median, 9.85 g/day for non-adjusted vs. 15.41 g/day for energy-adjusted) and PUFAs (median, 6.93 g/day for non-adjusted vs. 9.64 g/day for energy-adjusted) were primary contributors to total fatty acids. n-3 (median, 0.96 g/day for non-adjusted vs. 1.59 g/day for energy-adjusted) and n-6 PUFAs (median, 5.97 g/day for non-adjusted vs. 8.05 g/day for energy-adjusted) were primary contributors to PUFAs in this population. LA (median, 5.50 g/day for non-adjusted vs. 7.17g/day for energy-adjusted) was mainly consumed n-6 PUFAs and ALA (median, 0.93 g/day for non-adjusted vs. 1.53 g/day for energy-adjusted) was mainly consumed n-3 PUFAs. The median ratio of n-3 and n-6 PUFAs was 0.16 for the non-adjusted method and 0.20 for the adjusted method. The median of dietary cholesterol was 207.21 mg/day for the non-adjusted method and 161.49 mg/day for the energy-adjusted method. The median of total flavonoids was 48.08 mg/day for original data. The main contributors were isoflavones (15.94 mg/day for non-adjusted vs. 21.91 mg/day for energy-adjusted) and flavonols (median, 8.86 mg/day for non-adjusted vs. 1. 49 mg/day for energy-adjusted).

The associations between dietary fatty acids, total cholesterol, and the development of SC are presented in Table 3.3. A positive association between dietary intake of total cholesterol and SC was observed comparing the highest quartile to the lowest quartile in the standard logistic regression model (aOR, 1.57; 95% CI, 1.26-1.96), the energy-adjusted model (adjusted odds ratios with the residual method (rOR), 1.56; 95% CI, 1.23-1.93), the model with multiple imputations (miOR, 1.20; 95% CI, 1.09-1.33), and semi-Bayes shrinkage model (sbOR, 1.57; 95% CI, 1.29-1.97). Increased dietary intake of total cholesterol showed consistent dose-response associations with the increased odds of developing SC in the standard logistic regression model, energy-adjusted model, and model with multiple imputations. Nevertheless, there was a weak or non-linear relationship between total fatty acids and SC. Among the subtypes of dietary fatty acids, dietary SFAs were positively associated with SC (p-trend = 0.005; aOR, 1.11; 95% CI, 1.01-1.22 with 7 g/day increments as a continuous variable). Dietary MUFAs were positively associated with SC as a categorical variable, but a null association was observed as a continuous variable. We did not observe clear associations between dietary intake of PUFAs or their subtypes and stomach cancer.

The associations between dietary flavonoids and the development of SC are shown in Table 3.4. We did not find significant dose-response associations between total flavonoids and SC in the different models. Among subtypes of dietary flavonoids, increased dietary flavones showed dose-response associations with SC in the standard model and other models. The odds ratio of SC for the highest quartile of dietary flavones, when compared to the lowest quartile in the standard model, was 1.51 (95%CI, 1.21-1.89). Dietary flavanones may be inversely associated with the development of SC (aOR,0.87; 95%CI, 0.75-1.00 in the standard model), which was supported by the results from multiple imputations and semi-Bayes shrinkage methods. For dietary flavonols, flavan_3_ols, anthocyanidins, and isoflavonoids, there were no consistently significant associations with SC among different models.

As shown in Table 3.5, tea and soybean-related food were the primary sources of total flavonoids, 75.4% was from green tea, 4.3% tofu, 2.9% soybean in this population. For flavones, 38.9% was from green veggies, and 11.1% was from sweet pepper. Tangerines (75.7%) and orange (24.3%) were contributors of flavanones. 47.2% of anthocyanidins were from radish, and almost 100% of isoflavones were from soybean-related food. The associations between dietary flavonoids from different sources and SC are shown in Table 3.6. A dose-response association between total flavonoids from vegetables and SC was found in the standard model (*p*-trend=0.01; aOR,1.07; 95%CI, 1.00-1.13 with 10mg/day increase as a continuous variable). However, no significant associations were found between total flavonoids from fruits or tea and SC.

In Table 3.7, we did a sensitivity analysis to examine the associations between the same dietary exposures and SC among individuals who reported total energy intake between the upper and lower 2.5% (cases=1,907, controls=6,598). Although the analysis sample was not the same, the results from the sensitivity analysis were consistent with the leading results. Dietary SFAs, MUFAs, total cholesterol, and flavones were positively associated with the development of SC, while dietary flavanone was a protective factor for SC. A sensitivity analysis of the proxy interview is shown in Table 3.8. Consistent with the total population, the results from non-proxy participants (n=7,383) showed that total cholesterol was positively associated with the increased odds of SC in both standard and residual models. The dose-response associations of dietary SFAs and MUFAs with SC were only found in the standard model. Dietary flavanones were inversely associated with SC in the standard model. No significant association was observed between flavones and SC in both models. Among 1,049 proxy participants, 573 were SC cases and 476 were the controls. Compared with the non-proxy interview, the results from proxy interviews were inconsistent, especially for dietary flavonoids and its subtypes.

3.3 Interaction and Mediation

The interactions of dietary fatty acids, total cholesterol, flavonoids (High vs. Low) and the main risk factors (tobacco smoking, alcohol consumption, *H. pylori* infection, dietary sodium intake and family history of stomach cancer) on stomach cancer are examined in this study (Table 3.9- 3.13). After adjusting for potential confounding factors we mentioned above, we found no consistent interactions between these dietary exposures and tobacco smoking on SC in the standard and energy-adjusted models except for dietary anthocyanidins intake in Table 3.9. The ROR for the joint associations of tobacco smoking and high anthocyanidins intake on SC was statistically significant (ROR, 0.69; 95% CI, 0.54-0.90; rROR, 0.75; 95%CI, 0.58-0.97), while RERI suggested sub-additive biological interaction (RERI, -0.47; 95% CI, -0.86- -0.08; rRERI, -0.38; 95%CI, -0.74- -0.02). Similarly, we did not observe strong interactions between these dietary exposures and dietary sodium intake except for dietary isoflavonoids. The ROR for high sodium intake and high isoflavonoids intake was statistically significant (ROR, 0.63; 95% CI, 0.48-0.84; rROR, 0.73; 95% CI, 0.55-0.96) with suggested sub-additive biological interaction (RERI, -0.56; 95% CI, -0.93- -0.18; rRERI, -0.38; 95% CI, -0.73- -0.02). However, alcohol consumption (yes/no), *H. pylori* infection (positive/negative), and family history of SC (yes/no) did not appear to modify the association between dietary exposures and SC both in the standard and energy-adjusted models.

As inconsistent results between standard models and energy-adjusted models, we observed dietary SFAs interacted with tobacco smoking (ROR, 0.76; 95%CI, 0.59-0.99), alcohol consumption (ROR, 0.75; 95%CI, 0.57-0.98), and dietary sodium intake (ROR, 0.75; 95%CI, 0.57-0.99) for SC in the multiplicative scale of the standard model. Multiplicative interactions between dietary PUFAs and tobacco smoking (ROR, 0.75; 95%CI, 0.58-0.97), FAs (ROR, 0.75; 95%CI, 0.57-0.98), or n-6 PUFAs (ROR, 0.76; 95%CI, 0.58-0.99) and alcohol consumption, MUFAs (ROR, 0.70; 95%CI, 0.53-0.92) or flavones (ROR, 0.75; 95%CI, 0.57-0.99) and dietary sodium intake were also found in the standard model. Both multiplicative and additive interactions were found between dietary PUFAs and alcohol consumption (RERI, -0.36; 95%CI, -0.70- -0.01; ROR, 0.74; 95%CI, 0.56-0.96), total flavonoids and drinking alcohol (RERI, -0.33; 95%CI, -0.65- -0.02; ROR, 0.74; 95%CI, 0.56-0.97), total flavonoids and *H. pylori* infection (RERI, -0.45; 95%CI, -0.88- -0.02; ROR, 0.70; 95%CI, 0.51-0.95), FAs and dietary sodium intake (RERI, -0.46; 95%CI, -0.87- -0.04; ROR, 0.69; 95%CI, 0.52-0.92), n-6 PUFAs and dietary sodium intake (RERI, -0.41; 95%CI,

-0.80- -0.02; ROR, 0.71; 95%CI, 0.53-0.94). However, we did not find obvious interactions in the energy-adjusted model. Conversely, we found that dietary anthocyanidins interacted with dietary sodium (rRERI: 0.30; 95%CI, 0.00-0.60) in the additive scale and flavan_3_ols interacted with alcohol drinking (rROR, 0.76; 95%CI, 0.58-0.99) in the multiplicative scale of energy-adjusted model, but not in the standard model.

In Table 3.14, we observed no evidence of mediation by these risk factors on the associations between dietary fatty acids, total cholesterol, and SC, which was consistent with the results using residual methods shown in Table 3.15. However, as seen in Table 3.16, tobacco smoking mediated the associations between flavanones (8.8%, p=0.03), flavan_3_ols (59.8%, p=0.01), and SC. In the additional analysis using residual methods of Table 3.17, tobacco smoking still mediated the associations between flavanones (10.5%, p=0.03), flavan_3_ols (59.3%, p=0.01) and SC. Alcohol consumption, *H. pylori* infection, and dietary sodium intake did not have significant mediation effects between dietary flavonoids and SC.

3.4 Discussion

In this study, we have observed that higher intakes of dietary SFAs, MUFAs, and total cholesterol were associated with the development of stomach cancer. The associations were strong with a dose-response pattern. However, no apparent dose-response relationships were observed between the consumptions of total fatty acids, PUFAs and their subtypes, flavonoids and their subtypes, and SC. Also, no clear interaction was observed between dietary fatty acids, total cholesterol, flavonoids and main risk factors on SC except for tobacco smoking and anthocyanidins, and dietary sodium intake and isoflavonoids. The only SC related risk factor that mediated the associations between dietary factors and SC was tobacco smoking.

Dietary Fatty acids, Total cholesterol, and Flavonoids

Epidemiological and experimental studies have suggested that different subtypes of fatty acids appear to play some roles in the carcinogenesis and the development of stomach cancer [168]. Several case-control studies have reported that SFAs were positively associated with the development of SC[91–95], which is consistent with our results. However, other case-control studies[96–100] and one cohort study[101] reported null associations with SFAs. In this study, a high intake of dietary MUFAs showed a positive association with SC, consistent with two previous studies[91,93]. Nevertheless, the intake of vegetable oils, which is rich in oleic acid, has been inversely associated with SC in three case-control studies[97,98,169]. The conflicting findings might be associated with limited sample sizes and insufficient adjustment for potential confounding factors and might also be related to the complex composition of MUFAs. It has been suggested that the various sources of MUFAs, animal fat, and vegetable oils may differentially affect the association between MUFAs intake and SC[90].

PUFAs, which are involved in many critical biological functions, are essential nutrients for life, which cannot be produced endogenously[87]. However, very few studies have comprehensively investigated the intakes of all PUFA subtypes, n-3 and n-6 PUFAs in particular. In this study, we included most of PUFA subtypes and found, when the subtypes of PUFAs were separated, neither n-6 PUFAs (including LA and AA) nor n-3 PUFAs (including ALA, EPA, and DHA) were associated with SC. Like MUFAs, the different sources of PUFAs might be related to the inconsistent results of PUFAs on SC. Thiébaut et al. [170] reported that high consumption of alpha-linolenic acid (ALA) from fruit and vegetables was inversely associated with breast cancer, but

ALA from nut mixes and processed meat was positively related to the disease. PUFAs may also be related to carcinogenic compounds accumulated along the food chain in the primary source of dietary PUFAs[171]. In our study, we found that the consumption of fresh fish among the cases was higher than those among the controls, which might be confounded by other factors, such as rich toxins in fresh fish due to water contamination. Therefore, carefully identifying the sources of dietary fatty acids and minimizing the effects of confounding factors are necessary and essential for evaluating the association between subtypes of dietary fatty acids and SC.

Our finding suggested that a high intake of dietary cholesterol may increase the odds of stomach cancer, which is consistent with three previous case-control studies[92,94,112]. However, no significant association between dietary cholesterol and SC was found in a hospital-based case-control study in Italy (OR,1.11; 95%CI, 0.94-1.32)[102] and a population-based case-control study in Poland (OR, 0.90; 95%CI, 0.58-1.38) [113]. The reason for these inconsistent results is that most of the prior studies on dietary cholesterol with SC have been conducted in western countries, where the incidence of SC is relatively low[2]. Therefore, the power of these studies is low due to the relatively small number of stomach cancer cases, leading to inconsistent results. The mechanisms on the relationship between dietary intake of cholesterol and SC have been hypothesized. Controlled experiments in mice suggest an association between dietary cholesterol and cancer[107–110]. Hypercholesteremia, associated with high cholesterol intake, might be linked to elevated inflammatory activity, which plays a role in cancer development [172]. Jung et al. [173] also emphasized that hypercholesterolemia was a risk factor for the occurrence of gastric dysplasia. A preclinical study reported that cholesterol metabolism might play an essential role in *H. pylori* eradication[111], but we did not observe any effect modification between total dietary cholesterol and *H. pylori* on

SC. Hence, further studies are necessary to elucidate the influence of dietary cholesterol on *H. pylori* eradication therapy.

No clear association between total dietary flavonoids and the development of SC was found in this study. A recent meta-analysis on the association between dietary flavonoid intake and the risk of digestive tract cancers observed that there was no significant association between flavonoid intake and SC (OR, 0.88; 95% CI, 0.74-1.04)[174], which was supported our finding. They also suggested that higher dietary flavonoid intake might decrease the risk of SC in the European population, but not in America or Asia[174]. The potential reasons for different findings in different populations may include the various sources of flavonoids, diversity of dietary culture in storage, and preparation of food, particularly vegetables. For instance, we found a positive association between flavones intake and SC in this study. However, Zamora-Ros et al. [135]. observed a significant inverse association between flavones intake and SC risk among women in the European Prospective Investigation into Cancer and Nutrition (EPIC) study (HR, 0.88; 95%CI, 0.78-0.99 as a continuous variable). Diverse dietary culture may explain the district findings of this association. The primary sources of flavones in our population were vegetables, green veggies, and sweet pepper. The storage and preparation of food are various in different geographic locations. The common cooking style of vegetables in our population was braising and decocting, which was different from the cooking style of European countries. Therefore, the complexity of dietary flavonoids due to diverse diet culture needs to be investigated in further research. Additionally, we found that high flavanones intake is inversely related to the development of SC, which was confirmed in a Greek case-control study[132]. The primary source of dietary flavanones in our population was citrus fruits. A pooled analysis observed an inverse association between citrus fruit intake and SC, especially in people from low socio-economic status and in studies from Asia[175]. In the experimental studies, the mechanism of the potential protective effect is that flavanones may inhibit human gastric cancer cell proliferation, migration, and invasion[176,177].

Interaction and Mediation

Experimental and epidemiological evidence indicates that stomach cancer is the result of a long multistep and multifactorial process involving an interaction between *H. pylori* infection, environmental, and genetic factors[178]. However, when we assessed the interaction of dietary fatty acids with tobacco smoking, alcohol consumption, *H. pylori* infection, dietary sodium intake, and family history of stomach cancer for the disease, no consistent interactions were identified in the standard models and residual models. The power in the present study to perform such analysis was limited. The only published paper on the effect modification of fatty acids by smoking, alcohol, and BMI in the U.S. population[101] concluded that there was no apparent effect modification of dietary fatty acids intake by tobacco smoking and alcohol drinking on the development of the disease, which is consistent with our results. Like dietary fatty acids, no statistically significant interactions between these known risk factors and the intake of total cholesterol from dietary sources were found.

As mentioned above, the results of the associations between dietary flavonoids and SC in the epidemiologic studies have been inconsistent. Moreover, the literature on this issue is scarce and fails to identify a standard mechanism for interactions between dietary flavonoids and established risk factors on stomach cancer. Tobacco smoking, primarily responsible for oxidative stress in smokers, seems to be a moderate risk factor for SC[29]. In the EPIC cohort, total dietary flavonoid intake was inversely associated with SC risk in female ever-smokers but not in never-smokers, although no heterogeneity was found[135]. In a Swedish study, dietary quercetin intake was associated with a decreased SC risk in female smokers but not in female nonsmokers or male smokers [179]. These results suggest that the potential antioxidant properties of dietary flavonoids, which are attributed to their ability to modulate antioxidant pathways[180]. However, this observation has not been confirmed in this study; only dietary anthocyanidins negatively interacted with tobacco smoking in relation to SC. In addition to their potential effects on tobacco smoking, flavonoids might also prevent alcohol consumption from stomach cancer via oxidative damage of the gastric mucosa[181]. However, we did not observe interactions between dietary flavonoids and alcohol consumption on SC, which needs more evidence in future studies.

As for the interactions between dietary sodium intake and flavonoids, we observed significant sub-additive and multiplicative interactions between dietary sodium intake and isoflavonoids in the development of stomach cancer. This finding was supported by a recent meta-analysis reported that a high intake of fermented soy foods was associated with increased stomach cancer risk[182]. The result is biologically plausible, because soy is leading plant food that provides isoflavones, and fermented soy has large amounts of salt during preparation or fermentation in Asian counties. Although salt is not a carcinogen, experimental studies found that salt improves *H. pylori* colonization in the stomach and increases atrophic gastritis through inducing DNA synthesis and cell proliferation, leading to SC[21,183]. The interactions between *H. pylori* infection, family history of SC and dietary flavonoids could not be statistically confirmed in our study. The further exploration of complex interactions between genetic, metabolic, and microorganism that will inform our knowledge of the diet-cancer relationships.

To our knowledge, no previous epidemiological studies systematically evaluated whether established risk factors mediate the associations between dietary factors and stomach cancer. We applied mediation analysis to delineate the causal effects of dietary factors (fatty acids, total cholesterol, and flavonoids) by investigating variables on the causal pathway (tobacco smoking, alcohol consumption, *H. pylori* infection, and dietary sodium intake) that may be amenable to interventions. For instance, we found a 59.8% mediation effect in the association between dietary flavan_3_ols and SC due to tobacco smoking. The proportion of mediation effect by the residual method was 59.3%. If tobacco smoking were equalized, the proportion of dietary flavan_3_ols difference in SC would be eliminated. Additionally, 8.8% (10.5% in residual method) mediation effect observed in the association between dietary flavones and SC through tobacco smoking. Tobacco smoking among participants with high dietary intake of flavones is associated with about 8.8% increase in the odds ratio for the development of SC between participants with high and low dietary intake of flavones.

Dietary flavonoids have been considered as possible mediators of the beneficial effect of vegetables and fruit against cancer through antioxidant, anti-inflammatory, anti-proliferative activities, inhibition of bio-activating enzymes, and induction of detoxifying enzymes [184,185]. However, flavan_3_ols, which derived from the consumption of tea, were positively associated with SC on the NIE by tobacco smoking in this study. Although there is no precise biological mechanism for this mediation effect, the possible explanation is that the Chinese population drinks hot tea rather than cold tea, which leads to cellular damage to the upper digestive tract and therefore makes it more susceptible to carcinogenesis. A case-control study in Iran reported drinking strong and hot tea (OR = 2.64 and 2.85, respectively) were associated with SC[186]. In our study, the proportion of drinking hot tea was higher in stomach cancer cases relative to the controls (39.1% vs. 25.6%). The mediation effects explained by tobacco smoking can be related to the different effects of various food components or different potential risk factors. Similar consideration also holds for flavones, whose intake is derived from vegetables. Flavones are heat stable, but Chinese cooking style is easier to lose flavones from vegetables[187]. Alternatively, the bioavailability of dietary flavonoids is highly variable between individuals, which contributed to the different results in observation studies[188].

CHAPTER 4. RESULTS FOR INDEX-BASED DIETARY PATTERNS

4.1 Characteristics of Study Participants

The characteristics of stomach cancer cases and the controls are presented in Table 4.1. We included 1,327 stomach cancer cases and 6,056 controls in the analytic sample. There are 316 cases and 1,487 controls excluded from the analysis due to incomplete food frequency questionnaires (FFQs); total energy intake was less than 500 or more than 5,000 calories per day, or food items were less than four. Another 573 cases and 467 controls were excluded because their FFQs were obtained in proxy interviews, which suffer from substantial measurement errors. Compared to the controls, a high proportion of stomach cancer cases were men, less educated, and lower income. The daily energy intake was higher, and BMI was lower in the cases compared with those in the controls. Pack years of tobacco smoking, the proportion of family history of stomach cancer, and *H. pylori* infection were higher in the SC cases than in the controls.

4.2 Index-Based Dietary Patterns and Stomach Cancer

The daily intakes of specific food components in mCHEI for cases and controls are presented in Table 4.2. The stomach cancer cases had lower intakes of tubers (p<0.001), fruits (p=0.004) compared to the controls. In contrast, intakes of fish and seafood (p<0.001), red meat (p<0.001), sodium (p=0.007), alcohol (p<0.001) and fat (p<0.001) were significantly higher in the cases compared to the controls. Table 4.2 also lists the adjusted ORs and 95%CIs for the associations between stomach cancer and the daily intake of each food component in mCHEI. Intakes of fruits (OR, 0.93; 95%CI, 0.88-0.98) and poultry (OR, 0.97; 95%CI, 0.94-0.997) were inversely associated with stomach cancer, while intakes of sodium (OR, 1.06; 95%CI, 1.02-1.12) and alcohol (OR, 1.10; 95%CI, 1.04-1.16) were positively associated with the odds of stomach cancer in model

1 when adjusting for age, gender, county, and total energy intake. When adjusting for additional covariates in model 2, including tobacco smoking, pack-years of smoking, *H. pylori* infection, family history of stomach cancer, body mass index, education level, and income ten years ago, the point estimates of intakes of fruits, poultry, sodium, and alcohol changed slightly, however, the confidence intervals included null value, except sodium intake (OR, 1.08; 95%CI, 1.02-1.14). I addition, the intake of eggs showed an association with stomach cancer (OR, 1.09; 95%CI, 1.02-1.16) in model 2.

Table 4.3 summarizes the adjusted ORs and 95%CIs for the associations of stomach cancer with the scores of each food component in the mCHEI as well as HEI-2015. A higher score of sodium, reflecting less intake per day, was a protective factor associated with stomach cancer in both mCHEI and HEI-2015 (OR, 0.95; 95%CI, 0.91-0.99 for mCHEI; OR, 0.97; 95%CI, 0.94-0.99 for HEI-2015). In mCHEI, scores of tubers and alcohol were negatively associated with stomach cancer in model 1, while scores of whole grains and mixed beans (OR, 1.11; 95%CI, 1.02-1.22) and eggs (OR, 1.08; 95%CI, 1.02-1.13) were positively associated with stomach cancer in model 2. No obvious relationship between the remaining components of mCHEI or HEI-2015 and stomach cancer was observed.

Table 4.4 shows the relations between stomach cancer and the total scores of mCHEI and HEI-2015 as continuous variables. Better adherence to mCHEI (*p*-trend = 0.001; OR, 0.83; 95%CI, 0.77-0.90 with a 10-point increase as a continuous variable) was inversely associated with elevated odds of stomach cancer in the crude model. After adjustment for most stomach cancer risk factors, there were null associations for HEI-2015 (*p*-trend = 0.98; OR, 0.98; 95% CI, 0.87-1.10 with a 10-

point increase) and mCHEI (*p*-trend =0.22; OR, 1.05; 95% CI, 0.94-1.17 with a 10-point increase) in relation to the odds of stomach cancer. However, our data suggest that the relationship between stomach cancer and index-based dietary patterns were modified by BMI (*p* for interaction= 0.02 for mCHEI). No clear interactions were observed between index-based dietary pattern and gender, tobacco smoking, *H. pylori* infection, and family history of stomach cancer.

4.3 Discussion

In this large population-based case-control study, there was no observed association of total scores of adherence to mCHEI and HEI-2015 with stomach cancer, which is consistent with a study in the United States[144]. However, our data point out that better adherence to mCHEI and HEI-2015 on dietary sodium component was inversely associated with the odds of stomach cancer. It is worth noting that the associations of mCHEI with stomach cancer were modified by body mass index.

So far, few studies investigated the relationship between dietary adherence and stomach cancer, generated inconsistent results. In the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study, a relative MED adherence was associated with a significant reduction in stomach cancer risk (Hazard ratio (HR), 0.95; 95% CI, 0.91-0.99 with 1-unit increase). Similarly, an inverse association of alternate MED without alcohol with the risk of stomach cancer has been reported among men (*p* for trend: 0.019 for cardia, 0.016 for non-cardia) in the Netherlands Cohort Study (NLCS)[147]. Case-control studies also found that MED adherence was associated with reduced odds of stomach cancer[149–151]. However, similar to our findings, in the National Institutes of Health-AARP Diet and Health (NIH-AARP) study—a large U.S. prospective cohort study—HEI-2005 and alternate MED scores were not significantly associated with the risk of stomach cancer (Highest vs. lowest quintile HR, 0.92; 95%CI, 0.67-1.27 for cardia; HR, 0.88; 95%CI, 0.65-1.20 for non-cardia)[144]. Although the reason for the null association is unclear, the possible reason was that mCHEI and HEI-2015 were not explicitly designed to assess the development of stomach cancer. Some components in these dietary indexes may be null or even adverse association with the development of stomach cancer. Furthermore, HEI-2015 was designed to comply with the 2015-2020 Dietary Guidelines for Americans. Given improving the predictive capacity of these two dietary indexes associated with stomach cancer, we could further revise the dietary indexes by modifying food groups and weights based on our analysis about specific food components, then apply it in different populations to test validity.

Although different methods and criteria are applied to calculate the specific component scores in the mCHEI and HEI-2015, they both recommend a lower intake of dietary sodium, which was inversely associated with stomach cancer. Previous studies have reported that dietary salt intake was monotonically linked with an increased risk of stomach cancer in prospective studies[19]. Compared with HEI-2015, mCHEI was more sensitive to identify specific food components associated with stomach cancer in the Chinese population because it contains food items much more closely related to the common Chinese diet. Some components, such as a high intake of fruits, tubers, or poultry, and a low intake of red meat or alcohol, showed inverse associations with stomach cancer. However, other components showed adverse associations with stomach cancer. For example, a high intake of whole grains and mixed beans in mCHEI seems to increase the odds of stomach cancer. One reason for this finding may be due to the combination of grains and beans into one component, which makes it difficult to estimate the overall association. A high intake of eggs was also linked with the increased odds of stomach cancer. Of the foods most typical of the

Chinese diet, eggs contain high cholesterol. We previously reported a dose-response association between dietary cholesterol and stomach cancer[1], which might explain this relationship. Nevertheless, these results should be explained with caution, and further studies need to be carried out.

In the stratification analyses, we found that the associations between mCHEI and stomach cancer were modified by body mass index, which suggested that adherence to Chinese dietary guidelines was more beneficial for individuals with normal BMI compared to those with higher BMI. This observation is biologically plausible. However, we did not find other obvious interactions. We found that both the cases and controls with the highest quartile of mCHEI had the lowest proportion of tobacco smoking, alcohol consumption, and family history of stomach cancer (data not shown). Hence, the reason was probably due to a combination of various factors or limited sample size to detect the difference.

CHAPTER 5. RESULTS FOR GENE-DIET INTERACTION

5.1 Characteristics of Study Participants

In this study, a total of 788 stomach cancer cases and 2,398 controls from Dafeng and Ganyu County were included. Table 5.1 shows the general characteristics of the study participants. There were no significant differences between SC cases and controls in age and gender. However, the cases had a lower education level and lower income ten years ago than controls. The proportion of underweight (body mass index is less than 18.5 kg/m^2) was higher among the cases than controls. Tobacco smoking, measured as pack-years, was higher among the cases. The proportion of heavy alcohol consumption, based on ethanol amount in grams per day, was significantly higher among the cases than the controls. The cases were more likely to have a family history of stomach cancer than the controls (11.3% vs. 8.6%). The missing of *H. pylori* infection was higher among the cases than the controls (14.5% vs. 3.1%). Attrition analysis found no statistical differences in demographics between those included (n=3,186) and those who were excluded (n=7,049) except for income ten years ago, body mass index, tobacco smoking, alcohol consumption, and *H. pylori* infection, shown in Table 5.2.

5.2 Genetic Polymorphisms and Stomach Cancer

Table 5.3 presents the associations between 57 candidate SNPs and stomach cancer by performing four genetic effect models with corresponding adjusted and semi-Bayes adjusted ORs and their 95% CIs. We found that *WWOX* rs12828 (recessive) and *Gemin3* rs197412 (recessive) in the micro RNA pathway, *miR-300* rs12894467 (dominant) and *IKBKAP* rs2230793 (recessive) in the NF-κB pathway, *PLCE1* rs2274223 (dominant), *CHEK2* rs738722 (recessive), and *SEMA5B* rs9868873 (recessive) in GWAS, and *R267S* rs12934922 in Beta-carotene metabolism-related pathway (recessive) were positively associated with SC, while *E2F2* rs2075993 in the micro RNA pathway (dominant), *HEY2* rs3734637 (recessive) and *WNT8A* rs4835761 (dominant) in the stem cell pathway, *TERT* rs2736100 (dominant), and *FTO* rs8050136 (recessive) in GWAS were negatively associated with SC.

5.3 SNPs and Dietary Fatty Acids

The stratified associations of selected SNPs with the development of stomach cancer by dietary intake of total fatty acids are summarized in Table 5.4-5.7. In the stem cell pathway, associations were found for *Rex1* rs6815391 (aOR for log-additive, 1.25; 95%CI, 1.00-1.55; sbOR for log-additive, 1.24; 95%CI, 1.01-1.53), *IKBKAP* rs2230793 (aOR for recessive, 1.85; 95%CI, 1.18-2.89; sbOR for recessive, 1.60; 95%CI, 1.06-2.41) among those with low fatty acids intake. Among those with high fatty acids intake, *miR-300* rs12894467 was associated with SC (aOR for log-additive, 1.47; 95%CI, 1.17-1.84; sbOR for log-additive, 1.42; 95%CI, 1.14-1.77). In GWAS, associations were also observed for *TERT* rs2736100 (aOR for log-additive, 0.64; 95%CI, 0.51-0.81; sbOR for log-additive, 0.65; 95%CI, 0.52-0.81), *GKN2 -GKN1* rs4254535 (aOR for log-additive, 1.28; 95%CI, 1.02-1.60; sbOR for log-additive, 1.28; 95%CI, 1.03-1.59), and *CHEK2* rs738722 (aOR for log-additive, 1.37; 95%CI, 1.09-1.73; sbOR for log-additive, 1.32; 95%CI, 1.06-1.66) among low fatty acids intake. While *PLCE1* rs2274223 (aOR for log-additive, 1.31; 95%CI, 1.02-1.69; sbOR for log-additive, 1.28; 95%CI, 1.01-1.63) and *ZBTB12-C2* rs9267673 (aOR for recessive, 2.38; 95%CI, 1.22-4.66; sbOR for recessive, 1.89; 95%CI, 1.09-3.30) were associated with SC among those with high fatty acids intake. There were no associations between SNPs in the micro RNA, HIF, Beta-carotene metabolism pathway and SC in the stratified analyses.

The multiplicative and additive interactions are presented in Table 5.16. A potential interaction between *TERT* rs2736100 and dietary intake of total fatty acids on SC was observed on the multiplicative scale (ROR, 0.61; 95% CI, 0.39-0.94). Another significant interaction of *GKN2 GKN1* rs4254535 and dietary fatty acids on SC was observed on both additive and multiplicative scale (RERI, -0.67; 95% CI, -1.27- -0.07; ROR, 0.59; 95% CI, 0.39-0.90). These associations persisted even after the semi-Bayes adjustment.

5.4 SNPs and Dietary Cholesterol

Table 5.8-5.11 display the adjusted and semi-Bayes adjusted ORs by stratifying for dietary intake of total cholesterol. Among those with high intake of dietary cholesterol, associations were observed for *WWOX* rs12828 (aOR for log-additive, 1.23; 95%CI, 1.01-1.51; sbOR for log-additive, 1.23; 95%CI, 1.01-1.49), *E2F2* rs2075993 (aOR for log-additive, 0.74; 95%CI, 0.60-0.92; sbOR for log-additive, 0.75; 95%CI, 0.61-0.92), *miR-300* rs12894467 (aOR for log-additive, 1.47; 95%CI, 1.17-1.84; sbOR for log-additive, 1.45; 95%CI, 1.17-1.81), *TERT -CLPTM1L* rs4975616 (aOR for recessive, 2.43; 95%CI, 1.21-4.87; sbOR for recessive, 1.79; 95%CI, 1.01-3.19), *CHRNA3* rs8042374 (aOR for recessive, 2.11; 95%CI, 1.32-3.36; sbOR for recessive, 1.72; 95%CI, 1.13-2.62), *SEMA5B* rs9868873 (aOR for recessive, 2.97; 95%CI, 1.65-5.37; sbOR for recessive, 2.23; 95%CI, 1.34-3.70). Among those with lower intake of dietary cholesterol, associations were observed for *WNT8A* rs4835761 (aOR for dominant, 0.72; 95%CI, 0.53-0.97; sbOR for dominant, 0.73; 95%CI, 0.55-0.98), *Notch4* rs915894 (aOR for dominant, 0.67; 95%CI, 0.49-0.92; sbOR for dominant, 0.71; 95%CI, 0.53-0.96), *IKBKAP* rs2230793 (aOR for recessive, 1.61; 95%CI, 1.04-2.49; sbOR for recessive, 1.49; 95%CI, 1.00-2.23), *TERT* rs2736100 (aOR for log-additive, 0.71; 95%CI, 0.57-0.88; sbOR for log-additive, 0.71; 95%CI, 0.58-0.88), *CHEK2* rs738722 (aOR for log-additive, 1.39; 95%CI, 1.03-1.88; sbOR for log-additive, 1.34; 95%CI, 1.07-1.68). *R267S* rs12934922 in the dominate model was significantly associated with increased odds of SC among those with low cholesterol intake (aOR, 1.37; 95%CI, 1.04-1.82; sbOR, 1.36; 95%CI, 1.04-1.77), while inversely associated with SC among those with high cholesterol intake (aOR, 0.67; 95%CI, 0.47-0.96; sbOR, 0.70; 95%CI, 0.50-0.97).

In Table 5.17, we observed that dietary cholesterol interacted with *R267S* rs12934922 (ROR, 0.48; 95% CI, 0.30-0.77; RERI, -0.86; 95% CI, -1.47- -0.25), *E2F2* rs2075993 (ROR, 0.59; 95%CI, 0.39-0.91; RERI, -0.63; 95% CI, -1.21- -0.05), and *Notch4* rs915894 (ROR, 0.58; 95%CI, 0.38-0.91; RERI, -0.67; 95% CI, -1.30- -0.04) on SC in both multiplicative and additive scale of the standard models, and these interactions persisted after semi-Bayes adjustment.

5.5 SNPs and Dietary Flavonoids

In Table 5.12-5.15, we listed the stratified associations of selected SNPs with SC by dietary flavonoids with adjusted and semi-Bayes adjusted ORs and their CIs. Among those with high intake of dietary flavonoids, associations were observed for *WWOX* rs12828 (aOR for recessive, 1.59; 95%CI, 1.12-2.26; sbOR for recessive, 1.48; 95%CI, 1.06-2.05), *miR-300* rs12894467 (aOR for log-additive, 1.43; 95%CI, 1.15-1.78; sbOR for log-additive, 1.42; 95%CI, 1.15-1.76), *PLCE1* rs2274223 (aOR for log-additive, 1.34; 95%CI, 1.05-1.72; sbOR for log-additive, 1.38; 95%CI, 1.03-1.84), *TERT* rs2736100 (aOR for log-additive, 0.77; 95%CI, 0.63-0.95; sbOR for log-additive, 0.78; 95%CI, 0.64-0.96), *CHRNA3* rs8042374 (aOR for recessive, 1.93; 95%CI, 1.24-3.00; sbOR for recessive, 1.63; 95%CI, 1.09-2.44). Among those with lower intake of dietary flavonoids, associations were observed for *Gemin3* rs197412 (aOR for log-additive, 1.33; 95%CI, 1.06-1.66;

sbOR for log-additive, 1.31; 95%CI, 1.06-1.64), *HEY2* rs3734637 (aOR for recessive, 0.32; 95%CI, 0.13-0.77; sbOR for recessive, 0.50; 95%CI, 0.27-0.90), *Rex1* rs6815391 (aOR for recessive, 1.65; 95%CI, 1.08-2.52; sbOR for recessive, 1.51; 95%CI, 1.02-2.24), *IKBKAP* rs1538660 (aOR for dominant, 0.65; 95%CI, 0.48-0.89; sbOR for dominant, 0.71; 95%CI, 0.53-0.96), *IKBKAP* rs2230793 (aOR for recessive, 1.90; 95%CI, 1.18-3.07; sbOR for recessive, 1.74; 95%CI, 1.13-2.68), *IKBKAP* rs3204145 (aOR for dominant, 0.65; 95%CI, 0.48-0.89; sbOR for dominant, 0.72; 95%CI, 0.53-0.96), *TERT* rs2736100 (aOR for log-additive, 0.73; 95%CI, 0.59-0.92; sbOR for log-additive, 0.74; 95%CI, 0.60-0.92), *GKN2 -GKN1* rs4254535 (aOR for recessive, 1.84; 95%CI, 1.12-3.02; sbOR for recessive, 1.66; 95%CI, 1.07-2.60), *CHEK2* rs738722 (aOR for log-additive, 1.37; 95%CI, 1.08-1.73; sbOR for log-additive, 1.32; 95%CI, 1.05-1.67), *ZBTB12-C2* rs9267673 (aOR for recessive, 2.88; 95%CI, 1.33-6.21; sbOR for recessive, 2.05; 95%CI, 1.10-3.80).

In Table 5.18, both multiplicative and additive interactions were observed between *IKBKAP* rs1538660 and high flavonoids intake on SC (ROR, 0.58; 95% CI, 0.38-0.88, and RERI, -0.60; 95% CI, -1.12- -0.07), but the additive interactions did not remain after semi-Bayes adjustment.

5.6 Genetic Risk Scores

Thirteen SNPs associated with stomach cancer in the main effect analyses (Table 5.3) were selected to compute the PRS and weighted MGI. The associations between quartiles of PRS and weighted MGI with SC are presented in Table 5.19. There was a dose-response relationship between increased score of PRS and SC (*p*-trend <0.001). Compared to those with the lowest quartile of PRS, an adjusted OR was 2.52 (95%CI, 1.77-3.59) for those with the highest quartile of PRS. Similarly, an increased score of weighted MGI (*p*-trend <0.001) was monotonically associated with elevated odds of developing SC. A positive association between SC and highest versus lowest scores of weighted MGI was observed with an adjusted OR of 2.54 (95%CI, 1.77-3.65). However, no clear interaction was observed between genetic risk scores (PRS and weighted MGI) and dietary fatty acids, cholesterol, and flavonoids, when adjusting for potential confounders (Table 5.20).

5.7 Discussion

In this study, we found that SNPs of certain genes (*miR-300* rs12894467, *IKBKAP* rs2230793, *PLCE1* rs2274223, *R267S* rs12934922, *TERT* rs2736100, *CHEK2* rs738722, *WWOX* rs12828, *E2F2* rs2075993, *HEY2* rs3734637, *WNT8A* rs4835761, *Gemin3* rs197412, *FTO* rs8050136, and *SEMA5B* rs9868873) were associated with the development of stomach cancer. Furthermore, some interactions and heterogeneity of the associations were observed between several SNPs and dietary fatty acids, cholesterol, and flavonoids on stomach cancer.

Genetic Polymorphisms and Stomach Cancer

To our knowledge, this is the first study that observed associations between SNPs of some genes (*CHEK2* rs738722, *WWOX* rs12828, *HEY2* rs3734637, *WNT8A* rs4835761, *Gemin3* rs197412, *FTO* rs8050136, *SEMA5B* rs9868873, *R267S* rs12934922, *E2F2* rs2075993, *miR-300* rs12894467, and *IKBKAP* rs2230793) and development of SC. As for *PLCE1* rs2274223 and *TERT* rs2736100, several observational studies have investigated the associations of these two SNPs with the development of SC.

In our study, SNPs of *WWOX*, *Gemin3*, and *E2F2* in the miRNA related pathway were validated. *WWOX* is a tumor suppressor gene that maps to the common fragile site FRA16D region in chromosome 16q23.3-24.1, which was reported to be downregulated in stomach cancer and other tumors[189]. In miRNA processing, the Argonaute protein family, along with *Gemin3* and *Gemin4*, selectively bind to the guide strand to facilitate the formation of a miRNA-RNA-induced silencing complex (RISC)[190]. However, recent results of a meta-analysis of the Gemin3 rs197412 SNP showed no significant difference in cancer risk for TT relative to TC + CC[191]. The E2F2 gene encodes a member of the E2F transcription factor family, which has been investigated the prognostic significance of E2F mRNA expression in human SC[192]. This present work firstly identifies significant SNPs (*WWOX* rs12828, *Gemin3* rs197412, *E2F2* rs2075993) in miRNA related pathways and hence it would be meaningful to understand the functions and mechanisms of these SNPs in the process of the development of SC.

In the stem cell-related pathway, the Notch signaling pathway induces the expression of the HEY2 gene. Prior studies indicated that the canonical Notch signaling pathway that inhibits chief cell differentiation is frequently activated in SC[193]. WNT - β-catenin - TCF pathway seems to be a critical pathway in gastrointestinal carcinoma[194]. *WNT8B* showed 63.2% total-amino-acid identity to *WNT8A*, might play critical roles in SC through activation of this pathway[195]. To our knowledge, there is no evidence on the association of SNPs in *HEY2* and *WNT8B* with SC. Given the molecular basis for stem cell-related pathway, investigation of SNPs in stem cell-related pathway with SC merits further research.

In GWAS, *CHEK2* is a tumor suppressor gene involved in pathways such as DNA repair, cell cycle arrest, and apoptosis following DNA damage. Mutations of *CHEK2* have been identified in various types of cancer, including SC[196,197]. *FTO* is an obesity-related gene, and the *FTO* expression is associated with a variety of malignant cancers, including SC[198]. The semaphorins are a large family of guidance molecules that are involved in processes such as cell migration, axonal guidance, and axonal fasciculation[199]. Although the role of *SEMA5B* in tumors was unclear, various cancer cells express both semaphorins and their receptor, and experimental evidence shows that these signals can either promote or impede the various hallmarks of cancer[200]. *PLCE1,* which is located on chromosome 10q23, encodes a phospholipase that hydrolyzes phosphatidyl-inositol 4,5-bisphosphate to 1,2-diacylglycerol and inositol 1,4,5-trisphosphate[201]. The G allele of *PLCE1* rs2274223 was significantly correlated with the susceptibility of SC in East Asians based on the results of case-control studies and meta-analysis of these studies [49,202], consistent with our findings. *TERT* encodes the telomerase catalytic subunit, which maintains the length of telomeric DNA and chromosomal stability[203]. Two population-based studies have reported the positive association between *TERT* rs2736100 with stomach cancer[204,205].

Genetic Polymorphisms and Dietary Fatty Acids on Stomach cancer

In our stratification analysis, we found that the negative association between the G allele of *TERT* rs2736100 and SC was more pronounced among individuals with low dietary fatty acids intake. Furthermore, our formal interaction test indicated an interaction between *TERT* rs2736100 and dietary fatty acids on SC. So far, few studies have reported the gene-environment interactions on SC. The only gene-environment interaction study conducted by Zhang et al[205] reported that smokers with TG/GG of *TERT* rs2736100 increased the odds of developing SC compared to never-smokers with TT (OR, 3.12; 95%CI, 1.82-4.61). Another SNP interacted with dietary fatty acids on the development of SC in this study was *GKN2 -GKN1* rs4254535. Similarly, few studies focused on the association between this SNP and cancer. One genome-wide association study (GWAS) of lung cancer showed no correlation between rs4254535 and lung cancer[206]. As mentioned before, these two SNPs were identified by GWAS. Since 2005, GWAS have been conducted for identifying SNPs in genes and non-coding domains[207]. However, the complete mechanisms of these SNPs and combined effects with dietary factors are still needed to be explored by future studies that focus on the functions of those SNPs on cancers, including SC.

Genetic Polymorphisms and Cholesterol on Stomach cancer

Our results indicated that TT carriers of *R267S* rs12934922 would relate to the development of SC. In the stratification analysis, we observed a higher odds ratio (OR) of this SNP in relation to SC among individuals with a low intake of dietary cholesterol and lower OR in relation to SC among those with a high intake of dietary cholesterol. Thus, a gene-environment interaction has been suggested between *R267S* rs12934922 and dietary cholesterol on SC. However, the interactions of this SNP with dietary cholesterol have not been studied. Previous research found a high frequency of *R267S* rs12934922 in the human beta-carotene 15, 15'-monooxygenase 1 (BCMO1) gene, which influences the plasma carotenoid levels and retinol concentrations[69,70]. A meta-analysis study by Zhou et al[208] revealed an inverse association between the intake of β-carotene and stomach cancer. Further, we found that A allele of *E2F2* rs2075993 is associated with reduced stomach cancer among those with high intake of dietary cholesterol compared with those with low intake of dietary cholesterol; on the contrary, the A allele of *Notch4* rs915894 is associated with reduced stomach cancer among those with low intake of dietary cholesterol relative to those with high intake of dietary cholesterol. The Notch4 gene plays a vital role in promoting carcinogenesis and metastasis in SC progression[209]. Taken together, the mechanisms of these SNPs have not yet been fully elucidated, but biological plausibility suggests that the associations between these SNPs and SC that be modified by dietary cholesterol.

Genetic Polymorphisms and Dietary Flavonoids on Stomach cancer

We also found three SNPs (*IKBKAP* rs1538660, *IKBKAP* rs2230793, and *IKBKAP* rs3204145) in the Nuclear factor-kappa B pathway for their association with SC among individuals with low intake of flavonoids, while *miR-300* rs12894467 was associated with SC among individuals with high intake of flavonoids. Nuclear factor-kappa B (NF-κB) refers to a group of transcription factors that play a crucial role in inflammatory and immune responses[56]. Previous research has demonstrated that the NF-κB signaling cascade may be the central mediator of inflammation-induced carcinogenesis, including gastrointestinal malignancies[210]. *IKBKAP*, known as *ELP1*, is a gene encoding the I kappa B kinase complex-associated protein, an inhibitor of NF-κB proteins[211]. A recent study of the Chinese population found that the *NFKB1* rs3755867 was associated with the susceptibility of SC, and *NFKBIA* rs696 was associated with cardia cancer and *NFKBIA* rs2233406 was associated with non-cardia cancer[212]. However, studies on the association between *IKBKAP* and SC are limited. As for *miR-300,* it has been reported that *miR-300* up-regulation might exert some antagonistic function by targeting *p53* in SC cell proliferation[213]. Furthermore, the interaction of *IKBKAP* rs1538660 and dietary flavonoids was found. Dietary flavonoids, as potent antioxidants, have been known to play essential roles in the inactivation of transcription NF-κB mediated I kappa B kinase complex (IKK) pathways[214]. Thus, we speculated that dietary flavonoids inhibit NF-κB activation, promoting anti-tumor activities, thereby decreasing the SC risk. However, detailed functional studies are further required to explore the potential biologic mechanisms for the associations of those SNPs in the Nuclear factor-kappa B pathway and SC development that interact with dietary flavonoids.

The carcinogenesis of SC is a very complex process, and a single genetic variant is unlikely to contribute to SC development. Hence, the combination of individual genetic variants from different pathways may provide new perspectives on SC carcinogenesis. In this current study, we found that individuals in China with high genetic risk scores (measured by a polygenic risk score and weighted multi-genetic index) were at a higher likelihood of developing SC than those with low genetic risk scores, suggesting that multiple genes from different pathways contribute to the development of SC. However, we did not observe interactions between genetic risk scores and dietary factors on SC, partially owing to the limited statistical power of the interaction study.

Most SC cases are sporadic, and the development of SC appears to be attributed to a complex combination of environmental factors and the accumulation of general and specific genetic alterations[215]. Particularly, gene-diet interactions may explain the considerable variation in SC among different populations by gene-dietary factor interaction studies, and further contribute to improved predictability of SC devleopment[73].

CHAPTER 6. CONCLUSION AND PUBLIC HEALTH IMPLICATIONS

6.1 Strengths

There are several positive attributes in this study. First, it is one of the largest population-based case-control studies for stomach cancer with systematically collected environmental and genetic information in the Chinese population. A relatively large sample size of the cases and combined controls increase the precision of measurements and statistical power. Detailed databases listing the fatty acids, total cholesterol, and flavonoid values for common Chinese foods were constructed, which produced a better assessment of nutrients. Second, the method of causal mediation analysis was applied to examine dietary exposure-mediator interactions on SC. To the best of our knowledge, this is the first study to measure how much of the effect of dietary factors on SC is mediated through known risk factors. Third, our study extends prior literature by focusing on a general Chinese population to examine the association between the two newest dietary indexes, mCHEI and HEI-2015, and the development of stomach cancer. Both were designed as a continuous scoring system, which is easy to conduct statistical analyses and interpret results. The comparability of the results from these two dietary indexes supports our findings on the relationships between index-based dietary patterns and stomach cancer. Finally, this is one of the first studies to evaluate the gene-diet interactions on stomach cancer with genetic risk scores.

6.2 Limitations

Some potential limitations of the study should be addressed. For specific aim 1, although we collected dietary history one year before the diagnosis for cases and one year before the interview for controls, the cases might have already changed their dietary pattern before their diagnosis. There might still be the possibility of reverse causality between dietary factors and stomach cancer.

However, the majority of dietary fatty acids and cholesterol were from high-fat foods. These foods might potentially result in stomach upset or gastric reflex, especially in stomach cancer cases, if they had early gastric symptoms, leading to reduced intake of foods with high fatty acids and cholesterol. If reverse causality does exist, we might observe the inversed association. Based on the observed positive associations with fatty acids and cholesterol, the possibility of reverse causality may be minimal.

As with other case-control studies, measurement bias and selection bias are also potential limitations. The estimations of dietary intakes of fatty acids, total cholesterol, and flavonoids, just like measurements of other nutrients, are prone to measurement bias. The conversion of food items into related nutrients is involved, which may lead to measurement errors. To reduce measurement errors, we mainly used the China Food Composition Tables 2010 to calculate total energy intake and nutrients. For food items that contained various foods (e.g., beef and mutton), we weighted certain foods to reflect more common consumption or to reflect preparation methods in the population. We also used residual energy adjustment in the logistic regression models. The results were consistent with those in the standard logistic regression models.

In this study, the participation rates were 40% among the SC cases and 87% among the controls, which might lead to potential selection bias. The reason for the low rate is that SC cases diagnosed at advanced stages were too ill to enroll. Among the recruited cases and controls, the exclusion of participants who had missing data for diet and other covariates might result in selection bias if data are not missing completely at random. Hence, sensitivity analyses were performed to test whether excluding participants with an extreme energy intake would cause potential selection bias.

Moreover, multiple imputations were used in the dietary analyses to compare the imputed estimates against the complete case analysis. However, we did not find the inconsistent associations when results from the primary analyses were compared with sensitivity analyses. For confounding bias, we adjusted for potential confounding factors in all analyses based on prior knowledge and confounding assessment. Furthermore, our mediation analysis for estimating path specific associations of dietary factors on SC via known risk factors could be subject to uncontrolled factors induced mediator-outcome confounding.

For specific aim 2, we used the modified CHEI instead of the original index due to lacking the amount of cooking oil. When we re-calculated ORs and 95%CIs of total scores in the new CHEI (without the score of dietary fat) associated with stomach cancer in sensitivity analyses, the results were similar to our main findings. Second, the exclusion of the data obtained by proxy interviews might raise some concerns about selection bias. However, compared with non-proxy interviewers, proxy interviewers over-reported most of the food components in mCHEI, resulting in measurement errors. Also, the demographic characteristics were significantly different between the proxy and non-proxy interviewers. Third, we were unable to include subtypes of stomach cancer, which could explain the variations of our results. However, the majority of stomach cancer in China is non-cardia (or distal) stomach cancer. Further studies should focus on the evaluation of the associations by tumor location and morphology. Lastly, residual confounding is probably existing after adjusting for many covariates in our study.

For specific aim 3, first, although the study enrolled a large number of cases and controls, the subsample that had SNP data was much smaller. On the one hand, false-positive or inflated findings from multiple comparisons or sparse data using SNP data may happen. Semi-Bayes methods could provide conservative and accurate estimates. On the other hand, there were differences in the demographic and health behaviors of participants included and omitted from the analysis, which might have resulted in selection bias. Second, the effect of single SNP on SC is usually small; therefore, genetic risk scores were conducted to estimate the cumulative contribution of related SNPs on SC with different dietary factors.

6.3 Public Health Implications

The findings from this study suggest positive associations between high intakes of dietary SFAs, MUFAs, total cholesterol, and the development of stomach cancer in a large population-based case-control study in China. Our study highlights that reducing the intake of dietary sodium might prevent stomach cancer. The findings might shed some light on potential etiological roles of dietary nutrients on stomach cancer, and consequently, the possible dietary intervention could be implemented to prevent stomach cancer in the Chinese population. Additionally, a better understanding of genetic and environmental factors for stomach cancer would help to identify high-risk individuals in personalized risk prediction and intervention.

TABLES

Table 1.1. Research gaps in the literature

	SC incidence
Aim 1	
FAs, SFAs, MUFAs, PUFAs	Many
Total Cholesterol	Few
Flavonoids	Few
Nutrients→ risk factors	No
Aim 2	
Index-Based Dietary Patterns	Few
Index-Based Dietary Patterns *risk factors	Few
Aim 3	
FAs* Gene	No
Total Cholesterol * Gene	No
Flavonoids * Gene	No

Table 2.1. Data collection in Jiangsu Four Cancers Study from Zhao, et al.[153]

Categories	Contents
Demographic and socioeconomic data	Age
	Gender
	Place of birth
	Place of residence
	Household composition
	Education
	Income
Residential environment	Nearly sources of environmental pollution
	Type and size of residence
	Household ventilation
	Type of fuel used for heating and cooking
Health behaviors	Diet (FFQ)
	Tobacco smoking and passive smoking
	Alcohol drinking
	Tea drinking
	Physical activity
Medical history	
Occupational history and related exposures	Pesticides
Family history of cancer	
Reproductive history among women	Age at menarche
	Age at menopause
	History of pregnancy
	Breast-feeding practices
	Contraception
	Hormone replacement therapy

Table 2.2. Demographic characteristics of total stomach cancer cases and population controls (cases=2,216, controls=8,019)

Variables	Stomach cancer (n=2,216) n (%)	Controls (n=8,019) n (%)	*P*-value[a]
Study area			
Dafeng	644 (29.1)	2,536 (31.6)	
Ganyu	570 (25.7)	2,010 (25.1)	
Chuzhou	470 (21.2)	1,180 (14.7)	
Tongshan	532 (24.0)	2,293 (28.6)	**<0.001**
Gender			
Male	1,632 (73.7)	5,767 (71.9)	
Female	584 (26.4)	2,252 (28.1)	0.107
Age			
Mean (SD)	63.8 (11.2)	63.9 (11.4)	0.695
<50	237 (10.7)	884 (11.0)	
50-<60	473 (21.3)	1,794 (22.4)	
60-<70	745 (33.6)	2,565 (32.0)	
≥70	761 (34.3)	2,776 (34.6)	0.481
Education			
Illiterate	1,096 (49.6)	3,831 (47.8)	
Primary school	773 (34.9)	2,515 (31.4)	
Middle school	279 (12.6)	1,320 (16.5)	
High school or above	62 (2.8)	335 (4.2)	
Missing	6 (0.3)	18 (0.2)	**<0.001**
Income ten years ago (Yuan/year)			
<1,000	525 (23.7)	1,710 (21.3)	
1,000-<1,500	437 (19.7)	1,530 (19.1)	
1,500-<2,500	563 (25.4)	2,074 (25.9)	
≥2,500	630 (28.4)	2,572 (32.1)	
Missing	61 (2.8)	133 (1.7)	**0.007**
Body mass index (kg/m^2)			
<18.5	327 (14.8)	454 (5.7)	
18.5-<24	1,480 (66.8)	4,839 (60.3)	
24-<28	315 (14.2)	2,230 (27.8)	
≥28	70 (3.2)	453 (5.7)	
Missing	24 (1.0)	43 (0.5)	**<0.001**
Physical activity ten years ago			
No	1,364 (61.6)	4,723 (58.9)	
Yes	852 (38.5)	3,296 (41.1)	**0.024**
Tobacco smoking			
Never	923 (41.7)	4,292 (53.5)	
Ever	1,293 (58.3)	3,727 (46.5)	**<0.001**
Pack-years of tobacco smoking			
0	923 (41.7)	4,292 (53.5)	
1-<20	255 (11.5)	811 (10.1)	
20-<40	339 (15.3)	1,133 (14.1)	
≥40	510 (23.0)	1,241 (15.5)	
Missing	189 (8.5)	542 (6.8)	**<0.001**
Alcohol consumption			
Never	1,073 (48.4)	4,303 (53.7)	

Ever	1,143 (51.6)	3,716 (46.3)	**<0.001**
Grams ethanol/day in the 1990's[b]			
Never	1,288 (58.1)	5,054 (63.0)	
Low-risk drinking	151 (6.8)	533 (6.7)	
High-risk drinking	745 (33.6)	2,279 (28.4)	
Missing	32 (1.4)	153 (1.9)	**<0.001**
Family history of stomach cancer			
No	2,022 (91.2)	7,644 (95.3)	
Yes	194 (8.8)	375 (4.7)	**<0.001**
H. pylori infection			
Negative	377 (17.1)	1,918 (23.9)	
Positive	1,247 (56.3)	4,748 (59.2)	
Missing	592 (26.7)	1,353 (16.9)	**<0.001**

[a]: Chi-square test for the frequency and T-test for the mean; Numbers in bold face indicate statistically significant.

[b]: Low-risk drinking: men (≤ 25g ethanol/day) and women (≤ 15g ethanol/day); High-risk drinking: men (>25g ethanol/day) and women (>15g ethanol/day based on the 2016 Chinese Dietary Guide.

Table 2.3. Gene names and dbsnp numbers of 57 candidate SNPs in the JFC study

Gene	SNP	Gene	SNP	Gene	SNP
Micro RNA		**Stem Cell**		**GWAS**	
CXCL12	rs1804429	HEY1	rs1046472	RUNX1	rs2014300
IL15	rs10519613	Oct4	rs13409	PLCE1	rs2274223
WWOX	rs12828	AXIN1	rs1981492	GPC5	rs2352028
Gemin3	rs197412	DVL2	rs222851	TERT	rs2736100
Gemin4	rs7813	FZD3	rs2241802	CRPP1 -CRP	rs2808630
miR-196a2	rs11614913	Dec1	rs2269700	PLCE1	rs3781264
pre-miR-146a	rs2910164	Oct4	rs3130932	CLPTM1L	rs401681
Rbl2	rs3929	WNT2	rs3729629	GKN2 -GKN1	rs4254535
miR-26a1	rs7372209	HEY2	rs3734637	CCR4 -GLB1	rs4678680
THBS1	rs2292305	Ctbp2	rs3740535	TERT - CLPTM1L	rs4975616
Ago2	rs4961280	WNT2	rs4730775	CHEK2	rs738722
Ran	rs14035	WNT8A	rs4835761	TGM5	rs748404
CDK6	rs42031	Notch4	rs520692	IL1RAP	rs7626795
E2F2	rs2075993	Rex1	rs6815391	CHRNA3	rs8042374
DOCK4	rs3801790	HES2	rs8708	FTO	rs8050136
KRAS	rs9266	Notch4	rs915894	ZBTB12 -C2	rs9267673
IL6R	rs4072391	IKBKAP	rs2230793	HLA-DQB1- HLA-DQA2	rs9275572
CTNNB1	rs2953	miR-300	rs12894467	SEMA5B	rs9868873
BCMO1		IKBKAP	rs3204145		
R267S	rs12934922				
A379V	rs7501331				

Table 3.1. Demographic characteristics of stomach cancer and population controls in the JFC study (Cases=1,900 Controls=6,532)

Variables	Stomach cancer (n=1,900) n (%)	Controls (n=6,532) n (%)	*p*-value[a]
Study area			
Dafeng	641 (33.7)	2,508 (38.4)	
Ganyu	527 (27.7)	1,872 (28.7)	
Chuzhou	454 (23.9)	1,109 (17.0)	
Tongshan	278 (14.6)	1,043 (16.0)	**<0.001**
Gender			
Male	1,401 (73.7)	4,713 (72.2)	
Female	499 (26.3)	1,819 (27.9)	0.17
Age			
Mean (SD)	64.1 (10.8)	64.0 (11.3)	0.73
<50	185 (9.7)	699 (10.7)	
50-<60	407 (21.4)	1,450 (22.2)	
60-<70	652 (34.3)	2,109 (32.3)	
≥70	656 (34.5)	2,274 (34.8)	0.31
Education			
Illiterate	954 (50.2)	3,215 (49.2)	
Primary school	663 (34.9)	2,027 (31.0)	
Middle school	224 (11.8)	1,007 (15.4)	
High school or above	55 (2.9)	270 (4.1)	
Missing	4 (0.2)	13 (0.2)	**<0.001**
Income ten years ago (Yuan/year)			
<1,000	465 (24.5)	1,393 (21.3)	
1,000-<1,500	383 (20.2)	1,218 (18.7)	
1,500-<2,500	496 (26.1)	1,707 (26.1)	
≥2,500	502 (26.4)	2,116 (32.4)	
Missing	54 (2.8)	98 (1.5)	**<0.001**
Body mass index (kg/m2)			
<18.5	298 (15.7)	410 (6.3)	
18.5-<24	1,277 (67.2)	3,970 (60.8)	
24-<28	255 (13.4)	1,743 (26.7)	
≥28	61 (3.2)	372 (5.7)	
Missing	9 (0.5)	37 (0.6)	**<0.001**
Exercise ten years ago			
No	1,304 (68.6)	4,564 (69.9)	
Yes	596 (31.4)	1,968 (30.1)	0.3
Total energy intake (Kcal/day)			
<1549.3	433 (22.8)	1,633 (25.0)	
1549.3-<2036.8	487 (25.6)	1,633 (25.0)	
2036.8-<2624.6	468 (24.6)	1,633 (25.0)	
≥2624.6	512 (27.0)	1,633 (25.0)	0.14
Dietary sodium intake (g/day)			
<0.55	367 (19.3)	1,633 (25.0)	

0.55-<1.04	504 (26.5)	1,633 (25.0)	
1.04-<2.00	479 (25.2)	1,633 (25.0)	
≥2.00	550 (29.0)	1,633 (25.0)	**<0.001**
Tobacco smoking			
Never	734 (38.6)	3,136 (48.0)	
Ever	1,166 (61.4)	3,396 (52.0)	**<0.001**
Pack-years of tobacco smoking			
0	734 (38.6)	3,136 (48.0)	
1-<20	219 (11.5)	746 (11.4)	
20-<40	303 (16.0)	1,028 (15.7)	
≥40	477 (25.1)	1,139 (17.4)	
Missing	167 (8.8)	483 (7.4)	**<0.001**
Alcohol drinking			
Never	903 (47.5)	3,223 (49.3)	
Ever	997 (52.5)	3,309 (50.7)	**0.02**
Grams ethanol/day in the 1990's[b]			
Never	1,034 (54.4)	3,692 (56.5)	
Low-risk drinking	132 (7.0)	495 (7.6)	
High-risk drinking	705 (37.1)	2,209 (33.8)	
Missing	29 (1.5)	136 (2.1)	**0.03**
Family history of stomach cancer			
No	1,711 (90.1)	6,170 (94.5)	
Yes	189 (10.0)	362 (5.5)	**<0.001**
H. pylori infection			
Negative	332 (17.5)	1,613 (24.7)	
Positive	1,062 (55.9)	3,811 (58.3)	
Missing	506 (26.6)	1,108 (17.0)	**<0.001**

[a]: On the basis of the chi-square test for frequency and T-test for the mean; Numbers in bold face indicate statistically significant

[b]: Low-risk drinking: men (≤25g ethanol/day) and women (≤15g ethanol/day); High-risk drinking: men (>25g ethanol/day) and women (>15g ethanol/day based on the 2016 Chinese Dietary Guide.

Table 3.2. Median intakes of dietary fatty acids, total cholesterol, and flavonoids in controls (n=6,532)

Variables	Non-energy adjusted		Energy adjusted (residual methods)	
	Median	Quartile 1- Quartile 3	Median	Quartile 1- Quartile 3
Total fatty acids (g/day)	24.75	14.85 - 40.17	36.66	27.20 - 47.48
SFAs (g/day)	7.14	4.35 - 11.56	10.19	7.59 - 13.33
MUFAs (g/day)	9.85	5.57 - 16.65	15.41	11.16 - 20.56
PUFAs (g/day)	6.93	4.28 - 10.80	9.64	7.38 - 12.21
n-6 PUFAs (g/day)	5.97	3.76 - 9.14	8.05	6.20 - 10.08
LA (g/day)	5.50	3.49 - 8.35	7.17	5.58 - 9.03
AA (g/day)	0.38	0.18 - 0.78	0.73	0.51 - 1.03
n-3 PUFAs (g/day)	0.96	0.54 - 1.70	1.59	1.16 - 2.12
ALA (g/day)	0.93	0.52 - 1.64	1.53	1.13 - 2.05
EPA (mg/day)	10.47	4.30 - 21.77	19.06	12.47 - 27.42
DHA (mg/day)	9.97	2.52 - 24.49	25.96	17.52 - 37.34
n-3/n-6 PUFAs ratio	0.16	0.13 - 0.20	0.20	0.18 - 0.22
Total fat (g/day)	31.07	18.84-48.98	43.39	31.67-57.20
Total cholesterol (mg/day)	207.21	107.24-352.09	161.49	65.98-298.38
Total flavonoids (mg/day)	48.08	24.19 - 133.40	-137.61	-156.71 - -63.59
Flavonols (mg/day)	8.86	4.26 - 18.50	1.49	-2.23 - 9.93
Flavones (mg/day)	3.50	2.00 - 5.74	2.92	1.53 - 4.75
Flavanones (mg/day)	0	0 - 0.38	0.63	0.36 - 0.90
Flavan_3_ols (mg/day)	4.50	1.73 - 53.30	-176.59	-179.73 - -127.80
Anthocyanidins (mg/day)	3.13	1.43 - 6.28	2.85	1.06 - 5.70
Isoflavones (mg/day)	15.94	7.52 - 28.31	21.91	14.29 - 31.39

Notes: SFAs: Saturated fatty acids; MUFAs: Monounsaturated fatty acids; PUFAs: Polyunsaturated fatty acids; n-6 PUFAs: including LA and AA; LA: Linoleic acid; AA: Arachidonic acid; n-3 PUFAs: including ALA, EPA and DHA; ALA: α-linolenic acid; EPA: Eicosapentaenoic acid; DHA: Docosahexaenoic acid.

Table 3.3. The associations between daily fatty acids or total cholesterol intake and stomach cancer (Cases=1,900, Controls=6,532)

Variables	Ca/Co	aOR (95%CI)[a]	rOR (95%CI)[a]	miOR (95%CI)[a]	sbOR(95%CI)[a]
Total fatty acids (g/day)					
Q1 (<14.85)	356/1,633	1.00	1.00	1.00	1.00
Q2 (14.85-<24.75)	431/1,633	**1.28 (1.04, 1.59)**	1.20 (0.98, 1.47)	0.95 (0.86, 1.05)	**1.24 (1.01, 1.52)**
Q3 (24.75-<40.17)	581/1,633	**1.58 (1.27, 1.97)**	**1.39 (1.13, 1.70)**	**1.18 (1.08, 1.30)**	**1.51 (1.22, 1.87)**
Q4 (40.17+)	532/1,633	**1.44 (1.10, 1.87)**	1.18 (0.95, 1.45)	1.12 (1.00, 1.27)	**1.37 (1.06, 1.76)**
p-value for trend		**0.002**	0.082	**<0.001**	
Per 25g increase[b]		1.09 (0.99, 1.19)			
SFAs (g/day)					
Q1 (<4.35)	361/1,633	1.00	1.00	1.00	1.00
Q2 (4.35-<7.14)	438/1,633	**1.26 (1.02, 1.56)**	1.20 (0.98, 1.46)	0.95 (0.86, 1.04)	1.23 (1.00, 1.51)
Q3 (7.14-<11.56)	566/1,633	**1.48 (1.19, 1.85)**	**1.37 (1.12, 1.69)**	**1.16 (1.06, 1.26)**	**1.43 (1.16, 1.76)**
Q4 (11.56+)	535/1,633	**1.42 (1.09, 1.84)**	**1.29 (1.04, 1.59)**	1.11 (0.99, 1.24)	1.36 (1.06, 1.74)
p-value for trend		**0.005**	**0.01**	**<0.001**	
Per 7g increase[b]		**1.11 (1.01, 1.22)**			
MUFAs (g/day)					
Q1 (<5.57)	356/1,633	1.00	1.00	1.00	1.00
Q2 (5.57-<9.85)	435/1,633	1.19 (0.96, 1.47)	1.14 (0.93, 1.39)	0.95 (0.86, 1.04)	1.16 (0.95, 1.43)
Q3 (9.85-<16.65)	572/1,633	**1.50 (1.20, 1.86)**	**1.43 (1.16, 1.76)**	**1.20 (1.10, 1.31)**	**1.45 (1.18, 1.78)**
Q4 (16.65+)	537/1,633	1.41 (1.09, 1.82)	1.17 (0.95, 1.45)	1.10 (0.99, 1.23)	1.35 (1.06, 1.72)
p-value for trend		**0.002**	0.05	**<0.001**	
Per 10g increase[b]		1.05 (0.97, 1.14)			
PUFAs (g/day)					
Q1 (<4.28)	365/1,633	1.00	1.00	1.00	1.00
Q2 (4.28-<6.93)	461/1,633	1.21 (0.98, 1.50)	1.17 (0.96, 1.43)	1.00 (0.90, 1.10)	1.13 (0.92, 1.39)
Q3 (6.93-<10.80)	560/1,633	1.47 (1.17, 1.85)	1.20 (0.97, 1.47)	1.14 (1.04, 1.26)	**1.40 (1.13, 1.74)**
Q4 (10.80+)	514/1,633	1.16 (0.88, 1.52)	1.15 (0.93, 1.41)	1.03 (0.92, 1.16)	1.08 (0.83, 1.41)
p-value for trend		0.16	0.23	0.03	
Per 6g increase[b]		1.09 (0.99, 1.20)			
n-6 PUFAs (g/day)					
Q1 (<3.76)	372/1,633	1.00	1.00	1.00	1.00
Q2 (3.76-<5.97)	470/1,633	1.23 (1.00, 1.52)	1.14 (0.94, 1.39)	1.01 (0.92, 1.11)	1.17 (0.95, 1.43)
Q3 (5.97-<9.14)	538/1,633	1.36 (1.08, 1.71)	1.08 (0.88, 1.32)	1.10 (1.00, 1.20)	1.31 (1.05, 1.63)
Q4 (9.14+)	520/1,633	1.18 (0.90, 1.55)	1.15 (0.94, 1.41)	1.02 (0.90, 1.16)	1.12 (0.86, 1.45)
p-value for trend		0.21	0.28	0.15	
Per 5g increase[b]		1.10 (1.00, 1.21)			
LA (g/day)					
Q1 (<3.49)	380/1,633	1.00	1.00	1.00	1.00

Q2 (3.49-<5.50)	474/1,633	1.25 (1.01, 1.54)	1.14 (0.94, 1.39)	1.02 (0.93, 1.12)	1.20 (0.98, 1.47)
Q3 (5.50-<8.35)	522/1,633	1.26 (1.00, 1.58)	1.06 (0.86, 1.31)	1.06 (0.97, 1.17)	1.22 (0.98, 1.52)
Q4 (8.35+)	524/1,633	1.18 (0.90, 1.55)	1.14 (0.93, 1.40)	1.03 (0.91, 1.16)	1.13 (0.87, 1.46)
p-value for trend		0.31	0.32	0.22	
Per 5g increase[b]		**1.11 (1.00, 1.23)**			
AA (g/day)					
Q1 (<0.18)	394/1,633	1.00	1.00	1.00	1.00
Q2 (0.18-<0.38)	438/1,633	1.12 (0.91, 1.38)	1.08 (0.88, 1.32)	0.97 (0.87, 1.07)	1.09 (0.89, 1.33)
Q3 (0.38-<0.78)	553/1,633	**1.26 (1.03, 1.56)**	**1.26 (1.03, 1.56)**	**1.14 (1.04, 1.25)**	**1.22 (1.00, 1.49)**
Q4 (0.78+)	515/1,633	1.20 (0.95, 1.52)	1.05 (0.86, 1.30)	1.01 (0.91, 1.13)	1.13 (0.90, 1.42)
p-value for trend		0.08	0.4	0.08	
Per 1g increase[b]		1.01 (0.90, 1.14)			
n-3 PUFAs (g/day)					
Q1 (<0.54)	378/1,633	1.00	1.00	1.00	1.00
Q2 (0.54-<0.96)	417/1,633	1.11 (0.90, 1.37)	1.17 (0.95, 1.43)	0.92 (0.84, 1.02)	1.04 (0.85, 1.28)
Q3 (0.96-<1.70)	595/1,633	**1.48 (1.19, 1.84)**	**1.31 (1.07, 1.61)**	**1.24 (1.13, 1.35)**	**1.39 (1.13, 1.72)**
Q4 (1.70+)	510/1,633	1.18 (0.92, 1.53)	1.10 (0.89, 1.35)	1.00 (0.89, 1.13)	1.10 (0.86, 1.40)
p-value for trend		0.05	0.29	0.01	
Per 1g increase[b]		1.04 (0.96, 1.13)			
ALA (g/day)					
Q1 (<0.52)	380/1,633	1.00	1.00	1.00	1.00
Q2 (0.52-<0.93)	420/1,633	1.10 (0.89, 1.35)	1.14 (0.93, 1.40)	0.93 (0.85, 1.03)	1.05 (0.86, 1.29)
Q3 (0.93-<1.64)	589/1,633	**1.46 (1.18, 1.82)**	**1.30 (1.06, 1.60)**	**1.23 (1.12, 1.34)**	**1.40 (1.13, 1.72)**
Q4 (1.64+)	511/1,633	1.17 (0.91, 1.50)	1.07 (0.87, 1.32)	1.00 (0.89, 1.11)	1.10 (0.86, 1.40)
p-value for trend		0.06	0.36	**0.02**	
Per 1g increase[b]		1.04 (0.96, 1.13)			
EPA (mg/day)					
Q1 (<4.30)	398/1,633	1.00	1.00	1.00	1.00
Q2 (4.30-<10.47)	503/1,633	1.20 (0.98, 1.48)	0.94 (0.77, 1.14)	1.04 (0.95, 1.14)	1.20 (0.99, 1.46)
Q3 (10.47-<21.77)	450/1,633	1.10 (0.88, 1.37)	0.99 (0.80, 1.22)	0.98 (0.89, 1.07)	1.07 (0.87, 1.32)
Q4 (21.77+)	549/1,633	1.18 (0.93, 1.49)	1.09 (0.89, 1.33)	1.12 (1.01, 1.24)	1.15 (0.92, 1.44)
p-value for trend		0.37	0.32	**0.02**	
Per 20mg increase[b]		1.00 (0.96, 1.03)			
DHA (mg/day)					
Q1 (<2.52)	423/1,633	1.00	1.00	1.00	1.00
Q2 (2.52-<9.97)	448/1,633	1.13 (0.91, 1.39)	0.85 (0.70, 1.05)	0.92 (0.84, 1.01)	1.10 (0.90, 1.34)
Q3 (9.97-<24.49)	443/1,633	1.02 (0.81, 1.29)	0.83 (0.67, 1.03)	0.99 (0.90, 1.08)	0.99 (0.80, 1.24)
Q4 (24.49+)	586/1,633	1.35 (1.06, 1.72)	1.14 (0.93, 1.40)	1.23 (1.11, 1.37)	1.30 (1.03, 1.65)
p-value for trend		**0.03**	0.14	**<0.001**	

Per 20mg increase[b]		**1.04 (1.01, 1.08)**			
n-3/n-6 PUFAs					
Q1 (<0.13)	406/1,633	1.00	1.00	1.00	1.00
Q2 (0.13-<0.16)	449/1,633	1.00 (0.82, 1.23)	0.88 (0.72, 1.08)	0.97 (0.89, 1.07)	0.97 (0.80, 1.18)
Q3 (0.16-<0.20)	535/1,633	1.28 (1.05, 1.56)	1.11 (0.90, 1.34)	1.11 (1.01, 1.21)	1.24 (1.02, 1.49)
Q4 (0.20+)	510/1,633	1.13 (0.92, 1.39)	1.09 (0.90, 1.32)	1.03 (0.94, 1.14)	1.08 (0.88, 1.31)
p-value for trend		0.07	0.14	0.05	
Per 0.1 increase[b]		1.12 (0.98, 1.27)			
Total fat (g/day)					
Q1 (<18.84)	355/1,633	1.00	1.00	1.00	1.00
Q2 (18.84-<31.07)	463/1,633	1.31 (1.06, 1.61)	1.17 (0.96, 1.43)	1.01 (0.92, 1.11)	1.28 (1.05, 1.56)
Q3 (31.07-<48.98)	557/1,633	**1.43 (1.15, 1.78)**	**1.31 (1.06, 1.61)**	**1.14 (1.04, 1.25)**	**1.38 (1.12, 1.70)**
Q4 (48.98+)	525/1,633	1.30 (1.00, 1.69)	1.10 (0.89, 1.38)	1.05 (0.94, 1.18)	1.25 (0.98, 1.61)
p-value for trend		**0.04**	0.28	0.007	
Per 30g increase[b]		1.04 (0.95, 1.15)			
Total cholesterol (mg/day)					
Q1 (<107.24)	407/1,633	1.00	1.00	1.00	1.00
Q2 (107.24-<207.21)	429/1,633	1.06 (0.87, 1.29)	1.17 (0.96, 1.42)	0.89 (0.81, 0.98)	1.06 (0.87, 1.28)
Q3 (207.21-<352.09)	498/1,633	1.32 (1.08, 1.61)	1.45 (1.18, 1.77)	1.04 (0.94, 1.14)	1.29 (1.06, 1.57)
Q4 (352.09+)	566/1,633	**1.57 (1.26, 1.96)**	**1.56 (1.27, 1.93)**	**1.20 (1.09, 1.33)**	**1.59 (1.29, 1.97)**
p-value for trend		**<0.001**	**<0.001**	**<0.001**	
Per 250mg increase[b]		**1.13 (1.06, 1.22)**			

Notes: aOR: adjusted odds ratios; rOR: adjusted odds ratios with residual methods; miOR: adjusted odds ratios using multiple imputations; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; SFAs: Saturated fatty acids; MUFAs: Monounsaturated Fatty acids; PUFAs: Polyunsaturated fatty acids; n-6 PUFAs: including LA and AA; LA: Linoleic acid; AA: Arachidonic acid; n-3 PUFAs: including ALA, EPA and DHA; ALA: α-linolenic acid; EPA: Eicosapentaenoic acid; DHA: Docosahexaenoic acid; Ca/Co: Cases/Controls; Numbers in bold face indicate statistically significant.

[a]: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income 10 years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28), exercise 10 years ago (yes/no), dietary sodium intake (quartile level of raw data for aOR and energy-adjusted for rOR) and total energy intake (continuous, Kcal/day).

[b]: The rescaling units for the continuous were chosen based on the interquartile range (IQR) of controls and feasible intervention ranges.

Table 3.4. The associations between daily flavonoids intake and stomach cancer (Cases=1,900, Controls=6,532)

Variables	Ca /Co	aOR (95%CI)[a]	rOR (95%CI)[a]	miOR (95%CI)[a]	sbOR(95%CI)[a]
Total flavonoids (mg/day)					
Q1 (<24.19)	381/1,633	1.00	1.00	1.00	1.00
Q2 (24.19-<48.08)	525/1,633	**1.29 (1.05, 1.57)**	1.11 (0.91, 1.35)	1.10 (1.01, 1.21)	**1.29 (1.06, 1.57)**
Q3 (48.08-<133.40)	536/1,633	1.19 (0.96, 1.49)	**1.24 (1.02, 1.51)**	1.07 (0.97, 1.17)	1.19 (0.96, 1.48)
Q4 (133.40+)	458/1,633	1.09 (0.87, 1.37)	1.04 (0.84, 1.28)	0.93 (0.84, 1.03)	1.07 (0.86, 1.34)
p-value for trend		0.78	0.44	0.92	
Per 100 mg increase[b]		1.01 (0.99, 1.03)			
Flavonols (mg/day)					
Q1 (<4.26)	365/1,633	1.00	1.00	1.00	1.00
Q2 (4.26-<8.86)	579/1,633	**1.59 (1.31, 1.93)**	**1.21 (1.00, 1.46)**	**1.18 (1.08, 1.29)**	**1.53 (1.27, 1.85)**
Q3 (8.86-<18.50)	472/1,633	1.23 (0.99, 1.53)	1.07 (0.88, 1.31)	0.99 (0.90, 1.08)	1.20 (0.98, 1.48)
Q4 (18.50+)	484/1,633	1.26 (1.00, 1.59)	1.07 (0.86, 1.32)	0.97 (0.88, 1.08)	1.20 (0.96, 1.51)
p-value for trend		0.41	0.81	0.98	
Per 15 mg increase[b]		1.04 (0.98, 1.10)			
Flavones (mg/day)					
Q1 (<2.00)	351/1,633	1.00	1.00	1.00	1.00
Q2 (2.00-<3.50)	489/1,633	**1.28 (1.05, 1.57)**	1.16 (0.96, 1.41)	1.05 (0.95, 1.16)	**1.26 (1.04, 1.53)**
Q3 (3.50-<5.74)	543/1,633	**1.37 (1.12, 1.68)**	1.21 (0.99, 1.48)	**1.10 (1.01, 1.21)**	**1.38 (1.13, 1.68)**
Q4 (5.74+)	517/1,633	**1.51 (1.21, 1.89)**	**1.38 (1.13, 1.69)**	1.05 (0.94, 1.16)	**1.47 (1.18, 1.82)**
p-value for trend		**<0.001**	**0.002**	**0.02**	
Per 5 mg increase[b]		1.08 (0.98, 1.18)			
Flavanones (mg/day)					
No	1,243/3,922	1.00		1.00	1.00
Yes	657/2,610	**0.87 (0.75, 1.00)**		**0.91 (0.86, 0.96)**	**0.87 (0.75, 1.00)**
Q1 *			1.00		
Q2			1.08 (0.88, 1.31)		
Q3			0.89 (0.71, 1.12)		
Q4			0.94 (0.76, 1.17)		
p-value for trend			0.31		
Flavan_3_ols (mg/day)					
Q1 (<1.73)	395/1,633	1.00	1.00	1.00	1.00
Q2 (1.73-<4.50)	522/1,633	**1.38 (1.13, 1.69)**	**1.32 (1.08, 1.62)**	1.08 (0.99, 1.19)	**1.40 (1.15, 1.70)**
Q3 (4.50-<53.30)	542/1,633	**1.42 (1.15, 1.76)**	**1.41 (1.13, 1.76)**	1.07 (0.97, 1.17)	1.43 (1.16, 1.75)
Q4 (53.30+)	441/1,633	1.11 (0.89, 1.39)	1.09 (0.87, 1.37)	0.92 (0.83, 1.01)	1.10 (0.89, 1.37)
p-value for trend		0.46	0.53	0.66	
Per 50 mg increase[b]		1.00 (1.00, 1.01)			
Anthocyanidins (mg/day)					

Q1 (<1.43)	441/1,633	1.00	1.00	1.00	1.00
Q2 (1.43-<3.13)	482/1,633	1.08 (0.88, 1.31)	0.93 (0.76, 1.13)	1.05 (0.93, 1.17)	1.07 (0.88, 1.29)
Q3 (3.13-<6.28)	488/1,633	1.11 (0.90, 1.37)	0.89 (0.71, 1.11)	1.00 (0.90, 1.10)	1.12 (0.91, 1.37)
Q4 (6.28+)	489/1,633	1.21 (0.96, 1.53)	1.10 (0.87, 1.38)	0.97 (0.87, 1.08)	1.21 (0.96, 1.52)
p-value for trend		0.13	0.5	0.65	
Per 5 mg increase[b]		1.07 (1.03, 1.12)			
Isoflavonoids (mg/day)					
Q1 (<7.52)	437/1,633	1.00	1.00	1.00	1.00
Q2 (7.52-<15.94)	482/1,633	1.04 (0.85, 1.27)	1.16 (0.95, 1.41)	1.01 (0.92, 1.11)	1.04 (0.86, 1.26)
Q3 (15.94-<28.31)	462/1,633	0.86 (0.69, 1.06)	0.99 (0.81, 1.22)	0.95 (0.86, 1.04)	0.85 (0.69, 1.04)
Q4 (28.31+)	519/1,633	1.06 (0.84, 1.33)	1.12 (0.92, 1.37)	1.01 (0.91, 1.13)	1.04 (0.83, 1.30)
p-value for trend		0.99	0.57	0.7	
Per 20 mg increase[b]		1.06 (0.99, 1.13)			

Notes: aOR: adjusted odds ratios; rOR: adjusted odds ratios with residual methods; miOR: adjusted odds ratios using multiple imputations; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Ca/Co: Cases/Controls; Numbers in bold face indicate statistically significant

[a]: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28), exercise ten years ago (yes/no), dietary sodium intake (quartile level of raw data for aOR and energy-adjusted for rOR) and total energy intake (continuous, Kcal/day).

b: The rescaling units for the continuous were chosen based on the interquartile range (IQR) of controls and feasible intervention ranges.

*: More than 50 % of participants' intake 0.

Table 3.5. Main sources of dietary flavonoids among controls in the JFC study

	Top five Food sources (% of subclass)
Total flavonoids	Green tea (75.4%), Tofu (4.3%), Soybean (2.9%), Dried tofu (2.8%) and Tea-Oolong (2.7%)
Flavonols	Green tea (38.9%), Green veggies (11.1%), Sweet pepper (4.7%), Onion (4.5%) and Scallion (3.8%)
Flavones	Green veggies (44.2%), Sweet pepper (11.7%), Green tea (8.4%), Chives (5.9%) and Winter melon (5.2%)
Flavanones	Tangerines (75.7%), Orange (24.3%)
Flavan_3_ols	Green tea (92.0%), Tea Oolong (3.2%), Tea black (2.4%), Soybean (1.3%) and salted veggies (0.4%)
Anthocyanidins	Radish (47.2%), salted veggies (20.1%), beans (11.4%), Grapes (8.2%) and Eggplant (6.8%)
Isoflavones	Tofu (42.5%), Dried Tofu (29.3%), Soybeans (19.0%), salted veggies (5.7%) and Soy milk (1.5%)

Table 3.6. Adjusted odds ratios of stomach cancer according to the quartiles of total dietary flavonoids from different sources

	Ca/Co	aOR (95%CI)[a]	rOR (95%CI)[a]
Total flavonoids from vegetables (mg/day)			
Q1 (<4.58)	384/1,633	1.00	1.00
Q2 (4.58-<8.24)	481/1,633	**1.24 (1.02, 1.51)**	1.20 (0.99, 1.45)
Q3 (8.24-<14.49)	575/1,633	**1.46 (1.20, 1.79)**	**1.37 (1.12, 1.67)**
Q4 (14.49+)	460/1,633	**1.28 (1.01, 1.62)**	**1.40 (1.14, 1.71)**
p-value for trend		**0.01**	**<0.001**
Per 10 mg increase[b]		**1.07 (1.00,1.13)**	
Total flavonoids from fruits (mg/day)			
Q1 (<0.84)	475/1,633	1.00	1.00
Q2 (0.84-<2.16)	477/1,633	0.93 (0.77, 1.12)	0.93 (0.76, 1.13)
Q3 (2.16-<4.94)	448/1,633	0.96 (0.79, 1.17)	1.01 (0.83, 1.24)
Q4 (4.94+)	500/1,633	1.10 (0.89, 1.35)	**1.25 (1.03, 1.53)**
p-value for trend		0.38	**0.02**
Per 5 mg increase[b]		1.02 (0.98, 1.07)	
Total flavonoids from tea (mg/day)*			
No	1,423/4,777	1.00	
Yes	477/1,755	0.88 (0.74, 1.04)	
Q1			1.00
Q2			1.23 (0.99, 1.52)
Q3			0.99 (0.74, 1.32)
Q4			0.95 (0.74, 1.22)
p-value for trend			0.26

Notes: aOR: adjusted odds ratios; rOR: adjusted odds ratios with residual methods; Ca/Co: Cases/Controls; Numbers in bold face indicate statistically significant.

[a]: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28), exercise ten years ago (yes/no), dietary sodium intake (quartile level of raw data for aOR and energy-adjusted for rOR) and total energy intake (continuous, Kcal/day).

[b]: The rescaling units for the continuous were chosen based on interquartile range (IQR) of controls and feasible intervention ranges

*: More than 50% of participants' intake 0.

Table 3.7. Associations between dietary fatty acids, total cholesterol, flavonoids and stomach cancer excluding individuals with reported total energy intake in the upper and lower 2.5% (Cases=1,907, Controls=6,598)

Variables	Ca/Co	aOR (95%CI)[a]	rOR (95%CI)[a]
Total fatty acid (g/day)			
Q1	359/1,649	1.00	1.00
Q2	428/1,650	1.16 (0.93, 1.43)	1.19 (0.97, 1.45)
Q3	589/1,650	**1.52 (1.22, 1.90)**	**1.33 (1.08, 1.63)**
Q4	531/1,649	**1.34 (1.03, 1.75)**	1.19 (0.96, 1.47)
P for trend		**0.006**	0.08
SFAs (g/day)			
Q1	358/1,649	1.00	1.00
Q2	439/1,650	**1.24 (1.00, 1.54)**	**1.25 (1.02, 1.53)**
Q3	572/1,650	**1.51 (1.20, 1.88)**	**1.35 (1.10, 1.66)**
Q4	538/1,649	**1.46 (1.12, 1.89)**	**1.27 (1.03, 1.57)**
P for trend		**0.002**	**0.02**
MUFAs (g/day)			
Q1	361/1,650	1.00	1.00
Q2	435/1,649	1.23 (0.99, 1.52)	1.21 (0.99, 1.48)
Q3	574/1,649	**1.49 (1.20, 1.85)**	**1.43 (1.16, 1.75)**
Q4	537/1,650	**1.44 (1.11, 1.85)**	1.21 (0.97, 1.49)
P for trend		**0.002**	**0.04**
PUFAs (g/day)			
Q1	375/1,650	1.00	1.00
Q2	450/1,649	1.12 (0.90, 1.39)	1.18 (0.96, 1.44)
Q3	557/1,649	**1.40 (1.11, 1.76)**	1.21 (0.99, 1.49)
Q4	525/1,650	1.17 (0.89, 1.53)	1.18 (0.96, 1.45)
P for trend		0.13	0.14
n-6 PUFAs (g/day)			
Q1	377/1,650	1.00	1.00
Q2	473/1,649	1.20 (0.97, 1.49)	1.18 (0.97, 1.44)
Q3	535/1,650	**1.31 (1.04, 1.66)**	1.10 (0.90, 1.36)
Q4	522/1,649	1.13 (0.86, 1.49)	1.16 (0.95, 1.42)
P for trend		0.35	0.27
LA (g/day)			
Q1	380/1,650	1.00	1.00
Q2	478/1,649	1.21 (0.98, 1.50)	1.17 (0.96, 1.43)
Q3	522/1,649	1.25 (0.99, 1.58)	1.08 (0.88, 1.33)
Q4	527/1,650	1.13 (0.86, 1.49)	1.17 (0.96, 1.43)
P for trend		0.45	0.24
AA (g/day)			
Q1	394/1,649	1.00	1.00
Q2	441/1,650	1.12 (0.91, 1.37)	1.15 (0.94, 1.40)
Q3	551/1,649	**1.26 (1.02, 1.55)**	**1.27 (1.03, 1.56)**
Q4	521/1,650	1.22 (0.97, 1.54)	1.11 (0.90, 1.36)
P for trend		0.06	0.27
n-3 PUFAs (g/day)			
Q1	375/1,650	1.00	1.00
Q2	423/1,649	1.15 (0.93, 1.43)	1.13 (0.93, 1.38)

Q3	593/1,650	**1.47 (1.18, 1.83)**	**1.27 (1.04, 1.56)**
Q4	516/1,649	1.25 (0.96, 1.61)	1.09 (0.89, 1.34)
P for trend		**0.03**	0.30
ALA (g/day)			
Q1	374/1,649	1.00	1.00
Q2	429/1,650	1.15 (0.93, 1.42)	1.16 (0.95, 1.42)
Q3	586/1,649	**1.47 (1.18, 1.83)**	**1.29 (1.05, 1.58)**
Q4	518/1,650	1.24 (0.96, 1.60)	1.13 (0.92, 1.38)
P for trend		**0.04**	0.21
EPA (mg/day)			
Q1	401/1,650	1.00	1.00
Q2	503/1,649	1.21 (0.99, 1.48)	0.94 (0.77, 1.15)
Q3	453/1,650	1.09 (0.87, 1.35)	0.97 (0.79, 1.20)
Q4	550/1,649	1.19 (0.94, 1.51)	1.08 (0.88, 1.32)
P for trend		0.35	0.42
DHA (mg/day)			
Q1	431/1,646	1.00	1.00
Q2	447/1,653	1.11 (0.90, 1.37)	**0.81 (0.66, 0.99)**
Q3	446/1,649	1.03 (0.82, 1.30)	**0.80 (0.64, 0.99)**
Q4	583/1,650	**1.33 (1.04, 1.69)**	1.10 (0.90, 1.35)
P for trend		**0.04**	0.23
n-3/n-6 PUFAs			
Q1	413/1,649	1.00	1.00
Q2	450/1,650	1.00 (0.81, 1.22)	0.94 (0.77, 1.14)
Q3	535/1,650	**1.28 (1.05, 1.55)**	1.21 (0.99, 1.48)
Q4	509/1,649	1.14 (0.93, 1.39)	1.10 (0.90, 1.33)
P for trend		0.05	0.10
Total fat (g/day)			
Q1	359/1,649	1.00	1.00
Q2	462/1,650	**1.31 (1.06, 1.61)**	**1.23 (1.01, 1.50)**
Q3	560/1,649	**1.43 (1.14, 1.78)**	**1.27 (1.03, 1.56)**
Q4	526/1,650	**1.32 (1.01, 1.71)**	1.12 (0.90, 1.40)
P for trend		**0.03**	0.32
Total cholesterol (mg/day)			
Q1	408/1,649	1.00	1.00
Q2	436/1,650	1.05 (0.86, 1.28)	1.16 (0.95, 1.40)
Q3	500/1,650	**1.32 (1.08, 1.61)**	**1.39 (1.14, 1.70)**
Q4	563/1,649	**1.52 (1.22, 1.90)**	**1.51 (1.23, 1.87)**
P for trend		**<0.001**	**<0.001**
Total flavonoids (mg/day)			
Q1	378/1,650	1.00	1.00
Q2	524/1,649	**1.32 (1.08, 1.62)**	1.08 (0.89, 1.31)
Q3	549/1,649	1.24 (0.99, 1.55)	**1.24 (1.02, 1.51)**
Q4	456/1,650	1.10 (0.87, 1.38)	1.02 (0.83, 1.26)
P for trend		0.76	0.49
Flavonols (mg/day)			
Q1	368/1,650	1.00	1.00
Q2	575/1,649	**1.56 (1.28, 1.90)**	**1.28 (1.05, 1.55)**
Q3	478/1,650	1.24 (1.00, 1.54)	1.09 (0.89, 1.33)
Q4	486/1,649	1.26 (1.00, 1.58)	1.10 (0.89, 1.35)

P for trend		0.38	0.74
Flavones (mg/day)			
Q1	354/1,649	1.00	1.00
Q2	491/1,650	**1.28 (1.05, 1.56)**	1.10 (0.91, 1.34)
Q3	543/1,649	**1.38 (1.12, 1.69)**	1.18 (0.97, 1.44)
Q4	519/1,650	**1.48 (1.18, 1.85)**	**1.34 (1.10, 1.64)**
P for trend		**0.001**	**0.003**
Flavanones (mg/day)*			
No	1,254/3,979	1.00	
Yes	653/2,619	**0.86 (0.74, 0.99)**	
Q1			1.00
Q2			0.99 (0.81, 1.21)
Q3			0.84 (0.67, 1.06)
Q4			0.89 (0.72, 1.10)
P for trend			0.16
Flavan_3_ols (mg/day)			
Q1	393/1,650	1.00	1.00
Q2	529/1,649	**1.43 (1.17, 1.75)**	**1.35 (1.09, 1.67)**
Q3	542/1,649	**1.43 (1.15, 1.77)**	**1.68 (1.32, 2.13)**
Q4	443/1,650	1.13 (0.91, 1.42)	1.20 (0.95, 1.51)
P for trend		0.45	0.18
Anthocyanidins (mg/day)			
Q1	443/1,649	1.00	1.00
Q2	485/1,650	1.12 (0.92, 1.37)	0.95 (0.78, 1.16)
Q3	488/1,650	1.12 (0.90, 1.38)	0.88 (0.71, 1.10)
Q4	491/1,649	1.19 (0.94, 1.51)	1.09 (0.87, 1.37)
P for trend		0.19	0.60
Isoflavonoids (mg/day)			
Q1	443/1,649	1.00	1.00
Q2	484/1,650	1.05 (0.86, 1.28)	1.10 (0.91, 1.33)
Q3	463/1,649	0.87 (0.70, 1.08)	1.00 (0.82, 1.23)
Q4	517/1,650	1.02 (0.81, 1.28)	1.09 (0.89, 1.33)
P for trend		0.75	0.60

Notes: aOR: adjusted odds ratios; rOR: adjusted odds ratios with residual methods; SFAs: Saturated fatty acids; MUFAs: Monounsaturated Fatty acids; PUFAs: Polyunsaturated fatty acids; n-6 PUFAs: including LA and AA; LA: Linoleic acid; AA: Arachidonic acid; n-3 PUFAs: including ALA, EPA and DHA; ALA: α-linolenic acid; EPA: Eicosapentaenoic acid; DHA: Docosahexaenoic acid; Ca/Co: Cases/Controls; Numbers in bold face indicate statistically significant.

[a]: Adjusted for study area, age, gender, education level, income 10 years ago, tobacco smoking, alcohol drinking, family history of stomach cancer, *H. pylori* infection, body mass index, exercise 10 years ago, dietary sodium intake and total energy intake.

Table 3.8. Adjusted odds ratios and 95% CIs for associations between dietary fatty acids, total cholesterol, flavonoids and stomach cancer stratified by proxy interview (Non-proxy =7,383, Proxy=1,049)

	Non-proxy (n=7,383)			Proxy (n=1,049)		
Variables	Ca/Co	aOR (95%CI)[a]	rOR (95%CI)[a]	Ca/Co	aOR (95%CI)[a]	rOR (95%CI)[a]
Total fatty acid (g/day)						
Q1 (<14.85)	230/1,472	1.00	1.00	126/161	1.00	1.00
Q2 (14.85-<24.75)	286/1,527	**1.32 (1.03, 1.71)**	1.10 (0.87, 1.38)	145/106	1.12 (0.68, 1.84)	1.40 (0.80, 2.44)
Q3 (24.75-<40.17)	408/1,527	**1.59 (1.22, 2.07)**	**1.29 (1.02, 1.63)**	173/106	1.38 (0.82, 2.34)	1.32 (0.76, 2.28)
Q4 (40.17+)	403/1,530	**1.46 (1.07, 1.99)**	1.06 (0.83, 1.35)	129/103	1.34 (0.68, 2.65)	1.21 (0.67, 2.16)
p value for trend		**0.01**	0.44		0.27	0.70
Per 25g increase[b]		1.06 (0.95, 1.18)			1.03 (0.81, 1.32)	
SFAs (g/day)						
Q1 (<4.35)	232/1,480	1.00	1.00	129/153	1.00	1.00
Q2 (4.35-<7.14)	294/1,518	**1.30 (1.01, 1.67)**	1.08 (0.86, 1.37)	144/115	0.98 (0.60, 1.60)	1.33 (0.77, 2.28)
Q3 (7.14-<11.56)	402/1,535	**1.45 (1.12, 1.89)**	**1.32 (1.04, 1.67)**	164/98	1.38 (0.81, 2.33)	1.09 (0.63, 1.89)
Q4 (11.56+)	399/1,523	**1.37 (1.00, 1.86)**	1.15 (0.90, 1.47)	136/110	1.20 (0.63, 2.30)	1.21 (0.69, 2.15)
p value for trend		**0.046**	0.13		0.33	0.76
Per 7g increase[b]		1.07 (0.96, 1.19)			1.05 (0.84, 1.32)	
MUFAs (g/day)						
Q1 (<5.57)	230/1,488	1.00	1.00	126/145	1.00	1.00
Q2 (5.57-<9.85)	285/1,509	1.20 (0.93, 1.54)	1.08 (0.86, 1.36)	150/124	0.90 (0.56, 1.45)	1.10 (0.63, 1.92)
Q3 (9.85-<16.65)	406/1,539	**1.55 (1.20, 2.01)**	**1.35 (1.07, 1.71)**	166/94	1.16 (0.69, 1.95)	1.32 (0.76, 2.29)
Q4 (16.65+)	406/1,520	**1.48 (1.10, 1.99)**	1.09 (0.85, 1.40)	131/113	0.91 (0.48, 1.72)	1.05 (0.59, 1.87)
p value for trend		**0.003**	0.25		0.93	0.75
Per 10g increase[b]		1.03 (0.94, 1.13)			1.00 (0.82, 1.22)	
PUFAs (g/day)						
Q1 (<4.28)	239/1,463	1.00	1.00	126/170	1.00	1.00
Q2 (4.28-<6.93)	301/1,524	1.11 (0.86, 1.44)	1.11 (0.88, 1.39)	160/109	1.55 (0.95, 2.54)	1.12 (0.65, 1.94)
Q3 (6.93-<10.80)	394/1,532	**1.34 (1.03, 1.75)**	0.99 (0.78, 1.26)	166/101	1.63 (0.92, 2.88)	1.51 (0.86, 2.64)
Q4 (10.80+)	393/1,537	1.12 (0.81, 1.54)	1.11 (0.88, 1.40)	121/96	1.52 (0.73, 3.17)	1.10 (0.61, 1.98)
p value for trend		0.34	0.59		0.21	0.53
Per 6g increase[b]		1.07 (0.96, 1.20)			1.08 (0.85, 1.38)	
n-6 PUFAs (g/day)						
Q1 (<3.76)	244/1,458	1.00	1.00	128/175	1.00	1.00
Q2 (3.76-<5.97)	304/1,529	1.15 (0.89, 1.48)	1.04 (0.83, 1.30)	166/104	**1.67 (1.01, 2.76)**	1.25 (0.72, 2.15)

Q3 (5.97-<9.14)	383/1,530	1.25 (0.96, 1.64)	0.87 (0.68, 1.11)	155/103	1.45 (0.81, 2.57)	1.53 (0.88, 2.68)
Q4 (9.14+)	396/1,539	1.13 (0.82, 1.56)	1.12 (0.89, 1.40)	124/94	1.61 (0.78, 3.36)	1.25 (0.69, 2.26)
p value for trend		0.42	0.56		0.26	0.37
Per 5g increase[b]		1.07 (0.96, 1.20)			1.11 (0.87, 1.42)	
LA (g/day)						
Q1 (<3.49)	251/1,463	1.00	1.00	129/170	1.00	1.00
Q2 (3.49-<5.50)	310/1,521	1.12 (0.87, 1.44)	1.03 (0.82, 1.29)	164/112	1.46 (0.89, 2.38)	1.16 (0.67, 1.99)
Q3 (5.50-<8.35)	369/1,532	1.09 (0.83, 1.43)	0.88 (0.70, 1.12)	153/101	1.56 (0.87, 2.80)	1.29 (0.73, 2.28)
Q4 (8.35+)	397/1,540	1.08 (0.79, 1.49)	1.13 (0.90, 1.42)	127/93	1.58 (0.76, 3.30)	1.23 (0.67, 2.23)
p value for trend		0.72	0.47		0.2	0.47
Per 5g increase[b]		1.10 (0.97, 1.24)			1.14 (0.87, 1.49)	
AA (g/day)						
Q1 (<0.18)	253/1,496	1.00	1.00	141/137	1.00	1.00
Q2 (0.18-<0.38)	292/1,502	1.13 (0.88, 1.44)	1.03 (0.81, 1.30)	146/131	0.87 (0.55, 1.39)	1.05 (0.61, 1.82)
Q3 (0.38-<0.78)	393/1,536	**1.34 (1.04, 1.71)**	**1.27 (1.00, 1.62)**	160/97	0.91 (0.55, 1.50)	0.86 (0.50, 1.50)
Q4 (0.78+)	389/1,522	1.16 (0.88, 1.53)	0.95 (0.75, 1.21)	126/111	1.00 (0.57, 1.75)	1.00 (0.57, 1.75)
p value for trend		0.19	0.94		0.98	0.78
Per 1g increase[b]		0.95 (0.82, 1.10)			0.96 (0.72, 1.27)	
n-3 PUFAs (g/day)						
Q1 (<0.54)	241/1,473	1.00	1.00	137/160	1.00	1.00
Q2 (0.54-<0.96)	276/1,520	1.09 (0.85, 1.41)	1.11 (0.88, 1.40)	141/113	0.97 (0.60, 1.58)	1.14 (0.67, 1.93)
Q3 (0.96-<1.70)	410/1,533	**1.43 (1.10, 1.85)**	1.21 (0.95, 1.53)	185/100	1.37 (0.81, 2.32)	1.31 (0.77, 2.24)
Q4 (1.70+)	400/1,530	1.20 (0.89, 1.62)	1.05 (0.83, 1.33)	110/103	0.86 (0.44, 1.69)	1.08 (0.61, 1.93)
p value for trend		0.1	0.61		0.83	0.67
Per 1g increase[b]		1.02 (0.93, 1.12)			0.99 (0.81, 1.20)	
ALA (g/day)						
Q1 (<0.52)	247/1,474	1.00	1.00	133/159	1.00	1.00
Q2 (0.52-<0.93)	270/1,523	1.04 (0.81, 1.35)	1.08 (0.86, 1.37)	150/110	1.03 (0.63, 1.68)	1.18 (0.69, 2.00)
Q3 (0.93-<1.64)	411/1,533	**1.40 (1.09, 1.81)**	1.22 (0.97, 1.55)	178/100	1.35 (0.80, 2.27)	1.36 (0.79, 2.33)
Q4 (1.64+)	399/1,526	1.17 (0.87, 1.57)	1.01 (0.80, 1.28)	112/107	0.83 (0.43, 1.61)	1.13 (0.64, 2.00)
p value for trend		0.12	0.76		0.95	0.58
Per 1g increase[b]		1.02 (0.92, 1.12)			0.99 (0.81, 1.21)	
EPA (mg/day)						
Q1 (<4.30)	253/1,449	1.00	1.00	145/184	1.00	1.00
Q2 (4.30-<10.47)	332/1,523	1.10 (0.86, 1.41)	0.93 (0.73, 1.17)	171/110	**1.98 (1.26, 3.12)**	1.01 (0.61, 1.68)
Q3 (10.47-<21.77)	327/1,534	1.09 (0.84, 1.42)	0.99 (0.77, 1.27)	123/99	1.31 (0.78, 2.21)	0.87 (0.51, 1.50)

Q4 (21.77+)	415/1,550	1.18 (0.89, 1.56)	1.13 (0.89, 1.42)	134/83	1.51 (0.85, 2.66)	1.22 (0.71, 2.11)
p value for trend		0.31	0.23		0.24	0.59
Per 20mg increase[b]		1.01 (0.98, 1.05)			0.98 (0.85, 1.12)	
DHA (mg/day)						
Q1 (<2.52)	248/1,435	1.00	1.00	175/198	1.00	1.00
Q2 (2.52-<9.97)	307/1,528	1.04 (0.80, 1.34)	0.87 (0.68, 1.11)	141/105	**2.01 (1.25, 3.23)**	1.05 (0.63, 1.76)
Q3 (9.97-<24.49)	318/1,547	0.97 (0.73, 1.28)	0.87 (0.67, 1.12)	125/86	**1.86 (1.08, 3.20)**	0.89 (0.51, 1.56)
Q4 (24.49+)	454/1,546	1.28 (0.95, 1.71)	1.12 (0.89, 1.42)	132/87	**1.88 (1.05, 3.35)**	1.45 (0.83, 2.55)
p value for trend		0.08	0.22		**0.03**	0.28
Per 20mg increase[b]		**1.06 (1.02, 1.10)**			1.01 (0.88, 1.15)	
n-3/n-6 PUFAs						
Q1 (<0.13)	262/1,498	1.00	1.00	144/135	1.00	1.00
Q2 (0.13-<0.16)	309/1,528	0.92 (0.73, 1.18)	0.88 (0.70, 1.11)	140/105	1.24 (0.76, 2.03)	0.76 (0.45, 1.30)
Q3 (0.16-<0.20)	380/1,535	**1.30 (1.03, 1.63)**	1.12 (0.89, 1.41)	155/98	1.09 (0.67, 1.78)	0.81 (0.48, 1.38)
Q4 (0.20+)	376/1,495	1.14 (0.89, 1.46)	1.11 (0.88, 1.38)	134/138	0.73 (0.45, 1.19)	0.64 (0.38, 1.06)
p value for trend		0.06	0.15		0.19	0.12
Per 0.1 increase[b]		1.11 (0.96, 1.30)			0.95 (0.70, 1.29)	
Total fat (g/day)						
Q1 (<18.84)	239/1,487	1.00	1.00	116/146	1.00	1.00
Q2 (18.84-<31.07)	314/1,510	**1.29 (1.01, 1.65)**	1.14 (0.91, 1.43)	149/123	1.03 (0.64, 1.68)	0.95 (0.54, 1.67)
Q3 (31.07-<48.98)	389/1,533	**1.41 (1.09, 1.82)**	1.14 (0.89, 1.44)	168/100	1.15 (0.66, 1.99)	1.22 (0.69, 2.15)
Q4 (48.98+)	385/1,526	1.26 (0.93, 1.71)	1.02 (0.80, 1.31)	140/107	1.15 (0.58, 2.27)	0.97 (0.52, 1.79)
p value for trend		0.12	0.89		0.62	0.82
Per 30g increase[b]		1.03 (0.92, 1.16)			0.95 (0.74, 1.23)	
Total cholesterol (mg/day)						
Q1 (<107.24)	300/1,506	1.00	1.00	107/127	1.00	1.00
Q2 (107.24-<207.21)	318/1,503	1.06 (0.84, 1.33)	1.05 (0.85, 1.31)	111/130	0.87 (0.53, 1.42)	**2.30 (1.32, 3.99)**
Q3 (207.21-<352.09)	344/1,534	1.20 (0.95, 1.51)	**1.28 (1.01, 1.61)**	154/99	**1.76 (1.05, 2.93)**	**2.30 (1.34, 3.96)**
Q4 (352.09+)	365/1,513	**1.52 (1.17, 1.96)**	**1.46 (1.15, 1.86)**	201/120	**1.89 (1.08, 3.30)**	**2.37 (1.36, 4.16)**
p value for trend		**0.001**	**0.001**		**0.005**	**0.007**
Per 250mg increase[b]		**1.13 (1.04, 1.22)**			**1.26 (1.02, 1.55)**	
Total flavonoids (mg/day)						
Q1 (<24.19)	279/1,467	1.00	1.00	102/166	1.00	1.00
Q2 (24.19-<48.08)	346/1,509	1.05 (0.83, 1.33)	1.06 (0.85, 1.33)	179/124	**2.60 (1.56, 4.33)**	1.42 (0.85, 2.36)
Q3 (48.08-<133.40)	382/1,527	1.09 (0.85, 1.40)	1.20 (0.95, 1.51)	154/106	**2.07 (1.15, 3.72)**	**2.04 (1.18, 3.52)**
Q4 (133.40+)	320/1,553	0.89 (0.69, 1.15)	0.93 (0.73, 1.17)	138/80	**2.33 (1.22, 4.42)**	1.72 (0.92, 3.21)

p value for trend		0.38	0.83		**0.05**	**0.03**
Per 100 mg increase[b]		0.99 (0.97, 1.01)			**1.04 (1.00, 1.08)**	
Flavonols (mg/day)						
Q1 (<4.26)	281/1,479	1.00	1.00	84/154	1.00	1.00
Q2 (4.26-<8.86)	409/1,504	**1.37 (1.09, 1.71)**	1.17 (0.94, 1.45)	170/129	**2.89 (1.76, 4.75)**	**1.79 (1.06, 3.02)**
Q3 (8.86-<18.50)	329/1,527	1.10 (0.86, 1.40)	1.00 (0.80, 1.26)	143/106	**3.00 (1.68, 5.33)**	**2.75 (1.56, 4.83)**
Q4 (18.50+)	308/1,546	0.99 (0.76, 1.29)	0.86 (0.67, 1.09)	176/87	**3.46 (1.85, 6.47)**	**2.80 (1.52, 5.18)**
p value for trend		0.45	0.15		**<0.001**	**<0.001**
Per 15 mg increase[b]		0.96 (0.89, 1.03)			**1.14 (1.00, 1.31)**	
Flavones (mg/day)						
Q1 (<2.00)	258/1,481	1.00	1.00	93/152	1.00	1.00
Q2 (2.00-<3.50)	346/1,510	1.13 (0.90, 1.42)	1.15 (0.93, 1.44)	143/123	**1.82 (1.11, 2.97)**	1.23 (0.73, 2.07)
Q3 (3.50-<5.74)	376/1,546	1.18 (0.93, 1.49)	1.14 (0.90, 1.43)	167/87	**3.14 (1.82, 5.41)**	**1.77 (1.04, 3.00)**
Q4 (5.74+)	347/1,519	1.27 (0.98, 1.64)	1.18 (0.93, 1.48)	170/114	**2.46 (1.37, 4.43)**	**2.14 (1.26, 3.62)**
p value for trend		0.07	0.21		**0.001**	**0.002**
Per 5 mg increase[b]		1.03 (0.90, 1.16)			1.07 (0.88, 1.30)	
Flavanones (mg/day)						
No	896/3,584	1.00		347/338	1.00	
Yes	431/2,472	**0.76 (0.64, 0.90)**		226/138	1.39 (0.95, 2.03)	
Q1 *			1.00			1.00
Q2			0.96 (0.76, 1.21)			1.45 (0.82, 2.56)
Q3			0.83 (0.63, 1.08)			0.91 (0.48, 1.72)
Q4			0.83 (0.64, 1.06)			1.23 (0.68, 2.21)
p value for trend			0.09			0.99
Flavan_3_ols (mg/day)						
Q1 (<1.73)	268/1,466	1.00	1.00	127/167	1.00	1.00
Q2 (1.73-<4.50)	355/1,526	**1.34 (1.06, 1.70)**	1.14 (0.90, 1.44)	167/107	**1.80 (1.09, 2.99)**	**1.88 (1.15, 3.08)**
Q3 (4.50-<53.30)	387/1,511	**1.47 (1.14, 1.89)**	**1.42 (1.10, 1.84)**	155/122	1.28 (0.75, 2.19)	1.26 (0.72, 2.20)
Q4 (53.30+)	317/1,553	1.06 (0.82, 1.36)	0.98 (0.76, 1.27)	124/80	1.32 (0.70, 2.48)	1.34 (0.70, 2.55)
p value for trend		0.76	0.89		0.66	0.73
Per 50 mg increase[b]		0.99 (0.98, 1.00)			1.02 (1.00, 1.04)	
Anthocyanidins (mg/day)						
Q1 (<1.43)	331/1,501	1.00	1.00	110/132	1.00	1.00
Q2 (1.43-<3.13)	356/1,509	1.14 (0.91, 1.43)	0.96 (0.76, 1.19)	126/124	0.77 (0.46, 1.29)	0.65 (0.37, 1.16)
Q3 (3.13-<6.28)	345/1,530	1.13 (0.89, 1.45)	0.94 (0.73, 1.21)	143/103	1.20 (0.68, 2.10)	0.77 (0.42, 1.42)
Q4 (6.28+)	295/1,516	1.25 (0.94, 1.66)	1.11 (0.85, 1.46)	194/117	1.46 (0.81, 2.63)	1.19 (0.64, 2.20)

p value for trend		0.16	0.54		0.09	0.25
Per 5 mg increase[b]		**1.07 (1.02, 1.12)**			1.04 (0.95, 1.13)	
Isoflavonoids (mg/day)						
Q1 (<7.52)	295/1,480	1.00	1.00	142/153	1.00	1.00
Q2 (7.52-<15.94)	315/1,491	0.93 (0.74, 1.18)	1.09 (0.87, 1.37)	167/142	1.13 (0.70, 1.81)	1.04 (0.62, 1.75)
Q3 (15.94-<28.31)	327/1,539	0.79 (0.62, 1.01)	1.02 (0.81, 1.29)	135/94	1.16 (0.66, 2.04)	0.73 (0.41, 1.31)
Q4 (28.31+)	390/1,546	1.02 (0.79, 1.32)	1.13 (0.90, 1.42)	129/87	1.20 (0.64, 2.27)	1.02 (0.56, 1.85)
p value for trend		0.92	0.4		0.58	0.74
Per 20 mg increase[b]		1.07 (0.99, 1.15)			1.01 (0.85, 1.21)	

Notes: aOR: adjusted odds ratios; rOR: adjusted odds ratios with residual methods; Ca/Co: Cases/Controls; Numbers in bold face indicate statistically significant.

[a]: Adjusted for study area, age, gender, education level, income 10 years ago, tobacco smoking, alcohol drinking, family history of stomach cancer, *H. pylori* infection, body mass index, exercise 10 years ago, dietary sodium intake and total energy intake.

[b]: The rescaling units for the continuous were chosen based on interquartile range (IQR) of controls and feasible intervention ranges.

*: More than 50 % of participants' intake 0.

Table 3.9. The interactions between dietary fatty acids, total cholesterol, flavonoids and tobacco smoking on stomach cancer

Tobacco Smoking		Ca/Co	aOR(95%CI)[a]	rOR (95%CI)[a]	RERI	ROR
Non-smoker	Low FAs (<24.75 g/day)	302/1,612	1.00	1.00	RERI: -0.19 (-0.59, 0.20)	ROR: 0.79 (0.61, 1.03)
Non-smoker	High FAs (≥24.75 g/day)	432/1,524	**1.50 (1.20, 1.87)**	1.15 (0.94, 1.41)	rRERI: 0.09 (-0.24, 0.41)	rROR: 1.02 (0.79, 1.31)
Smoker	Low FAs (<24.75 g/day)	485/1,654	**1.62 (1.31, 2.00)**	**1.41 (1.15, 1.72)**		
Smoker	High FAs (≥24.75 g/day)	681/1,742	**1.92 (1.54, 2.41)**	**1.65 (1.34, 2.02)**		
Non-smoker	Low SFAs (<7.14 g/day)	302/1,611	1.00	1.00	RERI: -0.27 (-0.67, 0.13)	ROR: **0.76 (0.59, 0.99)**
Non-smoker	High SFAs (≥7.14 g/day)	432/1,525	**1.47 (1.18, 1.84)**	1.20 (0.98, 1.47)	rRERI: 0.10 (-0.24, 0.43)	rROR: 1.01 (0.78, 1.31)
Smoker	Low SFAs (<7.14 g/day)	497/1,655	**1.65 (1.34, 2.04)**	**1.41 (1.16, 1.73)**		
Smoker	High SFAs (≥7.14 g/day)	669/1,741	**1.86 (1.49, 2.32)**	**1.71 (1.39, 2.10)**		
Non-smoker	Low MUFAs (<9.85 g/day)	298/1,597	1.00	1.00	RERI: -0.17 (-0.57, 0.23)	ROR: 0.80 (0.62, 1.04)
Non-smoker	High MUFAs (≥9.85 g/day)	436/1,539	**1.50 (1.20, 1.87)**	1.16 (0.95, 1.43)	rRERI: 0.17 (-0.16, 0.49)	rROR: 1.07 (0.82, 1.38)
Smoker	Low MUFAs (<9.85 g/day)	493/1,669	**1.61 (1.30, 1.99)**	**1.37 (1.12, 1.68)**		
Smoker	High MUFAs (≥9.85 g/day)	673/1,727	**1.94 (1.55, 2.42)**	**1.70 (1.38, 2.09)**		
Non-smoker	Low PUFAs (<6.93 g/day)	307/1,623	1.00	1.00	RERI: -0.32 (-0.72, 0.07)	ROR: **0.75 (0.58, 0.97)**
Non-smoker	High PUFAs (≥6.93 g/day)	427/1,513	**1.41 (1.13, 1.77)**	1.06 (0.86, 1.30)	rRERI: 0.06 (-0.25, 0.37)	rROR: 1.02 (0.79, 1.32)
Smoker	Low PUFAs (<6.93 g/day)	519/1,643	**1.68 (1.36, 2.07)**	**1.40 (1.15, 1.71)**		
Smoker	High PUFAs (≥6.93 g/day)	647/1,753	**1.77 (1.40, 2.22)**	**1.52 (1.24, 1.87)**		
Non-smoker	Low n-6 PUFAs (<5.97 g/day)	316/1,622	1.00	1.00	RERI: -0.26 (-0.63, 0.11)	ROR: 0.79 (0.61, 1.02)
Non-smoker	High n-6 PUFAs (≥5.97 g/day)	418/1,514	**1.29 (1.03, 1.61)**	1.02 (0.83, 1.26)	rRERI: 0.06 (-0.24, 0.37)	rROR: 1.04 (0.80, 1.34)
Smoker	Low n-6 PUFAs (<5.97 g/day)	526/1,644	**1.62 (1.32, 1.99)**	**1.39 (1.14, 1.70)**		
Smoker	High n-6 PUFAs (≥5.97 g/day)	640/1,752	**1.65 (1.31, 2.07)**	**1.48 (1.21, 1.82)**		
Non-smoker	Low n-3 PUFAs (<0.96 g/day)	307/1,596	1.00	1.00	RERI: -0.03 (-0.40, 0.34)	ROR: 0.89 (0.69, 1.16)
Non-smoker	High n-3 PUFAs (≥0.96 g/day)	427/1,540	**1.37 (1.10, 1.71)**	1.07 (0.87, 1.32)	rRERI: 0.13 (-0.18, 0.44)	rROR: 1.07 (0.83, 1.39)
Smoker	Low n-3 PUFAs (<0.96 g/day)	488/1,670	**1.52 (1.23, 1.87)**	**1.37 (1.12, 1.67)**		
Smoker	High n-3 PUFAs (≥0.96 g/day)	678/1,726	**1.86 (1.49, 2.32)**	**1.58 (1.28, 1.94)**		
Non-smoker	Low Cholesterol (<207.21 mg/day)	325/1,600	1.00	1.00	RERI: -0.05 (-0.43, 0.34)	ROR: 0.87 (0.67, 1.12)
Non-smoker	High Cholesterol (≥207.21 mg/day)	409/1,536	**1.47 (1.20, 1.80)**	**1.50 (1.22, 1.83)**	rRERI: -0.16 (-0.55, 0.24)	rROR: 0.81 (0.63, 1.05)
Smoker	Low Cholesterol (<207.21 mg/day)	511/1,666	**1.53 (1.25, 1.87)**	**1.58 (1.30, 1.93)**		
Smoker	High Cholesterol (≥207.21 mg/day)	655/1,730	**1.95 (1.58, 2.40)**	**1.92 (1.56, 2.36)**		
Non-smoker	Low Total Flavonoids (<48.08mg/day)	423/1,853	1.00	1.00	RERI: -0.19 (-0.52, 0.14)	ROR: 0.86 (0.66, 1.11)

Non-smoker	High Total Flavonoids (≥48.08mg/day)	311/1,283	1.09 (0.88, 1.35)	**1.24 (1.01, 1.52)**	rRERI: -0.25 (-0.60, 0.11)	rROR: 0.80 (0.62, 1.04)
Smoker	Low Total Flavonoids (<48.08mg/day)	483/1,413	**1.53 (1.26, 1.85)**	**1.56 (1.29, 1.89)**		
Smoker	High Total Flavonoids (≥48.08mg/day)	683/1,983	**1.43 (1.17, 1.75)**	**1.55 (1.28, 1.89)**		
Non-smoker	Low Flavonols (<8.86mg/day)	418/1,826	1.00	1.00	RERI: -0.13 (-0.45, 0.19)	ROR: 0.91 (0.70, 1.18)
Non-smoker	High Flavonols (≥8.86mg/day)	316/1,310	1.02 (0.82, 1.25)	1.07 (0.87, 1.31)	rRERI: -0.17 (-0.49, 0.16)	rROR: 0.88 (0.68, 1.13)
Smoker	Low Flavonols (<8.86mg/day)	526/1,440	**1.49 (1.23, 1.80)**	**1.51 (1.25, 1.82)**		
Smoker	High Flavonols (≥8.86mg/day)	640/1,956	**1.38 (1.13, 1.68)**	**1.41 (1.16, 1.72)**		
Non-smoker	Low Flavones (<3.50mg/day)	350/1,709	1.00	1.00	RERI: 0.07 (-0.27, 0.41)	ROR: 0.99 (0.76, 1.28)
Non-smoker	High Flavones (≥3.50mg/day)	384/1,427	1.22 (0.99, 1.50)	1.14 (0.93, 1.39)	rRERI: 0.10 (-0.23, 0.42)	rROR: 1.03 (0.79, 1.33)
Smoker	Low Flavones (<3.50mg/day)	490/1,557	**1.42 (1.16, 1.74)**	**1.39 (1.14, 1.69)**		
Smoker	High Flavones (≥3.50mg/day)	676/1,839	**1.71 (1.40, 2.10)**	**1.63 (1.34, 1.98)**		
Non-smoker	Flavanones	230/1,140	1.00	1.00	RERI: 0.18 (-0.13, 0.49)	ROR: 1.11 (0.85, 1.46)
Non-smoker	No Flavanones	504/1,996	1.05 (0.85, 1.31)	1.08 (0.87, 1.33)	rRERI: 0.20 (-0.10, 0.51)	rROR: 1.12 (0.87, 1.46)
Smoker	Flavanones	427/1,470	**1.33 (1.05, 1.67)**	**1.33 (1.08, 1.64)**		
Smoker	No Flavanones	739/1,926	**1.56 (1.25, 1.93)**	**1.61 (1.30, 1.98)**		
Non-smoker	Low Flavan_3_ols (<4.50 mg/day)	418/1,833	1.00	1.00	RERI: -0.11 (-0.43, 0.22)	ROR: 0.91 (0.70, 1.18)
Non-smoker	High Flavan_3_ols (≥4.50 mg/day)	316/1,303	1.08 (0.87, 1.32)	1.08 (0.87, 1.33)	rRERI: -0.11 (-0.43, 0.22)	rROR: 0.91 (0.70, 1.18)
Smoker	Low Flavan_3_ols (<4.50 mg/day)	499/1,433	**1.48 (1.22, 1.80)**	**1.48 (1.22, 1.80)**		
Smoker	High Flavan_3_ols (≥4.50 mg/day)	667/1,963	**1.45 (1.19, 1.77)**	**1.45 (1.19, 1.78)**		
Non-smoker	Low Anthocyanidins (<3.13 mg/day)	326/1,625	1.00	1.00	RERI: **-0.47 (-0.86, -0.08)**	ROR: **0.69 (0.54, 0.90)**
Non-smoker	High Anthocyanidins (≥3.13 mg/day)	408/1,511	**1.31 (1.07, 1.62)**	1.16 (0.94, 1.44)	rRERI: **-0.38 (-0.74, -0.02)**	rROR: **0.75 (0.58, 0.97)**
Smoker	Low Anthocyanidins (<3.13 mg/day)	597/1,641	**1.71 (1.40, 2.08)**	**1.63 (1.34, 1.97)**		
Smoker	High Anthocyanidins (≥3.13 mg/day)	569/1,755	**1.55 (1.25, 1.92)**	**1.41 (1.13, 1.75)**		
Non-smoker	High Isoflavonoids (≥15.94 mg/day)	371/1,512	1.00	1.00	RERI: 0.10 (-0.20, 0.40)	ROR: 1.07 (0.83, 1.38)
Non-smoker	Low Isoflavonoids (<15.94 mg/day)	363/1,624	1.02 (0.82, 1.26)	1.04 (0.85, 1.27)	rRERI: -0.02 (-0.33, 0.29)	rROR: 0.97 (0.75, 1.26)

Smoker	High Isoflavonoids (≥15.94 mg/day)	610/1,754	**1.37 (1.13, 1.67)**	**1.44 (1.18, 1.75)**
Smoker	Low Isoflavonoids (<15.94 mg/day)	556/1,642	**1.49 (1.21, 1.84)**	**1.46 (1.19, 1.78)**

Notes: aOR: adjusted odds ratios; rOR: adjusted odds ratios with residual methods; SFAs: Saturated fatty acids; MUFAs: Monounsaturated fatty acids; PUFAs: Polyunsaturated fatty acids; RERI, relative excess risk due to interaction; ROR, ratio of odds ratios; rRERI, relative excess risk due to interaction with residual methods; rROR, ratio of odds ratios with residual methods; Ca/Co: Cases/Controls; Numbers in bold face indicate statistically significant.

[a] Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income 10 years ago (<1000, 1000 to <1500, 1500 to<2500, ≥2500), alcohol consumption (continuous, g ethanol/day), *H. pylori* infection (positive/negative), family history of stomach cancer (yes/no), BMI (<18.5, 18.5 to <24, 24 to <28, ≥28), exercise 10 years ago (yes/no), dietary sodium intake (quartile levels of raw and energy-adjusted values), total energy intake (continuous, kcal/day).

Table 3.10. The interactions between dietary fatty acids, total cholesterol, flavonoids and alcohol consumption on stomach cancer

Alcohol Drinking		Ca/Co	aOR(95%CI)[a]	rOR (95%CI)[a]	RERI	ROR
Non-drinker	Low FAs (<24.75 g/day)	425/1,954	1.00	1.00	RERI: -0.34 (-0.70, 0.02)	ROR: **0.75 (0.57, 0.98)**
Non-drinker	High FAs (≥24.75 g/day)	609/1,738	1.46 (1.19, 1.79)	1.13 (0.94, 1.36)	rRERI: 0.03 (-0.26, 0.32)	rROR: 1.02 (0.78, 1.33)
Drinker	Low FAs (<24.75 g/day)	362/1,312	1.23 (0.99, 1.53)	1.04 (0.85, 1.28)		
Drinker	High FAs (≥24.75 g/day)	504/1,528	1.35 (1.08, 1.70)	1.20 (0.97, 1.48)		
Non-drinker	Low SFAs (<7.14 g/day)	429/1,943	1.00	1.00	RERI: -0.34 (-0.69, 0.01)	ROR: **0.75 (0.57, 0.98)**
Non-drinker	High SFAs (≥7.14 g/day)	605/1,749	**1.40 (1.14, 1.72)**	1.16 (0.96, 1.40)	rRERI: 0.05 (-0.24, 0.34)	rROR:1.04 (0.80, 1.35)
Drinker	Low SFAs (<7.14 g/day)	370/1,323	1.23 (0.99, 1.53)	1.03 (0.84, 1.26)		
Drinker	High SFAs (≥7.14 g/day)	496/1,517	**1.29 (1.03, 1.61)**	**1.24 (1.00, 1.54)**		
Non-drinker	Low MUFAs (<9.85 g/day)	429/1,927	1.00	1.00	RERI: -0.26 (-0.60, 0.09)	ROR: 0.80 (0.61, 1.05)
Non-drinker	High MUFAs (≥9.85 g/day)	605/1,765	**1.42 (1.16, 1.74)**	1.16 (0.96, 1.40)	rRERI: 0.06 (-0.23, 0.35)	rROR: 1.05 (0.80, 1.37)
Drinker	Low MUFAs (<9.85 g/day)	362/1,339	1.19 (0.95, 1.47)	1.03 (0.84, 1.26)		
Drinker	High MUFAs (≥9.85 g/day)	504/1,501	**1.35 (1.08, 1.69)**	**1.25 (1.01, 1.55)**		
Non-drinker	Low PUFAs (<6.93 g/day)	448/1,976	1.00	1.00	RERI: **-0.36 (-0.70, -0.01)**	ROR: **0.74 (0.56, 0.96)**
Non-drinker	High PUFAs (≥6.93 g/day)	586/1,716	**1.35 (1.10, 1.66)**	1.17 (0.97, 1.41)	rRERI: -0.26 (-0.57, 0.05)	rROR: 0.79 (0.60, 1.03)
Drinker	Low PUFAs (<6.93 g/day)	378/1,290	1.24 (1.00, 1.54)	1.18 (0.97, 1.45)		
Drinker	High PUFAs (≥6.93 g/day)	488/1,550	1.24 (0.98, 1.55)	1.09 (0.88, 1.35)		
Non-drinker	Low n-6 PUFAs (<5.97 g/day)	457/1,973	1.00	1.00	RERI: -0.32 (-0.65, 0.02)	ROR: **0.76 (0.58, 0.99)**
Non-drinker	High n-6 PUFAs (≥5.97 g/day)	577/1,719	**1.26 (1.02, 1.55)**	1.13 (0.94, 1.36)	rRERI: -0.25 (-0.56, 0.06)	rROR: 0.79 (0.61, 1.04)
Drinker	Low n-6 PUFAs (<5.97 g/day)	385/1,293	1.22 (0.99, 1.51)	1.17 (0.96, 1.44)		
Drinker	High n-6 PUFAs (≥5.97 g/day)	481/1,547	1.16 (0.93, 1.46)	1.05 (0.85, 1.31)		
Non-drinker	Low n-3 PUFAs (<0.96 g/day)	442/1,926	1.00	1.00	RERI: -0.12 (-0.44, 0.21)	ROR: 0.90 (0.68, 1.17)
Non-drinker	High n-3 PUFAs (≥0.96 g/day)	592/1,766	**1.33 (1.09, 1.63)**	1.06 (0.88, 1.27)	rRERI: 0.04 (-0.24, 0.32)	rROR: 1.04 (0.79, 1.35)
Drinker	Low n-3 PUFAs (<0.96 g/day)	353/1,340	1.11 (0.89, 1.38)	1.03 (0.84, 1.26)		
Drinker	High n-3 PUFAs (≥0.96 g/day)	513/1,500	**1.32 (1.06, 1.65)**	1.13 (0.91, 1.39)		
Non-drinker	Low Cholesterol (<207.21 mg/day)	463/1,932	1.00	1.00	RERI: -0.30 (-0.66, 0.06)	ROR: 0.78 (0.60, 1.02)
Non-drinker	High Cholesterol (≥207.21 mg/day)	571/1,760	**1.53 (1.26, 1.84)**	**1.45 (1.21, 1.74)**	rRERI: -0.18 (-0.53, 0.17)	rROR: 0.85 (0.65, 1.11)
Drinker	Low Cholesterol (<207.21 mg/day)	373/1,334	1.18 (0.96, 1.45)	1.14 (0.93, 1.38)		
Drinker	High Cholesterol (≥207.21 mg/day)	493/1,506	**1.41 (1.14, 1.75)**	**1.41 (1.14, 1.74)**		
Non-drinker	Low Total Flavonoids (<48.08mg/day)	568/2,152	1.00	1.00	RERI: **-0.33 (-0.65, -0.02)**	ROR: **0.74 (0.56, 0.97)**

Non-drinker	High Total Flavonoids (≥48.08mg/day)	466/1,540	1.11 (0.92, 1.35)	**1.22 (1.01, 1.47)**	rRERI: -0.30 (-0.62, 0.02)	rROR: 0.76 (0.58, 1.00)
Drinker	Low Total Flavonoids (<48.08mg/day)	338/1,114	1.22 (1.00, 1.50)	1.19 (0.97, 1.46)		
Drinker	High Total Flavonoids (≥48.08mg/day)	528/1,726	1.00 (0.82, 1.23)	1.11 (0.91, 1.36)		
Non-drinker	Low Flavonols (<8.86mg/day)	585/2,122	1.00	1.00	RERI: -0.21 (-0.50, 0.08)	ROR: 0.82 (0.63, 1.07)
Non-drinker	High Flavonols (≥8.86mg/day)	449/1,570	1.02 (0.84, 1.23)	1.03 (0.85, 1.24)	rRERI: -0.15 (-0.43, 0.14)	rROR: 0.87 (0.67, 1.14)
Drinker	Low Flavonols (<8.86mg/day)	359/1,144	1.16 (0.95, 1.41)	1.12 (0.92, 1.37)		
Drinker	High Flavonols (≥8.86mg/day)	507/1,696	0.96 (0.78, 1.18)	1.01 (0.82, 1.23)		
Non-drinker	Low Flavones (<3.50mg/day)	476/2,005	1.00	1.00	RERI: -0.31 (-0.65, 0.03)	ROR: 0.77 (0.59, 1.00)
Non-drinker	High Flavones (≥3.50mg/day)	558/1,687	**1.36 (1.13, 1.65)**	**1.27 (1.06, 1.52)**	rRERI: -0.18 (-0.50, 0.14)	rROR: 0.85 (0.65, 1.11)
Drinker	Low Flavones (<3.50mg/day)	364/1,261	1.20 (0.97, 1.48)	1.13 (0.92, 1.38)		
Drinker	High Flavones (≥3.50mg/day)	502/1,579	**1.26 (1.02, 1.55)**	1.22 (0.99, 1.50)		
Non-drinker	Flavanones	316/1,325	1.00	1.00	RERI: -0.04 (-0.34, 0.27)	ROR: 0.96 (0.73, 1.27)
Non-drinker	No Flavanones	718/2,367	1.18 (0.97, 1.43)	**1.25 (1.03, 1.51)**	rRERI: -0.23 (-0.56, 0.09)	rROR: 0.81 (0.62, 1.06)
Drinker	Flavanones	341/1,285	1.07 (0.85, 1.35)	1.18 (0.95, 1.47)		
Drinker	No Flavanones	525/1,555	1.21 (0.98, 1.51)	1.20 (0.97, 1.49)		
Non-drinker	Low Flavan_3_ols (<4.50 mg/day)	575/2,133	1.00	1.00	RERI: -0.23 (-0.54, 0.08)	ROR: 0.81 (0.62, 1.06)
Non-drinker	High Flavan_3_ols (≥4.50 mg/day)	459/1,559	1.15 (0.95, 1.39)	1.19 (0.98, 1.44)	rRERI: -0.31 (-0.63, 0.01)	rROR: **0.76 (0.58, 0.99)**
Drinker	Low Flavan_3_ols (<4.50 mg/day)	342/1,133	1.16 (0.94, 1.43)	1.21 (0.98, 1.49)		
Drinker	High Flavan_3_ols (≥4.50 mg/day)	524/1,707	1.08 (0.88, 1.32)	1.09 (0.89, 1.33)		
Non-drinker	Low Anthocyanidins (<3.13 mg/day)	500/1,929	1.00	1.00	RERI: -0.18 (-0.48, 0.13)	ROR: 0.85 (0.65, 1.11)
Non-drinker	High Anthocyanidins (≥3.13 mg/day)	534/1,763	1.17 (0.96, 1.42)	1.09 (0.89, 1.32)	rRERI: -0.21 (-0.51, 0.08)	rROR: 0.82 (0.63, 1.07)
Drinker	Low Anthocyanidins (<3.13 mg/day)	423/1,337	1.13 (0.92, 1.38)	1.14 (0.94, 1.38)		
Drinker	High Anthocyanidins (≥3.13 mg/day)	443/1,503	1.12 (0.90, 1.39)	1.01 (0.81, 1.27)		
Non-drinker	Low Isoflavonoids (<15.94 mg/day)	506/1,943	1.00	1.00	RERI: -0.23 (-0.53, 0.06)	ROR: 0.80 (0.61, 1.05)
Non-drinker	High Isoflavonoids (≥15.94 mg/day)	528/1,749	1.02 (0.84, 1.24)	1.04 (0.87, 1.25)	rRERI: -0.16 (-0.45, 0.12)	rROR: 0.86 (0.66, 1.11)

Drinker	Low Isoflavonoids (<15.94 mg/day)	413/1,323	1.17 (0.95, 1.44)	1.13 (0.93, 1.38)
Drinker	High Isoflavonoids (≥15.94 mg/day)	453/1,517	0.96 (0.77, 1.19)	1.00 (0.81, 1.24)

Notes: aOR: adjusted odds ratios; rOR: adjusted odds ratios with residual methods; SFAs: Saturated fatty acids; MUFAs: Monounsaturated fatty acids; PUFAs: Polyunsaturated fatty acids; RERI, relative excess risk due to interaction; ROR, ratio of odds ratios; rRERI, relative excess risk due to interaction with residual methods; rROR, ratio of odds ratios with residual methods; Ca/Co: Cases/Controls; Numbers in bold face indicate statistically significant.

[a] Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income 10 years ago (<1000, 1000 to <1500, 1500 to<2500, ≥2500), smoking (continuous, pack-years), *H. pylori* infection (positive/negative), family history of stomach cancer (yes/no), BMI (<18.5, 18.5 to <24, 24 to <28, ≥28), exercise 10 years ago (yes/no), dietary sodium intake (quartile levels of raw and energy-adjusted values), total energy intake (continuous, kcal/day).

Table 3.11. The interactions between dietary fatty acids, total cholesterol, flavonoids and *H. pylori* infection on stomach cancer

***H. pylori* Infection**		Ca/Co	aOR(95%CI)[a]	rOR (95%CI)[a]	RERI	ROR
Negative	Low FAs (<24.75 g/day)	135/849	1.00	1.00	RERI: -0.06 (-0.47, 0.35)	ROR: 0.88 (0.65, 1.20)
Negative	High FAs (≥24.75 g/day)	197/764	**1.44 (1.08, 1.92)**	1.23 (0.94, 1.62)	rRERI: -0.04 (-0.42, 0.33)	rROR: 0.92 (0.68, 1.26)
Positive	Low FAs (<24.75 g/day)	431/1,874	**1.39 (1.10, 1.76)**	**1.36 (1.08, 1.71)**		
Positive	High FAs (≥24.75 g/day)	631/1,937	**1.77 (1.38, 2.27)**	**1.55 (1.22, 1.95)**		
Negative	Low SFAs (<7.14 g/day)	139/861	1.00	1.00	RERI: -0.10 (-0.51, 0.31)	ROR:0.87 (0.64, 1.18)
Negative	High SFAs (≥7.14 g/day)	193/752	**1.40 (1.05, 1.86)**	1.24 (0.94, 1.63)	rRERI:0.02 (-0.35, 0.39)	rROR:0.97 (0.71, 1.31)
Positive	Low SFAs (<7.14 g/day)	436/1,873	**1.40 (1.11, 1.77)**	**1.32 (1.05, 1.67)**		
Positive	High SFAs (≥7.14 g/day)	626/1,938	**1.70 (1.33, 2.18)**	**1.59 (1.26, 2.00)**		
Negative	Low MUFAs (<9.85 g/day)	138/839	1.00	1.00	RERI:0.00 (-0.40, 0.39)	ROR:0.92 (0.68, 1.26)
Negative	High MUFAs (≥9.85 g/day)	194/774	**1.40 (1.05, 1.86)**	1.17 (0.89, 1.53)	rRERI:0.13 (-0.22, 0.47)	rROR:1.06 (0.78, 1.44)
Positive	Low MUFAs (<9.85 g/day)	428/1,869	**1.35 (1.07, 1.71)**	**1.26 (1.00, 1.58)**		
Positive	High MUFAs (≥9.85 g/day)	634/1,942	**1.75 (1.37, 2.24)**	**1.55 (1.23, 1.95)**		
Negative	Low PUFAs (<6.93 g/day)	150/859	1.00	1.00	RERI: 0.08 (-0.28, 0.43)	ROR: 1.01 (0.74, 1.37)
Negative	High PUFAs (≥6.93 g/day)	182/754	1.20 (0.90, 1.60)	1.09 (0.83, 1.43)	rRERI: -0.01 (-0.35, 0.34)	rROR: 0.97 (0.72, 1.32)
Positive	Low PUFAs (<6.93 g/day)	438/1,870	**1.29 (1.03, 1.63)**	**1.32 (1.05, 1.65)**		
Positive	High PUFAs (≥6.93 g/day)	624/1,941	**1.57 (1.22, 2.01)**	**1.40 (1.12, 1.77)**		
Negative	Low n-6 PUFAs (<5.97 g/day)	154/861	1.00	1.00	RERI: 0.07 (-0.27, 0.41)	ROR: 1.03 (0.76, 1.40)
Negative	High n-6 PUFAs (≥5.97 g/day)	178/752	1.11 (0.83, 1.47)	1.12 (0.85, 1.46)	rRERI: -0.11 (-0.47, 0.26)	rROR: 0.90 (0.66, 1.23)
Positive	Low n-6 PUFAs (<5.97 g/day)	448/1,873	**1.28 (1.02, 1.61)**	**1.37 (1.10, 1.72)**		
Positive	High n-6 PUFAs (≥5.97 g/day)	614/1,938	**1.46 (1.14, 1.87)**	**1.39 (1.10, 1.74)**		
Negative	Low n-3 PUFAs (<0.96 g/day)	147/858	1.00	1.00	RERI: 0.22 (-0.13, 0.56)	ROR: 1.12 (0.83, 1.53)
Negative	High n-3 PUFAs (≥0.96 g/day)	185/755	1.18 (0.89, 1.57)	1.09 (0.83, 1.44)	rRERI: 0.05 (-0.29, 0.39)	rROR: 1.01 (0.75, 1.38)
Positive	Low n-3 PUFAs (<0.96 g/day)	420/1,855	1.22 (0.97, 1.53)	**1.29 (1.03, 1.62)**		
Positive	High n-3 PUFAs (≥0.96 g/day)	642/1,956	**1.62 (1.27, 2.06)**	**1.43 (1.14, 1.81)**		
Negative	Low Cholesterol (<207.21 mg/day)	134/782	1.00	1.00	RERI: -0.23 (-0.69, 0.24)	ROR:0.78 (0.57, 1.06)

Negative	High Cholesterol (≥207.21 mg/day)	198/831	**1.66 (1.26, 2.19)**	**1.68 (1.28, 2.22)**	rRERI: -0.26 (-0.73, 0.22)	rROR:0.76 (0.56, 1.04)
Positive	Low Cholesterol (<207.21 mg/day)	491/1,990	**1.49 (1.18, 1.89)**	**1.50 (1.19, 1.90)**		
Positive	High Cholesterol (≥207.21 mg/day)	571/1,821	**1.93 (1.52, 2.45)**	**1.93 (1.52, 2.44)**		
Negative	Low Total Flavonoids (<48.08mg/day)	145/823	1.00	1.00	RERI: **-0.45 (-0.88, -0.02)**	ROR: **0.70 (0.51, 0.95)**
Negative	High Total Flavonoids (≥48.08mg/day)	187/790	1.28 (0.97, 1.68)	1.30 (0.99, 1.71)	rRERI: -0.26 (-0.67, 0.15)	rROR: 0.79 (0.58, 1.07)
Positive	Low Total Flavonoids (<48.08mg/day)	553/1,948	**1.57 (1.25, 1.96)**	**1.48 (1.18, 1.85)**		
Positive	High Total Flavonoids (≥48.08mg/day)	509/1,863	**1.39 (1.10, 1.76)**	**1.51 (1.20, 1.91)**		
Negative	Low Flavonols (<8.86mg/day)	157/795	1.00	1.00	RERI: -0.29 (-0.67, 0.09)	ROR: 0.79 (0.58, 1.08)
Negative	High Flavonols (≥8.86mg/day)	175/818	1.09 (0.83, 1.44)	1.14 (0.87, 1.50)	rRERI: -0.27 (-0.65, 0.12)	rROR: 0.80 (0.59, 1.09)
Positive	Low Flavonols (<8.86mg/day)	568/1,985	**1.46 (1.17, 1.82)**	**1.46 (1.17, 1.81)**		
Positive	High Flavonols (≥8.86mg/day)	494/1,826	**1.27 (1.01, 1.60)**	**1.33 (1.06, 1.68)**		
Negative	Low Flavones (<3.50mg/day)	147/807	1.00	1.00	RERI: 0.06 (-0.30, 0.42)	ROR: 0.99 (0.73, 1.35)
Negative	High Flavones (≥3.50mg/day)	185/806	1.23 (0.94, 1.62)	1.14 (0.87, 1.49)	rRERI: 0.12 (-0.22, 0.46)	rROR: 1.06 (0.78, 1.44)
Positive	Low Flavones (<3.50mg/day)	475/1,967	**1.31 (1.04, 1.65)**	**1.26 (1.01, 1.57)**		
Positive	High Flavones (≥3.50mg/day)	587/1,844	**1.60 (1.27, 2.03)**	**1.52 (1.22, 1.90)**		
Negative	No Flavanones	217/1,001	1.00	1.00	RERI: -0.36 (-0.74, 0.03)	ROR: 0.75 (0.54, 1.03)
Negative	Flavanones	115/612	1.08 (0.82, 1.42)	1.03 (0.78, 1.35)	rRERI: -0.27 (-0.63, 0.09)	rROR: 0.81 (0.60, 1.10)
Positive	No Flavanones	725/2,304	**1.44 (1.19, 1.75)**	**1.43 (1.16, 1.76)**		
Positive	Flavanones	337/1,507	1.16 (0.93, 1.45)	1.19 (0.95, 1.49)		
Negative	Low Flavan_3_ols (<4.50 mg/day)	147/796	1.00	1.00	RERI: -0.16 (-0.54, 0.21)	ROR: 0.86 (0.63, 1.17)
Negative	High Flavan_3_ols (≥4.50 mg/day)	185/817	1.17 (0.89, 1.53)	1.17 (0.89, 1.54)	rRERI: -0.16 (-0.53, 0.22)	rROR: 0.86 (0.64, 1.17)
Positive	Low Flavan_3_ols (<4.50 mg/day)	539/1,964	**1.41 (1.13, 1.76)**	**1.41 (1.12, 1.76)**		
Positive	High Flavan_3_ols (≥4.50 mg/day)	523/1,847	**1.41 (1.12, 1.78)**	**1.42 (1.12, 1.80)**		

Negative	Low Anthocyanidins (<3.13 mg/day)	151/772	1.00	1.00	RERI: -0.23 (-0.63, 0.17)	ROR: 0.81 (0.59, 1.10)
Negative	High Anthocyanidins (≥3.13 mg/day)	181/841	1.29 (0.97, 1.71)	1.19 (0.89, 1.58)	rRERI: -0.23 (-0.61, 0.16)	rROR: 0.82 (0.60, 1.11)
Positive	Low Anthocyanidins (<3.13 mg/day)	541/1,966	**1.46 (1.16, 1.83)**	**1.44 (1.15, 1.79)**		
Positive	High Anthocyanidins (≥3.13 mg/day)	521/1,845	**1.52 (1.19, 1.93)**	**1.40 (1.10, 1.77)**		
Negative	High Isoflavonoids (≥15.94 mg/day)	165/758	1.00	1.00	RERI: 0.05 (-0.29, 0.39)	ROR: 1.02 (0.75, 1.38)
Negative	Low Isoflavonoids (<15.94 mg/day)	167/855	1.08 (0.82, 1.42)	1.13 (0.86, 1.48)	rRERI: -0.13 (-0.49, 0.24)	rROR: 0.89 (0.65, 1.20)
Positive	High Isoflavonoids (≥15.94 mg/day)	548/1,924	**1.29 (1.04, 1.61)**	**1.39 (1.11, 1.73)**		
Positive	Low Isoflavonoids (<15.94 mg/day)	514/1,887	**1.42 (1.12, 1.79)**	**1.39 (1.10, 1.74)**		

Notes: aOR: adjusted odds ratios; rOR: adjusted odds ratios with residual methods; SFAs: Saturated fatty acids; MUFAs: Monounsaturated fatty acids; PUFAs: Polyunsaturated fatty acids; RERI, relative excess risk due to interaction; ROR, ratio of odds ratios; rRERI, relative excess risk due to interaction with residual methods; rROR, ratio of odds ratios with residual methods; Ca/Co: Cases/Controls; Numbers in bold face indicate statistically significant.

[a] Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income 10 years ago (<1000, 1000 to <1500, 1500 to<2500, ≥2500), smoking (continuous, pack-years), alcohol consumption (continuous, g ethanol/day), family history of stomach cancer (yes/no), BMI (<18.5, 18.5 to <24, 24 to <28, ≥28), exercise 10 years ago (yes/no), dietary sodium intake (quartile levels of raw and energy-adjusted values), total energy intake (continuous, kcal/day).

Table 3.12. The interactions between dietary fatty acids, total cholesterol, flavonoids and dietary sodium intake on stomach cancer

Dietary Sodium Intake		Ca/Co	aOR(95%CI)[a]	rOR (95%CI)[a]	RERI	ROR
Low sodium	Low FAs (<24.75 g/day)	502/2,230	1.00	1.00	RERI: **-0.46 (-0.87, -0.04)**	ROR: **0.69 (0.52, 0.92)**
Low sodium	High FAs (≥24.75 g/day)	369/1,036	**1.61 (1.30, 1.99)**	**1.26 (1.03, 1.54)**	rRERI: -0.14 (-0.48, 0.21)	rROR: 0.87 (0.66, 1.15)
High sodium	Low FAs (<24.75 g/day)	285/1,036	**1.36 (1.10, 1.68)**	**1.24 (1.01, 1.51)**		
High sodium	High FAs (≥24.75 g/day)	744/2,230	**1.51 (1.24, 1.83)**	**1.36 (1.14, 1.63)**		
Low sodium	Low SFAs (<7.14 g/day)	500/2,203	1.00	1.00	RERI: -0.33 (-0.73, 0.05)	ROR: **0.75 (0.57, 0.99)**
Low sodium	High SFAs (≥7.14 g/day)	371/1,063	**1.48 (1.20, 1.83)**	**1.37 (1.12, 1.68)**	rRERI: -0.25 (-0.61, 0.12)	rROR: 0.80 (0.61, 1.05)
High sodium	Low SFAs (<7.14 g/day)	299/1,063	**1.31 (1.06, 1.62)**	**1.29 (1.06, 1.57)**		
High sodium	High SFAs (≥7.14 g/day)	730/2,203	**1.45 (1.20, 1.77)**	**1.41 (1.18, 1.69)**		
Low sodium	Low MUFAs (<9.85 g/day)	495/2,217	1.00	1.00	RERI: -0.44 (-0.86, -0.03)	ROR: **0.70 (0.53, 0.92)**
Low sodium	High MUFAs (≥9.85 g/day)	376/1,049	**1.61 (1.30, 1.98)**	**1.35 (1.10, 1.65)**	rRERI: -0.19 (-0.55, 0.17)	rROR: 0.83 (0.63, 1.10)
High sodium	Low MUFAs (<9.85 g/day)	296/1,049	**1.35 (1.09, 1.67)**	**1.26 (1.03, 1.53)**		
High sodium	High MUFAs (≥9.85 g/day)	733/2,217	**1.51 (1.25, 1.83)**	**1.42 (1.18, 1.69)**		
Low sodium	Low PUFAs (<6.93 g/day)	542/2,253	1.00	1.00	RERI: -0.26 (-0.64, 0.12)	ROR: 0.79 (0.60, 1.06)
Low sodium	High PUFAs (≥6.93 g/day)	329/1,013	**1.39 (1.12, 1.73)**	**1.24 (1.01, 1.51)**	rRERI: -0.29 (-0.64, 0.07)	rROR: 0.78 (0.59, 1.03)
High sodium	Low PUFAs (<6.93 g/day)	284/1,013	**1.27 (1.03, 1.57)**	**1.33 (1.09, 1.62)**		
High sodium	High PUFAs (≥6.93 g/day)	745/2,253	**1.40, 1.15, 1.70)**	**1.28 (1.08, 1.52)**		
Low sodium	Low n-6 PUFAs (<5.97 g/day)	543/2,246	1.00	1.00	RERI: **-0.41 (-0.80, -0.02)**	ROR: **0.71 (0.53, 0.94)**
Low sodium	High n-6 PUFAs (≥5.97 g/day)	328/1,020	**1.38 (1.11, 1.72)**	1.15 (0.95, 1.41)	rRERI: -0.20 (-0.54, 0.14)	rROR: 0.83 (0.63, 1.10)
High sodium	Low n-6 PUFAs (<5.97 g/day)	299/1,020	**1.37 (1.11, 1.68)**	**1.30 (1.06, 1.58)**		
High sodium	High n-6 PUFAs (≥5.97 g/day)	730/2,246	**1.34 (1.10, 1.63)**	**1.25 (1.05, 1.48)**		
Low sodium	Low n-3 PUFAs (<0.96 g/day)	512/2,225	1.00	1.00	RERI: -0.34 (-0.74, 0.06)	ROR: 0.75 (0.56, 1.00)
Low sodium	High n-3 PUFAs (≥0.96 g/day)	359/1,041	**1.53 (1.24, 1.89)**	**1.22 (1.00, 1.49)**	rRERI: -0.18 (-0.52, 0.17)	rROR: 0.85 (0.64, 1.12)
High sodium	Low n-3 PUFAs (<0.96 g/day)	283/1,041	**1.29 (1.04, 1.60)**	**1.27 (1.04, 1.55)**		
High sodium	High n-3 PUFAs (≥0.96 g/day)	746/2,225	**1.48 (1.22, 1.79)**	**1.31 (1.10, 1.56)**		
Low sodium	Low Cholesterol (<207.21 mg/day)	495/2,108	1.00	1.00	RERI: -0.07 (-0.43, 0.30)	ROR: 0.92 (0.70, 1.21)
Low sodium	High Cholesterol (≥207.21 mg/day)	376/1,158	**1.45 (1.18, 1.79)**	**1.43 (1.17, 1.76)**	rRERI: -0.03 (-0.39, 0.33)	rROR: 0.94 (0.71, 1.23)
High sodium	Low Cholesterol (<207.21 mg/day)	341/1,158	1.15 (0.94, 1.40)	1.18 (0.97, 1.43)		
High sodium	High Cholesterol (≥207.21 mg/day)	688/2,108	**1.53 (1.27, 1.84)**	**1.59 (1.32, 1.91)**		
Low sodium	Low Total Flavonoids (<48.08mg/day)	526/2,053	1.00	1.00	RERI: -0.16 (-0.48, 0.16)	ROR: 0.87 (0.66, 1.14)

Low sodium	High Total Flavonoids (≥48.08mg/day)	345/1,213	1.08 (0.87, 1.33)	1.10 (0.90, 1.34)	rRERI: 0.05 (-0.26, 0.35)	rROR: 1.02 (0.78, 1.34)
High sodium	Low Total Flavonoids (<48.08mg/day)	380/1,213	**1.26 (1.04, 1.52)**	1.16 (0.96, 1.41)		
High sodium	High Total Flavonoids (≥48.08mg/day)	649/2,053	1.17 (0.97, 1.42)	**1.31 (1.10, 1.56)**		
Low sodium	High Flavonols (≥8.86mg/day)	311/1,193	1.00	1.00	RERI: -0.11 (-0.44, 0.23)	ROR: 0.90 (0.68, 1.19)
Low sodium	Low Flavonols (<8.86mg/day)	560/2,073	1.13 (0.91, 1.40)	1.08 (0.88, 1.33)	rRERI: -0.15 (-0.47, 0.17)	rROR: 0.88 (0.67, 1.15)
High sodium	High Flavonols (≥8.86mg/day)	645/2,073	**1.26 (1.02, 1.57)**	**1.29 (1.06, 1.59)**		
High sodium	Low Flavonols (<8.86mg/day)	384/1,193	**1.28 (1.02, 1.62)**	1.23 (0.99, 1.53)		
Low sodium	Low Flavones (<3.50mg/day)	503/2,121	1.00	1.00	RERI: -0.34 (-0.72, 0.04)	ROR: **0.75 (0.57, 0.99)**
Low sodium	High Flavones (≥3.50mg/day)	368/1,145	**1.46 (1.19, 1.80)**	1.21 (0.99, 1.47)	rRERI: 0.04 (-0.28, 0.36)	rROR: 1.00 (0.77, 1.32)
High sodium	Low Flavones (<3.50mg/day)	337/1,145	**1.30 (1.06, 1.59)**	1.15 (0.95, 1.40)		
High sodium	High Flavones (≥3.50mg/day)	692/2,121	**1.42 (1.18, 1.71)**	**1.40 (1.17, 1.67)**		
Low sodium	Flavanones	296/1,254	1.00	1.00	RERI: 0.13 (-0.17, 0.43)	ROR: 1.10 (0.83, 1.45)
Low sodium	No Flavanones	575/2,012	1.11 (0.90, 1.36)	1.20 (0.98, 1.48)	rRERI: -0.10 (-0.43, 0.24)	rROR: 0.90 (0.69, 1.18)
High sodium	Flavanones	361/1,356	1.10 (0.88, 1.39)	**1.29 (1.04, 1.60)**		
High sodium	No Flavanones	668/1,910	**1.34 (1.09, 1.64)**	**1.40 (1.13, 1.73)**		
Low sodium	Low Flavan_3_ols (<4.50 mg/day)	523/2,007	1.00	1.00	RERI: 0.11 (-0.18, 0.40)	ROR: 1.10 (0.83, 1.44)
Low sodium	High Flavan_3_ols (≥4.50 mg/day)	348/1,259	1.01 (0.82, 1.24)	1.04 (0.85, 1.27)	rRERI: 0.05 (-0.25, 0.35)	rROR: 1.04 (0.79, 1.35)
High sodium	Low Flavan_3_ols (<4.50 mg/day)	394/1,259	1.12 (0.92, 1.35)	1.17 (0.96, 1.42)		
High sodium	High Flavan_3_ols (≥4.50 mg/day)	635/2,007	**1.23 (1.02, 1.47)**	**1.27 (1.05, 1.52)**		
Low sodium	Low Anthocyanidins (<3.13 mg/day)	625/2,340	1.00	1.00	RERI: -0.00 (-0.34, 0.33)	ROR: 0.98 (0.73, 1.32)
Low sodium	High Anthocyanidins (≥3.13 mg/day)	246/926	1.14 (0.91, 1.43)	0.89 (0.70, 1.13)	rRERI: **0.30 (0.00, 0.60)**	rROR: 1.33 (0.98, 1.80)
High sodium	Low Anthocyanidins (<3.13 mg/day)	298/926	1.13 (0.92, 1.39)	1.05 (0.86, 1.28)		
High sodium	High Anthocyanidins (≥3.13 mg/day)	731/2,340	**1.27 (1.07, 1.51)**	**1.24 (1.05, 1.46)**		
Low sodium	Low Isoflavonoids (<15.94 mg/day)	559/2,212	1.00	1.00	RERI: **-0.56 (-0.93, -0.18)**	ROR: **0.63 (0.48, 0.84)**
Low sodium	High Isoflavonoids (≥15.94 mg/day)	312/1,054	1.20 (0.97, 1.49)	1.17 (0.96, 1.43)	rRERI: **-0.38 (-0.73, -0.02)**	rROR: **0.73 (0.55, 0.96)**

High sodium	Low Isoflavonoids (<15.94 mg/day)	360/1,054	**1.49 (1.22, 1.81)**	**1.40 (1.16, 1.70)**
High sodium	High Isoflavonoids (≥15.94 mg/day)	669/2,212	1.14 (0.94, 1.37)	**1.19 (1.01, 1.42)**

Notes: aOR: adjusted odds ratios; rOR: adjusted odds ratios with residual methods; SFAs: Saturated fatty acids; MUFAs: Monounsaturated Fatty acids; PUFAs: Polyunsaturated fatty acids; RERI, relative excess risk due to interaction; ROR, ratio of odds ratios; rRERI, relative excess risk due to interaction with residual methods; rROR, ratio of odds ratios with residual methods; Ca/Co: Cases/Controls; Numbers in bold face indicate statistically significant.

[a] Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income 10 years ago (<1000, 1000 to <1500, 1500 to<2500, ≥2500), smoking (continuous, pack-years), alcohol consumption (continuous, g ethanol/day), *H. pylori* infection (positive/negative), family history of stomach cancer (yes/no), BMI (<18.5, 18.5 to <24, 24 to <28, ≥28), exercise 10 years ago (yes/no), total energy intake (continuous, kcal/day).

Table 3.13. The interactions between dietary fatty acids, total cholesterol, flavonoids and family history of stomach cancer on stomach cancer

Family history of SC		Ca/Co	aOR(95%CI)[a]	rOR (95%CI)[a]	RERI	ROR
No	Low FAs (<24.75 g/day)	720/3,122	1.00	1.00	RERI: 0.22 (-0.70, 1.14)	ROR: 0.99 (0.62, 1.60)
No	High FAs (≥24.75 g/day)	991/3,048	**1.31 (1.10, 1.56)**	1.14 (0.98, 1.32)	rRERI: 0.57 (-0.28, 1.43)	rROR: 1.28 (0.81, 2.04)
Yes	Low FAs (<24.75 g/day)	67/144	**1.76 (1.20, 2.59)**	**1.55 (1.11, 2.17)**		
Yes	High FAs (≥24.75 g/day)	122/218	**2.30 (1.67, 3.15)**	**2.26 (1.62, 3.14)**		
No	Low SFAs (<7.14 g/day)	728/3,120	1.00	1.00	RERI: 0.17 (-0.73, 1.07)	ROR: 0.99 (0.62, 1.59)
No	High SFAs (≥7.14 g/day)	983/3,050	**1.26 (1.06, 1.49)**	**1.19 (1.02, 1.39)**	rRERI: 0.43 (-0.45, 1.31)	rROR: 1.16 (0.73, 1.83)
Yes	Low SFAs (<7.14 g/day)	71/146	**1.77 (1.21, 2.58)**	**1.64 (1.18, 2.28)**		
Yes	High SFAs (≥7.14 g/day)	118/216	**2.20 (1.60, 3.03)**	**2.26 (1.62, 3.16)**		
No	Low MUFAs (<9.85 g/day)	720/3,111	1.00	1.00	RERI: 0.36 (-0.55, 1.28)	ROR: 1.07 (0.66, 1.71)
No	High MUFAs (≥9.85 g/day)	991/3,059	**1.31 (1.11, 1.55)**	**1.20 (1.03, 1.40)**	rRERI: 0.34 (-0.53, 1.22)	rROR: 1.10 (0.70, 1.75)
Yes	Low MUFAs (<9.85 g/day)	71/155	**1.70 (1.16, 2.47)**	**1.67 (1.20, 2.33)**		
Yes	High MUFAs (≥9.85 g/day)	118/207	**2.37 (1.72, 3.26)**	**2.22 (1.59, 3.09)**		
No	Low PUFAs (<6.93 g/day)	763/3,122	1.00	1.00	RERI: 0.33 (-0.54, 1.20)	ROR: 1.10 (0.68, 1.79)
No	High PUFAs (≥6.93 g/day)	948/3,048	**1.20 (1.00,1.43)**	1.04 (0.90, 1.21)	rRERI: 0.56 (-0.24, 1.37)	rROR: 1.35 (0.85, 2.14)
Yes	Low PUFAs (<6.93 g/day)	63/144	**1.65 (1.12, 2.44)**	**1.50 (1.06, 2.12)**		
Yes	High PUFAs (≥6.93 g/day)	126/218	**2.18 (1.59, 3.00)**	**2.10 (1.53, 2.89)**		
No	Low n-6 PUFAs (<5.97 g/day)	779/3,118	1.00	1.00	RERI: 0.49 (-0.33, 1.32)	ROR: 1.26 (0.78, 2.04)
No	High n-6 PUFAs (≥5.97 g/day)	932/3,052	1.11 (0.93, 1.32)	1.02 (0.88, 1.18)	rRERI: 0.31 (-0.48, 1.10)	rROR: 1.18 (0.75, 1.88)
Yes	Low n-6 PUFAs (<5.97 g/day)	63/148	**1.52 (1.03, 2.24)**	**1.61 (1.15, 2.26)**		
Yes	High n-6 PUFAs (≥5.97 g/day)	126/214	**2.12 (1.54, 2.92)**	**1.94 (1.40, 2.68)**		
No	Low n-3 PUFAs (<0.96 g/day)	735/3,121	1.00	1.00	RERI: 0.55 (-0.34, 1.44)	ROR: 1.20 (0.74, 1.96)
No	High n-3 PUFAs (≥0.96 g/day)	976/3,049	**1.27 (1.07, 1.51)**	1.08 (0.93, 1.25)	rRERI: 0.60 (-0.22, 1.41)	rROR: 1.35 (0.85, 2.15)
Yes	Low n-3 PUFAs (<0.96 g/day)	60/145	**1.56 (1.05, 2.33)**	**1.49 (1.04, 2.12)**		
Yes	High n-3 PUFAs (≥0.96 g/day)	129/217	**2.38 (1.74, 3.26)**	**2.16 (1.57, 2.96)**		
No	Low Cholesterol (<207.21 mg/day)	741/3,066	1.00	1.00	RERI: 0.46 (-0.51, 1.42)	ROR: 1.09 (0.69, 1.73)
No	High Cholesterol (≥207.21 mg/day)	970/3,104	**1.36 (1.17, 1.59)**	**1.33 (1.14, 1.55)**	rRERI: 0.99 (-0.15, 2.13)	rROR: 1.38 (0.86, 2.22)
Yes	Low Cholesterol (<207.21 mg/day)	95/200	**1.69 (1.22, 2.33)**	**1.58 (1.17, 2.12)**		
Yes	High Cholesterol (≥207.21 mg/day)	94/162	**2.51 (1.78, 3.53)**	**2.90 (1.99, 4.21)**		
No	High Total Flavonoids (≥48.08mg/day)	889/3,062	1.00	1.00	RERI: 0.01 (-0.80, 0.81)	ROR: 0.99 (0.62, 1.57)

No	Low Total Flavonoids (<48.08mg/day)	822/3,108	1.03 (0.88, 1.20)	0.94 (0.81, 1.10)	rRERI: -0.51 (-1.28, 0.27)	rROR: 0.76 (0.48, 1.21)
Yes	High Total Flavonoids (≥48.08mg/day)	105/204	**1.76 (1.29, 2.41)**	**1.99 (1.45, 2.74)**		
Yes	Low Total Flavonoids (<48.08mg/day)	84/158	**1.80 (1.26, 2.56)**	**1.42 (1.01, 2.03)**		
No	High Flavonols (≥8.86mg/day)	870/3,085	1.00	1.00	RERI: 0.14 (-0.67, 0.96)	ROR: 1.04 (0.66, 1.66)
No	Low Flavonols (<8.86mg/day)	841/3,085	1.08 (0.93, 1.27)	1.06 (0.92, 1.24)	rRERI: -0.50 (-1.36, 0.36)	rROR: 0.74 (0.47, 1.18)
Yes	High Flavonols (≥8.86mg/day)	86/181	**1.72 (1.22, 2.41)**	**2.09 (1.47, 2.95)**		
Yes	Low Flavonols (<8.86mg/day)	103/181	**1.95 (1.40, 2.71)**	**1.65 (1.19, 2.28)**		
No	Low Flavones (<3.50mg/day)	767/3,096	1.00	1.00	RERI: 0.49 (-0.37, 1.35)	ROR: 1.19 (0.75, 1.90)
No	High Flavones (≥3.50mg/day)	944/3,074	**1.21 (1.04, 1.41)**	**1.17 (1.01, 1.36)**	rRERI: 0.44 (-0.43, 1.31)	rROR: 1.18 (0.74, 1.86)
Yes	Low Flavones (<3.50mg/day)	73/170	**1.58 (1.10, 2.26)**	**1.62 (1.17, 2.24)**		
Yes	High Flavones (≥3.50mg/day)	116/192	**2.27 (1.66, 3.12)**	**2.23 (1.60, 3.11)**		
No	Flavanones	591/2,432	1.00	1.00	RERI: 0.51 (-0.31, 1.34)	ROR: 1.26 (0.78, 2.02)
No	No Flavanones	1120/3,738	1.13 (0.97, 1.32)	1.12 (0.96, 1.31)	rRERI: 0.47 (-0.35, 1.29)	rROR: 1.23 (0.77, 1.98)
Yes	Flavanones	66/178	**1.53 (1.05, 2.22)**	**1.55 (1.06, 2.26)**		
Yes	No Flavanones	123/184	**2.17 (1.59, 2.96)**	**2.14 (1.57, 2.92)**		
No	Low Flavan_3_ols (<4.50 mg/day)	829/3,108	1.00	1.00	RERI: -0.02 (-0.82, 0.78)	ROR: 0.97 (0.61, 1.54)
No	High Flavan_3_ols (≥4.50 mg/day)	882/3,062	1.04 (0.90, 1.21)	1.07 (0.92, 1.25)	rRERI: -0.34 (-1.18, 0.50)	rROR: 0.81 (0.51, 1.28)
Yes	Low Flavan_3_ols (<4.50 mg/day)	88/158	**1.79 (1.27, 2.51)**	**1.98 (1.40, 2.79)**		
Yes	High Flavan_3_ols (≥4.50 mg/day)	101/204	**1.80 (1.30, 2.50)**	**1.71 (1.23, 2.37)**		
No	Low Anthocyanidins (<3.13 mg/day)	826/3,074	1.00	1.00	RERI: -0.03 (-0.85, 0.79)	ROR: 0.94 (0.60, 1.49)
No	High Anthocyanidins (≥3.13 mg/day)	885/3,096	1.10 (0.94, 1.29)	1.01 (0.86, 1.19)	rRERI: 0.19 (-0.66, 1.04)	rROR: 1.11 (0.68, 1.78)
Yes	Low Anthocyanidins (<3.13 mg/day)	97/192	**1.80 (1.30, 2.48)**	**1.70 (1.27, 2.27)**		
Yes	High Anthocyanidins (≥3.13 mg/day)	92/170	**1.87 (1.33, 2.63)**	**1.90 (1.29, 2.79)**		
No	High Isoflavonoids (≥15.94 mg/day)	860/3,056	1.00	1.00	RERI: -0.11 (-0.95, 0.74)	ROR: 0.91 (0.56, 1.46)
No	Low Isoflavonoids (<15.94 mg/day)	851/3,114	1.10 (0.94, 1.30)	1.03 (0.84, 1.26)	rRERI: -0.01 (-0.30, 0.28)	rROR: 0.99 (0.76, 1.29)

Yes	High Isoflavonoids (≥15.94 mg/day)	121/210	**1.82 (1.36, 2.45)**	1.18 (0.93, 1.50)
Yes	Low Isoflavonoids (<15.94 mg/day)	68/152	**1.82 (1.24, 2.67)**	1.20 (0.94, 1.52)

Notes: aOR: adjusted odds ratios; rOR: adjusted odds ratios with residual methods; SFAs: Saturated fatty acids; MUFAs: Monounsaturated fatty acids; PUFAs: Polyunsaturated fatty acids; RERI, relative excess risk due to interaction; ROR, ratio of odds ratios; rRERI, relative excess risk due to interaction with residual methods; rROR, ratio of odds ratios with residual methods; Ca/Co: Cases/Controls; Numbers in bold face indicate statistically significant.

[a] Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income 10 years ago (<1000, 1000 to <1500, 1500 to<2500, ≥2500), smoking (continuous, pack-years), alcohol consumption (continuous, g ethanol/day), *H. pylori* infection (positive/negative), BMI (<18.5, 18.5 to <24, 24 to <28, ≥28), exercise 10 years ago (yes/no), dietary sodium intake (quartile levels of raw and energy-adjusted values), total energy intake (continuous, kcal/day).

Table 3.14. Mediation effects of the modifiable risk factors on the relationships between dietary fatty acids, cholesterol (High vs. Low) and stomach cancer

	NDE OR (95%CI)[a]	NIE OR (95%CI)[a]	Total Effect	Mediated (%)	*p* for NIE
Total fatty acids and SC					
Tobacco smoking	**1.30 (1.09, 1.50)**	1.00 (0.99, 1.01)	**1.30 (1.09, 1.51)**	1.1	0.62
Alcohol drinking	**1.30 (1.09, 1.52)**	1.00 (0.99, 1.00)	**1.30 (1.09, 1.52)**	Not mediated	-
H. pylori infection	**1.31 (1.09, 1.53)**	1.01 (1.00, 1.01)	**1.32 (1.10, 1.54)**	2.4	0.20
Dietary sodium intake	**1.40 (1.16, 1.63)**	0.98 (0.93, 1.04)	**1.37 (1.15, 1.59)**	Not mediated	-
SFAs and SC					
Tobacco smoking	**1.25 (1.05, 1.45)**	1.00 (0.99, 1.01)	**1.25 (1.05, 1.45)**	1.8	0.46
Alcohol drinking	**1.25 (1.04, 1.45)**	1.00 (1.00, 1.00)	**1.25 (1.04, 1.45)**	Not mediated	-
H. pylori infection	**1.26 (1.05, 1.47)**	1.01 (1.00, 1.02)	**1.27 (1.05, 1.48)**	3.8	0.12
Dietary sodium intake	**1.32 (1.10, 1.54)**	0.99 (0.94, 1.05)	**1.31 (1.10, 1.52)**	Not mediated	-
MUFAs and SC					
Tobacco smoking	**1.31 (1.10, 1.52)**	1.00 (0.99, 1.01)	**1.31 (1.11, 1.52)**	1.1	0.60
Alcohol drinking	**1.30 (1.09, 1.51)**	1.00 (1.00, 1.00)	**1.30 (1.09, 1.51)**	Not mediated	-
H. pylori infection	**1.32 (1.10, 1.53)**	1.01 (1.00, 1.01)	**1.33 (1.11, 1.54)**	2.5	0.17
Dietary sodium intake	**1.40 (1.17, 1.63)**	0.98 (0.93, 1.04)	**1.37 (1.16, 1.59)**	Not mediated	-
PUFAs and SC					
Tobacco smoking	1.17 (0.98, 1.37)	1.00 (0.99, 1.01)	1.17 (0.98, 1.37)	Not mediated	-
Alcohol drinking	1.20 (0.99, 1.41)	1.00 (0.99, 1.00)	1.20 (0.99, 1.40)	Not mediated	-
H. pylori infection	**1.21 (1.00, 1.42)**	1.00 (0.99. 1.01)	**1.21 (1.00, 1.42)**	2.2	0.4
Dietary sodium intake	**1.28 (1.06, 1.50)**	1.00 (0.94, 1.07)	**1.28 (1.07, 1.49)**	1.0	0.95
n-6 PUFAs and SC					
Tobacco smoking	1.11 (0.93, 1.29)	1.00 (0.99, 1.01)	1.11 (0.93, 1.29)	Not mediated	-
Alcohol drinking	1.13 (0.93, 1.32)	1.00 (0.99, 1.00)	1.13 (0.93, 1.32)	Not mediated	-
H. pylori infection	1.13 (0.94, 1.33)	1.00 (1.00, 1.01)	1.14 (0.94, 1.33)	4.1	0.32
Dietary sodium intake	**1.21 (1.00, 1.42)**	0.99 (0.93, 1.05)	**1.20 (1.00, 1.40)**	Not mediated	-
n-3 PUFAs and SC					
Tobacco smoking	**1.28 (1.08, 1.48)**	1.00 (0.99, 1.01)	**1.28 (1.08, 1.48)**	Not mediated	-
Alcohol drinking	**1.27 (1.06, 1.48)**	1.00 (1.00, 1.00)	**1.27 (1.06, 1.48)**	0.0	0.97
H. pylori infection	**1.29 (1.08, 1.51)**	1.01 (1.00, 1.02)	**1.30 (1.09, 1.52)**	2.4	0.28
Dietary sodium intake	**1.37 (1.14, 1.60)**	0.99 (0.93, 1.05)	**1.36 (1.14, 1.57)**	Not mediated	-
Cholesterol and SC					
Tobacco smoking	**1.35 (1.15, 1.54)**	1.00 (0.99, 1.01)	**1.35 (1.15, 1.54)**	0.1	0.96
Alcohol drinking	**1.39 (1.18, 1.59)**	1.00, 0.99, 1.00)	**1.39 (1.18, 1.59)**	Not mediated	-
H. pylori infection	**1.37 (1.17, 1.57)**	1.00 (1.00, 1.01)	**1.37 (1.17, 1.58)**	1.1	0.31
Dietary sodium intake	**1.40 (1.19, 1.61)**	1.01 (0.97, 1.06)	**1.42 (1.22, 1.63)**	4.1	0.6

Notes: NDE, natural direct effect; NIE, natural indirect effect. Not mediated: natural direct or indirect effect to be larger than the total effect, the proportion mediated is not meaningful; Numbers in bold face indicate statistically significant.

[a] Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income 10 years ago (<1000, 1000 to <1500, 1500 to<2500, ≥2500), smoking (continuous, pack-years), alcohol consumption (continuous, g ethanol/day), *H. pylori* infection (positive/negative), family history of stomach cancer (yes/no), BMI (<18.5, 18.5 to <24, 24 to <28, ≥28), exercise 10 years ago (yes/no), dietary sodium intake (quartile levels), total energy intake (continuous, kcal/day), except for the corresponding variables used for mediation.

Table 3.15. Mediation effects of the modifiable risk factors on the relationships between dietary fatty acids, cholesterol (High vs. Low) and stomach cancer using residual methods

	rNDE OR (95%CI)[a]	rNIE OR (95%CI)[a]	Total Effect	Mediated (%)	*p* for rNIE
Total Fatty acids and SC					
Tobacco smoking	1.16 (1.00, 1.32)	1.00 (0.99, 1.01)	1.16 (1.00, 1.32)	Not mediated	-
Alcohol drinking	1.14 (0.97, 1.30)	1.00 (0.99, 1.01)	1.13 (0.97, 1.30)	Not mediated	-
H. pylori infection	1.16 (0.99, 1.33)	1.00 (1.00, 1.01)	1.16 (0.99, 1.33)	1.8	0.45
Dietary sodium intake	**1.20 (1.02, 1.38)**	1.02 (0.96, 1.09)	1.23 (1.06, 1.40)	12.9	0.44
SFAs and SC					
Tobacco smoking	**1.21 (1.04, 1.38)**	1.00 (0.98, 1.01)	**1.20 (1.03, 1.37)**	Not mediated	-
Alcohol drinking	**1.18 (1.01, 1.35)**	1.00 (0.99, 1.01)	**1.18 (1.00, 1.35)**	Not mediated	-
H. pylori infection	**1.21 (1.03, 1.39)**	1.00 (1.00, 1.01)	**1.21 (1.03, 1.39)**	1.2	0.57
Dietary sodium intake	**1.26 (1.07, 1.45)**	1.01 (0.95, 1.07)	**1.27 (1.09, 1.45)**	4.2	0.76
MUFAs and SC					
Tobacco smoking	**1.21 (1.04, 1.38)**	1.00 (0.98, 1.01)	**1.20 (1.03, 1.37)**	Not mediated	-
Alcohol drinking	**1.18 (1.01, 1.36)**	1.00 (0.99, 1.00)	**1.18 (1.01, 1.35)**	Not mediated	-
H. pylori infection	**1.22 (1.04, 1.39)**	1.00 (0.99, 1.01)	**1.22 (1.04, 1.40)**	1.1	0.63
Dietary sodium intake	**1.26 (1.07, 1.45)**	1.01 (0.96, 1.07)	**1.28 (1.10, 1.46)**	6.7	0.62
PUFAs and SC					
Tobacco smoking	1.08 (0.93, 1.23)	0.99 (0.98, 1.01)	1.07 (0.92, 1.22)	Not mediated	-
Alcohol drinking	1.06 (0.91, 1.22)	1.00 (1.00, 1.01)	1.06 (0.91, 1.22)	2.0	0.57
H. pylori infection	1.07 (0.92, 1.22)	1.00 (0.99, 1.01)	1.07 (0.92, 1.23)	2.2	0.68
Dietary sodium intake	1.13 (0.96, 1.30)	1.01 (0.94, 1.08)	1.14 (0.99, 1.30)	9.6	0.72
n-6 PUFAs and SC					
Tobacco smoking	1.05 (0.90, 1.19)	0.99 (0.98, 1.01)	1.04 (0.90, 1.18)	Not mediated	-
Alcohol drinking	1.03 (0.88, 1.18)	1.00 (1.00, 1.00)	1.03 (0.88, 1.18)	2.6	0.64
H. pylori infection	1.03 (0.88, 1.18)	1.00 (1.00, 1.01)	1.03 (0.88, 1.18)	5.1	0.59
Dietary sodium intake	1.08 (0.92, 1.24)	1.03 (0.96, 1.10)	1.11 (0.96, 1.26)	26.9	0.43
n-3 PUFAs and SC					
Tobacco smoking	1.12 (0.97, 1.28)	0.99 (0.98, 1.01)	1.12 (0.96, 1.27)	Not mediated	-
Alcohol drinking	1.07 (0.92, 1.23)	1.00 (0.99, 1.01)	1.07 (0.91, 1.22)	Not mediated	-
H. pylori infection	1.11 (0.95, 1.27)	1.00 (0.99, 1.01)	1.11(0.95, 1.27)	2.0	0.60
Dietary sodium intake	1.15 (0.98, 1.32)	1.02 (0.96, 1.09)	1.18 (1.01, 1.34)	15.7	0.47
Cholesterol and SC					
Tobacco smoking	**1.32 (1.13, 1.50)**	1.00 (0.99, 1.01)	**1.32 (1.13, 1.50)**	Not mediated	-
Alcohol drinking	**1.36 (1.17, 1.56)**	1.00 (1.00, 1.00)	**1.36 (1.17, 1.56)**	Not mediated	-
H. pylori infection	**1.37 (1.17, 1.57)**	1.00 (1.00, 1.01)	**1.37 (1.17, 1.57)**	1.5	0.27
Dietary sodium intake	**1.39 (1.19, 1.60)**	1.02 (0.98, 1.06)	**1.42 (1.22, 1.62)**	6.7	0.31

Notes: rNDE, natural direct effect with residual methods; rNIE, natural indirect effect with residual methods; SFAs: Saturated fatty acids; MUFAs: Monounsaturated fatty acids; PUFAs: Polyunsaturated fatty acids. Not mediated: natural direct or indirect effect to be larger than the total effect, the proportion mediated is not meaningful; Numbers in bold face indicate statistically significant.

[a] Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income 10 years ago (<1000, 1000 to <1500, 1500 to<2500, ≥2500), smoking (continuous, pack-years), alcohol consumption (continuous, g ethanol/day), *H. pylori* infection (positive/negative), family history of stomach cancer (yes/no), BMI (<18.5, 18.5 to <24, 24 to <28, ≥28), exercise 10 years ago (yes/no), dietary sodium intake (quartile levels), total energy intake (continuous, kcal/day), except for the corresponding variables used for mediation.

Table 3.16. Mediation effects of the modifiable risk factors on the relationships between dietary flavonoids (High vs. Low) and stomach cancer

	NDE OR (95%CI)[a]	NIE OR (95%CI)[a]	Total Effect	Mediated (%)	*p* for NIE
Total flavonoids and SC					
Tobacco smoking	1.00 (0.86, 1.14)	**1.03 (1.00, 1.05)**	1.02 (0.88, 1.17)	Not mediated	-
Alcohol drinking	1.00 (0.85, 1.15)	0.99 (0.97, 1.01)	0.99 (0.84, 1.14)	76.9	0.33
H. pylori infection	0.97 (0.82, 1.12)	1.00 (1.00, 1.01)	0.97 (0.83, 1.12)	Not mediated	-
Dietary sodium intake	1.01 (0.86, 1.16)	1.02 (0.98, 1.05)	1.02 (0.87, 1.17)	61.9	0.42
Flavonols and SC					
Tobacco smoking	0.96 (0.83, 1.10)	**1.03 (1.01, 1.06)**	0.99 (0.85, 1.14)	Not mediated	-
Alcohol drinking	0.95 (0.80, 1.09)	1.00 (0.98, 1.01)	0.94 (0.80, 1.08)	7.9	0.61
H. pylori infection	0.92 (0.78, 1.06)	1.00 (1.00, 1.01)	0.92 (0.78, 1.06)	Not mediated	-
Dietary sodium intake	0.93 (0.79, 1.07)	**1.05 (1.00, 1.10)**	0.98 (0.83, 1.12)	Not mediated	-
Flavones and SC					
Tobacco smoking	**1.21 (1.04, 1.38)**	**1.02 (1.00,1.03)**	**1.23 (1.06, 1.41)**	**8.8**	**0.03**
Alcohol drinking	**1.23 (1.05, 1.42)**	1.00 (0.99, 1.00)	**1.23 (1.05, 1.41)**	Not mediated	-
H. pylori infection	**1.23 (1.04, 1.41)**	1.00 (0.99, 1.01)	**1.23 (1.05, 1.41)**	1.0	0.63
Dietary sodium intake	**1.30 (1.10, 1.49)**	0.99 (0.95, 1.04)	**1.29 (1.10, 1.47)**	Not mediated	-
Flavanones and SC					
Tobacco smoking	0.89 (0.77, 1.02)	1.01 (1.00, 1.02)	0.90 (0.77, 1.03)	Not mediated	-
Alcohol drinking	**0.86 (0.74, 0.99)**	1.00 (1.00, 1.01)	**0.87 (0.74, 0.99)**	Not mediated	-
H. pylori infection	**0.86 (0.74, 0.99)**	1.00 (1.00, 1.00)	**0.86 (0.74, 0.99)**	Not mediated	-
Dietary sodium intake	**0.86 (0.73, 0.98)**	1.00 (0.98, 1.01)	**0.85 (0.73, 0.98)**	2.9	0.43
Flavan_3_ols and SC					
Tobacco smoking	1.02 (0.88, 1.16)	**1.03 (1.01, 1.05)**	1.05 (0.90, 1.19)	**59.8**	**0.01**
Alcohol drinking	1.07 (0.91, 1.22)	0.99 (0.97, 1.01)	1.06 (0.91, 1.21)	Not mediated	-
H. pylori infection	1.04 (0.89, 1.19)	1.00 (0.99, 1.00)	1.04 (0.89, 1.18)	Not mediated	-
Dietary sodium intake	1.05 (0.90, 1.20)	1.04 (1.00, 1.07)	1.09 (0.93, 1.24)	43.0	0.06
Anthocyanidins and SC					
Tobacco smoking	1.05 (0.89, 1.21)	1.01 (1.00, 1.02)	1.06 (0.90, 1.22)	10.6	0.21
Alcohol drinking	1.10 (0.93, 1.27)	1.00 (0.99, 1.00)	1.10 (0.93, 1.27)	Not mediated	-
H. pylori infection	1.09 (0.92, 1.26)	1.00 (1.00, 1.01)	1.10 (0.92, 1.27)	2.1	0.51
Dietary sodium intake	1.13 (0.94, 1.32)	1.05 (0.95, 1.14)	**1.18 (1.02, 1.35)**	27.9	0.32
Isoflavonoids and SC					
Tobacco smoking	0.94 (0.80, 1.09)	0.99 (0.98, 1.00)	0.94 (0.80, 1.08)	11.2	0.23
Alcohol drinking	0.93 (0.79, 1.08)	1.00 (1.00, 1.00)	0.93 (0.79, 1.08)	1.3	0.62
H. pylori infection	0.91 (0.77, 1.06)	1.00 (1.00, 1.01)	0.92 (0.77, 1.06)	Not mediated	-
Dietary sodium intake	1.01 (0.84, 1.17)	0.98 (0.92, 1.04)	0.99 (0.84, 1.14)	Not mediated	-

Notes: NDE, natural direct effect; NIE, natural indirect effect. Not mediated: natural direct or indirect effect to be larger than the total effect, the proportion mediated is not meaningful; Numbers in bold face indicate statistically significant.

[a] Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income 10 years ago (<1000, 1000 to <1500, 1500 to<2500, ≥2500), smoking (continuous, pack-years), alcohol consumption (continuous, g ethanol/day), *H. pylori* infection (positive/negative), family history of stomach cancer (yes/no), BMI (<18.5, 18.5 to <24, 24 to <28, ≥28), exercise 10 years ago (yes/no), dietary sodium intake (quartile levels), total energy intake (continuous, kcal/day), except for the corresponding variables used for mediation.

Table 3.17. Mediation effects of the modifiable risk factors on the relationships between dietary flavonoids (High vs. Low) and stomach cancer using residual methods

	rNDE OR (95%CI)[a]	rNIE OR (95%CI)[a]	Total Effect	Mediated (%)	*p* for rNIE
Total flavonoids and SC					
Tobacco smoking	1.09 (0.94, 1.24)	**1.02 (1.00, 1.04)**	1.11 (0.96, 1.27)	**19.2**	**0.04**
Alcohol drinking	1.11 (0.95, 1.27)	0.99 (0.97, 1.01)	1.10 (0.94, 1.25)	Not mediated	-
H. pylori infection	1.08 (0.93, 1.24)	1.00 (1.00, 1.01)	1.09 (0.93, 1.24)	2.4	0.45
Dietary sodium intake	1.11 (0.95, 1.27)	1.04 (0.99, 1.08)	1.15 (0.99, 1.31)	28.5	0.08
Flavonols and SC					
Tobacco smoking	0.99 (0.86, 1.13)	**1.03 (1.00, 1.05)**	1.02 (0.88, 1.16)	Not mediated	-
Alcohol drinking	0.98 (0.84, 1.12)	1.00 (0.98, 1.02)	0.98 (0.84, 1.12)	10.7	0.82
H. pylori infection	0.96 (0.83, 1.10)	1.00 (1.00, 1.01)	0.97 (0.83, 1.11)	Not mediated	-
Dietary sodium intake	0.98 (0.84, 1.12)	**1.05 (1.01, 1.09)**	1.03 (0.88, 1.17)	Not mediated	-
Flavones and SC					
Tobacco smoking	**1.16 (1.00, 1.31)**	**1.02 (1.00, 1.03)**	**1.18 (1.02, 1.34)**	**10.5**	**0.03**
Alcohol drinking	**1.20 (1.03, 1.36)**	1.00 (0.99, 1.01)	**1.19 (1.03, 1.36)**	Not mediated	-
H. pylori infection	**1.19 (1.02, 1.36)**	1.01 (1.00, 1.02)	**1.20 (1.03, 1.37)**	3.9	0.15
Dietary sodium intake	**1.21 (1.04, 1.38)**	1.03 (0.99, 1.08)	**1.25 (1.08, 1.42)**	15.5	0.14
Flavanones and SC					
Tobacco smoking	**0.87 (0.74, 0.99)**	1.01 (0.99, 1.02)	**0.87 (0.74, 1.00)**	Not mediated	-
Alcohol drinking	**0.87 (0.74, 1.00)**	1.00 (0.99, 1.00)	**0.87 (0.74, 1.00)**	1.4	0.53
H. pylori infection	0.87 (0.74, 1.00)	1.00 (1.00, 1.01)	0.87 (0.74, 1.01)	Not mediated	-
Dietary sodium intake	0.88 (0.74, 1.00)	**1.02 (1.00, 1.04)**	0.89 (0.76, 1.03)	Not mediated	-
Flavan_3_ols and SC					
Tobacco smoking	1.02 (0.87, 1.16)	**1.03 (1.01, 1.05)**	1.05 (0.90, 1.20)	**59.3**	**0.01**
Alcohol drinking	1.08 (0.92, 1.24)	0.99 (0.97, 1.01)	1.07 (0.91, 1.22)	Not mediated	-
H. pylori infection	1.04 (0.89, 1.20)	1.00 (0.99, 1.00)	1.04 (0.89, 1.20)	Not mediated	-
Dietary sodium intake	1.06 (0.90, 1.22)	1.03 (1.00, 1.06)	1.09 (0.93, 1.25)	36.0	0.05
Anthocyanidins and SC					
Tobacco smoking	0.97 (0.82, 1.12)	1.00 (0.99, 1.01)	0.97 (0.82, 1.13)	Not mediated	-
Alcohol drinking	1.00 (0.84, 1.16)	1.00 (1.00, 1.00)	1.00 (0.84, 1.16)	Not mediated	-
H. pylori infection	1.02 (0.86, 1.18)	1.00 (1.00, 1.01)	1.02 (0.86, 1.19)	8.4	0.54
Dietary sodium intake	0.97 (0.80, 1.14)	**1.16 (1.04, 1.28)**	1.13 (0.96, 1.29)	Not mediated	-
Isoflavonoids and SC					
Tobacco smoking	0.98 (0.84, 1.11)	0.99 (0.98, 1.00)	0.97 (0.83, 1.10)	27.1	0.18
Alcohol drinking	0.98 (0.84, 1.11)	1.00 (1.00, 1.00)	0.98 (0.84, 1.11)	Not mediated	-
H. pylori infection	0.97 (0.83, 1.11)	1.01 (1.00, 1.02)	0.98 (0.84, 1.12)	Not mediated	-
Dietary sodium intake	1.04 (0.88, 1.19)	1.01 (0.94, 1.07)	1.05 (0.91, 1.19)	17.7	0.82

Notes: rNDE, natural direct effect with residual methods; rNIE, natural indirect effect with residual methods. Not mediated: natural direct or indirect effect to be larger than the total effect, the proportion mediated is not meaningful; Numbers in bold face indicate statistically significant.

[a] Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income 10 years ago (<1000, 1000 to <1500, 1500 to<2500, ≥2500), smoking (continuous, pack-years), alcohol consumption (continuous, g ethanol/day), *H. pylori* infection (positive/negative), family history of stomach cancer (yes/no), BMI (<18.5, 18.5 to <24, 24 to <28, ≥28), exercise 10 years ago (yes/no), dietary sodium intake (quartile levels), total energy intake (continuous, kcal/day), except for the corresponding variables used for mediation.

Table 4.1. Demographic characteristics and main risk factors of stomach cancer and population controls (Cases=1,327, Controls=6,056)

Variables	Cases (n=1,327) n	Cases (n=1,327) %	Controls (n=6,056) n	Controls (n=6,056) %	*p*-value*
County					
Dafeng	498	37.5	2387	39.4	
Ganyu	328	24.7	1755	29	<0.001
Chuzhou	404	30.4	1039	17.2	
Tongshan	97	7.3	875	14.5	
Gender					
Male	1010	76.1	4382	72.4	0.005
Female	317	23.9	1674	27.6	
Age					
<50	128	9.7	648	10.7	
50-59	286	21.6	1366	22.6	0.12
60-69	478	36	1977	32.7	
≥70	435	32.8	2065	34.1	
Mean (SD)	63.9	10.5	63.8	11.1	0.84
Education					
Illiterate	659	49.8	2943	48.7	
Primary school	460	34.7	1902	31.5	0.001
Middle school	169	12.8	941	15.6	
High school or above	31	2.7	223	4.3	
Income 10 years ago (Yuan/year)					
<1000	315	24.4	1265	21.2	
1000-1499	261	20.2	1124	18.8	0.003
1500-2499	351	27.2	1604	26.9	
≥2500	364	28.2	1979	33.1	
Body mass index (kg/m2)					
<18.5	229	17.3	374	6.2	
18.5-<24	898	68.0	3681	61.1	<0.001
24-<28	157	11.9	1617	26.8	
≥28	37	2.8	355	5.9	
Daily energy intake (kcal/day): Mean (SD)	2244.1	847.0	2145.6	808.2	<0.001
Tobacco smoking					
Never	469	35.3	2859	47.2	<0.001
Ever	858	64.7	3197	52.8	
Pack-years of tobacco smoking					
Never	469	38.8	2859	50.8	
1 to 19	155	12.8	700	12.4	<0.001
20-39	223	18.4	979	17.4	
≥40	363	30.0	1087	19.3	
Alcohol drinking					
Never	610	46.0	2941	48.6	
Ever	717	54.0	3115	51.4	0.09
Family history of stomach cancer					
No	1179	88.9	5708	94.3	<0.001

Yes	148	11.2	348	5.8	
Exercise ten years ago					
No	950	71.6	4298	71	0.65
Yes	377	28.4	1758	29	
H. pylori infection					
No	239	23.5	1499	29.7	<0.001
Yes	779	76.5	3546	70.3	

* Based on the chi-square test; t-test for the mean.

Table 4.2. Distribution and odds ratios of modified Chinese Healthy Eating Index (mCHEI) components for cases and controls

		Intakes per day		Per IQR increase	
mCHEI components	Unit	Cases (n=1,327)	Controls (n=6,056)	Model 1	Model 2
Total grains	g	492.6±205.2 (287.7)	482.3±199.2 (282.8)	0.92 (0.78, 1.09)	0.88 (0.71, 1.09)
Whole grains and mixed beans	g	9.05±13.5 (9.7)	9.21±18.0 (9.7)	0.99 (0.96, 1.03)	1.01 (0.97, 1.05)
Tubers***	g	15.9±24.8 (16.9)	18.2±28.5 (18.4)	0.96 (0.91, 1.01)	0.98 (0.92, 1.04)
Total vegetables	g	221.9±163.2 (173.3)	217.0±173.5 (178.7)	1.02 (0.95, 1.09)	1.05 (0.96, 1.14)
Dark vegetables	g	120.1±110.3 (114.6)	123.9±134.4 (113.9)	0.95 (0.90, 1.01)	0.95 (0.88, 1.02)
Fruits**	g	38.4±46.5 (37.2)	44.2±59.9 (42.8)	**0.93 (0.88, 0.98)**	0.97 (0.91, 1.03)
Dairy	g	5.35±23.8 (0.0)	5.45±26.5 (0.0)	1.01 (0.99, 1.02)	1.01 (0.99, 1.02)
Soybeans	g	76.3±79.0 (73.0)	72.2±74.6 (70.8)	1.03 (0.97, 1.09)	1.02 (0.95, 1.10)
Fish and seafood***	g	26.3±41.5 (24.7)	23.1±36.6 (22.7)	1.02 (0.99, 1.06)	1.04 (0.99, 1.09)
Red meat***	g	51.7±51.4 (48.8)	44.1±47.0 (43.8)	1.01 (0.95, 1.08)	1.01 (0.92, 1.10)
Poultry	g	3.17±6.8 (3.7)	3.66±10.4 (3.3)	**0.97 (0.94, 0.997)**	0.99 (0.95, 1.03)
Eggs	g	39.4±42.6 (36.1)	40.2±46.0 (36.3)	1.03 (0.97, 1.08)	**1.09 (1.02, 1.16)**
Seeds and nuts	g	7.09±16.4 (6.8)	6.90±12.4 (6.8)	1.02 (0.99, 1.05)	1.02 (0.98, 1.06)
Sodium**	mg	1746.5±2461.9 (1393.2)	1558.4±1638.8 (1404.3)	**1.06 (1.02, 1.12)**	**1.08 (1.02, 1.14)**
Added sugars	g	7.51±7.8 (5.0)	7.44±10.6 (5.0)	1.00 (0.98, 1.03)	1.02 (0.99, 1.05)
Alcohol***	g	32.7±50.4 (57.1)	26.9±44.9 (42.9)	**1.10 (1.04, 1.16)**	1.04 (0.96, 1.12)
Fat***	g	42.4±29.8 (30.7)	38.7±28.3 (30.1)	1.01 (0.93, 1.10)	1.03 (0.93, 1.14)

Value presented as mean ±SD (IQR); t-test for normal distribution and Mann-Whitney test for non-normal distribution (*p<.05, **p<.01, ***p<.001); Numbers in bold face indicate statistically significant.
Model 1: Adjusted for age, gender, county, total energy intake.
Model 2: Adjusted for model 1 in addition to tobacco smoking (yes vs. no), pack year of smoking, *H. pylori* infection status, family history of stomach cancer, body mass index (continuous), education level (illiterate, primary, middle, high school or above), and income ten years ago (continuous).

Table 4.3. Odds ratios and 95% confidence intervals for stomach cancer by each component of dietary recommendation adherence scores

	OR (95%CI)			
	mCHEI score		HEI-2015 score	
Components	Model 1	Model 2	Model 1	Model 2
Total grains	1.07 (0.91, 1.26)	0.97 (0.80, 1.19)		
Whole grains and mixed beans	1.03 (0.96, 1.10)	**1.11 (1.02, 1.22)**		
Tubers	**0.94 (0.89, 0.99)**	0.98 (0.92, 1.05)		
Total vegetables	1.05 (1.00, 1.10)	1.06 (1.00, 1.12)	1.03 (0.99, 1.08)	1.05 (0.99, 1.11)
Dark vegetables	0.99 (0.96, 1.03)	1.00 (0.95, 1.05)		
Total fruits	0.97 (0.94, 1.00)	1.00 (0.96, 1.05)	0.94 (0.88, 1.01)	1.01 (0.93, 1.10)
Dairy	1.07 (0.94, 1.23)	1.15 (0.96, 1.38)	1.04 (0.96, 1.13)	1.10 (0.98, 1.23)
Soybeans	1.02 (0.97, 1.07)	1.00 (0.94, 1.06)		
Fish and seafood	1.03 (0.99, 1.07)	1.05 (1.00, 1.11)		
Red meat	0.99 (0.88, 1.11)	0.94 (0.81, 1.10)		
Poultry	0.94 (0.87, 1.01)	0.97 (0.88, 1.07)		
Eggs	1.02 (0.98, 1.06)	**1.08 (1.02, 1.13)**		
Seeds and nuts	1.00 (0.97, 1.03)	0.99 (0.96, 1.04)		
Sodium	**0.96 (0.93, 0.99)**	**0.95 (0.91, 0.99)**	**0.97 (0.95, 0.99)**	**0.97 (0.94, 0.99)**
Added sugars	1.12 (0.83, 1.52)	0.92 (0.65, 1.32)	1.04 (0.90, 1.20)	0.95 (0.79, 1.14)
Alcohol	**0.95 (0.93, 0.98)**	0.99 (0.95, 1.03)		
Fat	1.00 (0.99, 1.02)	0.99 (0.97, 1.02)	0.97 (0.94, 1.01)	0.96 (0.92, 1.01)
Whole fruit			0.96 (0.92, 1.00)	1.01 (0.96, 1.07)
Greens and beans			0.98 (0.94, 1.03)	1.00 (0.94, 1.06)
Whole grains			1.01 (0.98, 1.05)	1.00 (0.95, 1.05)
Total protein foods			1.04 (0.98, 1.10)	1.04 (0.97, 1.11)
Seafood and plant proteins			1.03 (0.96, 1.10)	1.02 (0.94, 1.11)
Refined grains			0.97 (0.91, 1.03)	1.01 (0.93, 1.08)
Saturated fats			0.97 (0.90, 1.04)	0.92 (0.83, 1.02)

Note: mCHEI, modified Chinese Healthy Eating Index; HEI, Healthy Eating Index; Numbers in bold face indicate statistically significant.
Model 1: Adjusted for age, gender, county, total energy intake.
Model 2: Adjusted for model 1 in addition to tobacco smoking (yes vs. no), pack year of smoking, *H. pylori* infection status, family history of stomach cancer, body mass index (continuous), education level (illiterate, primary, middle, high school or above), and income ten years ago (continuous).

Table 4.4. Odds ratios and 95% confidence intervals for stomach cancer by quartiles of dietary recommendation adherence scores

	Quartiles of dietary recommendation adherence scores					
	I	II	III	IV	*p*-trend	per 10-point increase
mCHEI score						
Total population						
Case/Control	379/1514	337/1514	328/1514	283/1514		
Crude	1.00	0.89 (0.76, 1.05)	0.87 (0.73, 1.02)	**0.75 (0.63, 0.89)**	**0.001**	**0.83 (0.77, 0.90)**
Model 1	1.00	1.00 (0.84, 1.18)	1.04 (0.88, 1.24)	0.98 (0.82, 1.18)	0.98	0.96 (0.88, 1.05)
Model 2	1.00	1.05 (0.85, 1.29)	1.03 (0.83, 1.28)	1.18 (0.94, 1.48)	0.22	1.05 (0.94, 1.17)
HEI-2015 score						
Total population						
Case/Control	360/1514	282/1514	397/1514	288/1514		
Crude	1.00	**0.80 (0.68, 0.95)**	1.10 (0.94, 1.29)	**0.78 (0.66, 0.93)**	0.26	0.94 (0.86, 1.02)
Model 1	1.00	**0.77 (0.65, 0.92)**	1.09 (0.92, 1.28)	0.85 (0.71, 1.01)	0.65	0.96 (0.88, 1.05)
Model 2	1.00	**0.72 (0.58, 0.90)**	1.09 (0.89, 1.34)	0.87 (0.69, 1.08)	0.98	0.98 (0.87, 1.10)

Note: mCHEI, modified Chinese Healthy Eating Index; HEI, Healthy Eating Index; Numbers in bold face indicate statistically significant.
Model 1: Adjusted for age, gender (only for total population), county, total energy intake.
Model 2: Adjusted for model 1 in addition to tobacco smoking (yes vs. no), pack year of smoking, *H. pylori* infection status, family history of stomach cancer, body mass index (continuous), education level (illiterate, primary, middle, high school or above), and income ten years ago (continuous).

Table 4.5. Odds ratios and 95% confidence intervals for stomach cancer per 10-point increase of dietary recommendation adherence scores in stratified analyses

	mCHEI score			HEI-2015		
	Crude	Model 1	Model 2	Crude	Model 1	Model 2
Gender						
Female	0.95 (0.81, 1.13)	1.04 (0.87, 1.25)	1.10 (0.89, 1.37)	1.07 (0.89, 1.27)	1.05 (0.87, 1.26)	1.06 (0.84, 1.34)
Male	**0.81 (0.73, 0.89)**	0.94 (0.85, 1.04)	1.02 (0.89, 1.16)	**0.90 (0.81, 0.99)**	0.93 (0.84, 1.03)	0.94 (0.82, 1.07)
p for interaction			0.13			0.12
Tobacco smoking						
Non-smoker	**0.86 (0.75, 0.98)**	0.97 (0.84, 1.12)	1.07 (0.90, 1.28)	0.96 (0.84, 1.11)	0.96 (0.83, 1.11)	0.98 (0.82, 1.18)
Smoker	**0.84 (0.76, 0.93)**	0.97 (0.87, 1.09)	1.00 (0.87, 1.15)	**0.90 (0.80, 0.998)**	0.94 (0.84, 1.05)	0.94 (0.82, 1.09)
p for interaction			0.62			0.97
H. pylori infection						
Negative	**0.80 (0.66, 0.97)**	1.04 (0.85, 1.28)	1.14 (0.91, 1.43)	0.89 (0.73, 1.08)	0.95 (0.78, 1.17)	1.04 (0.83, 1.31)
Positive	**0.78 (0.70, 0.87)**	0.96 (0.85, 1.08)	1.02 (0.90, 1.16)	0.90 (0.80, 1.01)	0.93 (0.83, 1.06)	0.96 (0.84, 1.10)
p for interaction			0.57			0.68
Family history of stomach cancer						
No	**0.84 (0.77, 0.91)**	0.95 (0.87, 1.04)	1.03 (0.92, 1.16)	0.94 (0.86, 1.02)	0.96 (0.88, 1.05)	0.98 (0.88, 1.11)
Yes	0.87 (0.65, 1.16)	1.12 (0.82, 1.53)	1.24 (0.85, 1.82)	0.99 (0.73, 1.35)	1.16 (0.84, 1.60)	1.09 (0.74, 1.61)
p for interaction			0.64			0.83
Body mass index						
<24 (kg/m^2)	**0.81 (0.74, 0.88)**	0.94 (0.86, 1.04)	0.97 (0.86, 1.10)	0.92 (0.84, 1.01)	0.94 (0.85, 1.04)	0.91 (0.80, 1.04)
≥24 (kg/m^2)	1.00 (0.82, 1.23)	1.09 (0.87, 1.36)	1.29 (0.98, 1.69)	1.06 (0.85, 1.32)	1.06 (0.84, 1.32)	1.19 (0.89, 1.60)
p for interaction			**0.02**			0.09

Note: mCHEI, modified Chinese Healthy Eating Index; HEI, Healthy Eating Index; Numbers in bold face indicate statistically significant.
Model 1: Adjusted for age, gender, county, total energy intake.
Model 2: Adjusted for model 1 in addition to tobacco smoking (yes vs. no), pack year of smoking, *H. pylori* infection status, family history of stomach cancer, body mass index (continuous), education level, and income ten years ago, except for the corresponding variables used for stratification.

Table 4.6. Score and weighting of modified Chinese Healthy Eating Index (mCHEI) in the Jiangsu case-control study

Components	Weighting	Standard for maximum points	Standard for 0 points	Case (n=1,327)	Control (n=6,056)	*p*-value
Total grains	5	≥2.5SP/1000kcal	0	4.95±0.4 (0.0)	4.94±0.4 (0.0)	0.94[b]
Whole grains and mixed beans	5	≥0.6SP/1000kcal	0	0.69±0.9 (0.8)	0.70±0.9 (0.8)	0.92[a]
Tubers	5	≥0.3SP/1000kcal	0	1.11±1.3 (1.3)	1.32±1.4 (1.5)	**<0.001[a]**
Total vegetables	5	≥1.9SP/1000kcal	0	2.53±1.4 (2.0)	2.52±1.4 (2.1)	0.85[a]
Dark vegetables	5	≥0.9SP/1000kcal	0	2.61±1.6 (2.9)	2.66±1.6 (3.0)	0.36[a]
Fruits	10	≥1.1SP/1000kcal	0	1.59±1.8 (1.7)	1.83±2.0 (1.9)	**<0.001[a]**
Dairy	5	≥0.5SP/1000kcal	0	0.10±0.4 (0.0)	0.11±0.5 (0.0)	0.57[b]
Soybeans	5	≥0.4SP/1000kcal	0	4.32±1.3 (0.7)	4.28±1.3 (1.0)	0.26[a]
Fish and seafood	5	≥0.6SP/1000kcal	0	1.75±1.5 (2.0)	1.61±1.5 (1.9)	**0.003[a]**
Red meat	5	≤0.4SP/1000kcal	≥3.5SP/1000kcal	4.68±0.6 (0.4)	4.74±0.5 (0.3)	**<0.001[b]**
Poultry	5	≥0.3SP/1000kcal	0	0.49±0.8 (0.6)	0.54±0.9 (0.6)	0.47[b]
Eggs	5	≥0.5SP/1000kcal	0	2.87±1.8 (3.7)	2.96±1.8 (3.7)	0.09[a]
Seeds and nuts	5	≥0.4SP/1000kcal	0	2.19±1.9 (4.0)	2.25±2.0 (4.4)	0.30[a]
Sodium	10	≤1000mg/1000kcal	≥3608mg/1000kcal	9.29±1.8 (0.0)	9.36±1.8 (0.0)	0.19[a]
Added sugars	5	≤10% of energy	≥20% of energy	4.99±0.2 (0.0)	4.98±0.2 (0.0)	0.97[b]
Alcohol	5	≤25g(men)/15g (women)	≥60g(men)/ 40g (women)	3.45±2.2 (4.6)	3.69±2.1 (2.6)	**<0.001[a]**
Fat	10	≤15.6g/1000kcal	≥32.6g/1000kcal	7.30±3.5 (4.8)	7.51±3.4 (4.5)	**0.049[a]**
Total	100			54.3±7.3 (9.3)	55.3±7.3 (9.4)	**<0.001[a]**

Note: Value presented as mean ±SD (IQR); Numbers in bold face indicate statistically significant.
[a]: t-test was used for continuous variable with normal distribution; [b]: Mann-Whitney test was used for continuous variable with non-normal distribution.

Table 4.7. Score and weighting of Healthy Eating Index-2015 (HEI) in the Jiangsu case-control study

Components	Weighting	Standard for maximum points	Standard for 0 points	Case (n=1,327)	Control (n=6,056)	*p*-value
Total fruit	5	≥0.8 cup/1000kcal	0	0.85±0.9 (0.9)	0.98±1.0 (1.0)	**<0.001[a]**
Whole fruit	5	≥0.4 cup/1000kcal	0	1.56±1.4 (1.9)	1.75±1.5 (2.0)	**<0.001[a]**
Total vegetables	5	≥1.1 cup/1000kcal	0	3.14±1.4 (2.7)	3.15±1.4 (2.8)	0.96[a]
Greens and beans	5	≥0.2 cup/1000kcal	0	4.23±1.3 (1.3)	4.25±1.3 (1.2)	0.57[a]
Whole grains	10	≥1.5 oz/1000kcal	0	0.53±1.7 (0.04)	0.51±1.7 (0.0)	**0.002[b]**
Dairy	10	≥1.3 cup/1000kcal	0	0.16±0.6 (0.0)	0.16±0.8 (0.0)	0.57[b]
Total protein foods	5	≥2.5 oz/1000kcal	0	4.31±1.1 (1.1)	4.23±1.2 (1.4)	**0.03[a]**
Seafood and plant proteins	5	≥0.8 oz/1000kcal	0	4.60±0.9 (0.0)	4.57±1.0 (0.0)	0.20[a]
Fatty acids	10	(PUFAs + MUFAs)/SFAs ≥2.5	(PUFAs + MUFAs)/SFAs ≤1.2	8.46±1.8 (2.3)	8.52±1.7 (2.2)	0.32[a]
Refined grains	10	≤1.8 oz/1000 kcal	≥4.3 oz/1000 kcal	0.14±1.0 (0.0)	0.17±1.1 (0.0)	0.58[b]
Sodium	10	≤1.1 g/ 1000 kcal	≥2.0 g/1000 kcal	8.73±3.0 (0.0)	8.87±2.8 (0.0)	0.25[b]
Added Sugars	10	≤6.5% of energy	≥26% of energy	9.96±0.3 (0.0)	9.96±0.5 (0.0)	0.90[b]
Saturated fats	10	≤8% of energy	≥16% of energy	9.85±0.8 (0.0)	9.89±0.7 (0.0)	**0.002[b]**
Total				55.4±6.7 (8.6)	55.7±6.9 (8.7)	0.13[a]

Note: Value presented as mean ±SD (IQR); Numbers in bold face indicate statistically significant.
[a]: t-test was used for continuous variable with normal distribution; [b]: Mann-Whitney test was used for continuous variable with non-normal distribution.

Table 5.1. Demographic characteristics and main risk factors of stomach cancer and population controls among participants with genetic data (Cases=788, Controls=2,398)

	Cases (n=788)		Controls (n=2,398)		
	n	%	n	%	*p*-value
County					
Dafeng	494	62.7	2,002	83.5	
Ganyu	294	37.3	396	16.5	**<0.001**
Gender					
Male	592	75.1	1,728	72.1	
Female	196	24.9	670	27.9	0.09
Age					
<50	84	10.7	281	11.7	
50-<60	175	22.2	512	21.4	
60-<70	277	35.2	818	34.1	
≥70	252	32.0	787	32.8	0.78
Education					
Illiterate	386	49.0	1,051	43.8	
Primary school	270	34.3	846	35.3	
Middle school	108	13.7	376	15.7	
High school or above	22	2.8	125	5.2	
Missing	2	0.3	0	0.0	**<0.001**
Income 10 years ago (Yuan/year)					
<1000	191	24.2	373	15.6	
1000-<1500	167	21.2	433	18.1	
1500-<2500	205	26.0	700	29.2	
≥2500	212	26.9	876	36.5	
Missing	13	1.7	16	0.7	**<0.001**
Body mass index (kg/m^2)					
<18.5	134	17.0	185	7.7	
18.5-<24	527	66.9	1,483	61.8	
24-<28	88	11.2	590	24.6	
≥28	31	3.9	136	5.7	
Missing	8	1.0	4	0.2	**<0.001**
Tobacco smoking					
Never	253	32.1	965	40.2	
Ever	535	67.9	1,433	59.8	**<0.001**
Pack-years of tobacco smoking					
Never	253	32.1	965	40.2	
1-<20	108	13.7	373	15.6	
20-<40	154	19.5	457	19.1	
≥40	238	30.2	525	21.9	
Missing	34	4.4	78	3.3	**<0.001**
Alcohol consumption					
Never	321	40.7	1,025	42.7	
Ever	467	59.3	1,373	57.3	0.32
Grams ethanol/day in the 1990's					

Never	388	49.2	1,192	49.7	
Low-risk	49	6.2	219	9.1	
High-risk	349	44.3	979	40.8	
Missing	2	0.3	8	0.3	**0.049**
Family history of stomach cancer					
No	699	88.7	2,192	91.4	
Yes	89	11.3	206	8.6	**0.02**
H. pylori infection					
No	155	19.7	564	23.5	
Yes	519	65.9	1,759	73.4	
Missing	114	14.5	75	3.1	**<0.001**

[a]: Chi-square test for the frequency; T-test for the mean; Numbers in bold face indicate statistically significant.

[b]: Low-risk drinking: men (≤ 25g ethanol/day) and women (≤ 15g ethanol/day); High-risk drinking: men (>25g ethanol/day) and women (>15g ethanol/day based on the 2016 Chinese Dietary Guide.

Table 5.2. Comparison of demographics and main risk factors between including and excluding participants (Included=3,186 Excluded=7,049)

	Include (N=3,186)			Exclude (N=7,049)		
Variables	Cases, n (%)	Controls, n (%)	Total, n (%)	Cases, n (%)	Controls, n (%)	Total, n (%)
County						
Dafeng	494 (62.7)	2,002 (83.5)	*2,496 (78.3)*	150 (10.5)	534 (9.5)	*684 (9.7)*
Ganyu	294 (37.3)	396 (16.5)	*690 (21.7)*	276 (19.3)	1,614 (28.7)	*1,890 (26.8)*
Chuzhou	0 (0.0)	0 (0.0)	*0 (0.0)*	470 (32.9)	1,180 (21.0)	*1,650 (23.4)*
Tongshan	0 (0.0)	0 (0.0)	*0(0.0)*	532 (37.3)	2,293 (40.8)	*2,825 (40.1)*
Gender						
Male	592 (75.1)	1,728 (72.1)	*2,320 (72.8)*	1,040 (72.8)	4,039 (71.9)	*5,079 (72.1)*
Female	196 (24.9)	670 (27.9)	*866 (27.2)*	388 (27.2)	1,582 (28.1)	*1,970 (27.9)*
Age						
<50	84 (10.7)	281 (11.7)	*365 (11.5)*	153 (10.7)	603 (10.7)	*756 (10.7)*
50-<60	175 (22.2)	512 (21.4)	*687 (21.6)*	298 (20.9)	1,282 (22.8)	*1,580 (22.4)*
60-<70	277 (35.2)	818 (34.1)	*1,095 (34.4)*	468 (32.8)	1,747 (31.1)	*2,215 (31.4)*
≥70	252 (32.0)	787 (32.8)	*1,039 (32.6)*	509 (35.6)	1,989 (35.4)	*2,498 (35.4)*
Education						
Illiterate	386 (49.0)	1,051 (43.8)	*1,437 (45.1)*	710 (49.7)	2,780 (49.5)	*3,490 (49.5)*
Primary school	270 (34.3)	846 (35.3)	*1,116 (35.0)*	503 (35.2)	1,669 (29.7)	*2,172 (30.8)*
Middle school	108 (13.7)	376 (15.7)	*484 (15.2)*	171 (12.0)	944 (16.8)	*1,115 (15.8)*
High school or above	22 (2.8)	125 (5.2)	*147 (4.6)*	40 (2.8)	210 (3.7)	*250 (3.5)*
Missing	2 (0.3)	0 (0.0)	*2 (0.1)*	4 (0.3)	18 (0.3)	*22 (0.3)*
Income ten years ago (Yuan/year)						
<1,000	191 (24.2)	373 (15.6)	*564 (17.7)*	334 (23.4)	1,337 (23.8)	*1,671 (23.7)*
1,000-<1,500	167 (21.2)	433 (18.1)	*600 (18.8)*	270 (18.9)	1,097 (19.5)	*1,367 (19.4)*
1,500-<2,500	205 (26.0)	700 (29.2)	*905 (28.4)*	358 (25.1)	1,374 (24.4)	*1,732 (24.6)*
≥2,500	212 (26.9)	876 (36.5)	*1,088 (34.1)*	418 (29.3)	1,696 (30.2)	*2,114 (30.0)*
Missing	13 (1.6)	16 (0.7)	*29 (0.9)*	48 (3.4)	117 (2.1)	*165 (2.3)*
Body mass index (kg/m2)						
<18.5	134 (17.0)	185 (7.7)	*319 (10.0)*	193 (13.5)	269 (4.8)	*462 (6.6)*
18.5-<24	527 (66.9)	1,483 (61.8)	*2,010 (63.1)*	953 (66.7)	3,356 (59.7)	*4,309 (61.1)*
24-<28	88 (11.2)	590 (24.6)	*678 (21.3)*	227 (15.9)	1,640 (29.2)	*1,867 (26.5)*
≥28	31 (3.9)	136 (5.7)	*167 (5.2)*	39 (2.7)	317 (5.6)	*356 (5.1)*
Missing	8 (1.0)	4 (0.2)	*12 (0.4)*	16 (1.1)	39 (0.7)	*55 (0.8)*
Tobacco smoking						
Never	253 (32.1)	965 (40.2)	*1,218 (38.2)*	670 (46.9)	3,327 (59.2)	*3,997 (56.7)*
Ever	535 (67.9)	1,433 (59.8)	*1,968 (61.8)*	758 (53.1)	2,294 (40.8)	*3,052 (43.3)*
Pack-years of tobacco smoking						
Never	253 (32.1)	965 (40.2)	*1,218 (38.2)*	670 (46.9)	3,327 (59.2)	*3,997 (56.7)*
1-<20	108 (13.7)	373 (15.6)	*481 (15.1)*	147 (10.3)	438 (7.8)	*585 (8.3)*
20-<40	154 (19.5)	457 (19.1)	*611 (19.2)*	185 (13.0)	676 (12.0)	*861 (12.2)*
≥40	238 (30.2)	525 (21.9)	*763 (23.9)*	272 (19.0)	716 (12.7)	*988 (14.0)*
Missing	35 (4.4)	78 (3.3)	*113 (3.5)*	154 (10.8)	464 (8.3)	*618 (8.8)*
Alcohol consumption						
Never	321 (40.7)	1,025 (42.7)	*1,346 (42.2)*	752 (52.7)	3,278 (58.3)	*4,030 (57.2)*
Ever	467 (59.3)	1,373 (57.3)	*1,840 (57.8)*	676 (47.3)	2,343 (41.7)	*3,019 (42.8)*

Grams ethanol/day in the 1990's						
Never	388 (49.2)	1,192 (49.7)	*1,580 (49.6)*	900 (63.0)	3,862 (68.7)	*4,762 (67.6)*
Low-risk	49 (6.2)	219 (9.1)	*268 (8.4)*	102 (7.1)	314 (5.6)	*416 (5.9)*
High-risk	349 (44.3)	979 (40.8)	*1,328 (41.7)*	396 (27.7)	1,300 (23.1)	*1,696 (24.1)*
Missing	2 (0.3)	8 (0.3)	*10 (0.3)*	30 (2.1)	145 (2.6)	*175 (2.5)*
Family history of stomach cancer						
No	699 (88.7)	2,192 (91.4)	*2,891 (90.7)*	1,323 (92.6)	5,452 (97.0)	*6,775 (96.1)*
Yes	89 (11.3)	206 (8.6)	*295 (9.3)*	105 (7.4)	169 (3.0)	*274 (3.9)*
H. pylori infection						
No	155 (19.7)	564 (23.5)	*719 (22.6)*	222 (15.5)	1,354 (24.1)	*1,576 (22.4)*
Yes	519 (65.9)	1,759 (73.4)	*2,278 (71.5)*	728 (51.0)	2,989 (53.2)	*3,717 (52.7)*
Missing	114 (14.5)	75 (3.1)	*189 (5.9)*	478 (33.5)	1,278 (22.7)	*1,756 (24.9)*

Note: Low-risk drinking: men (≤25g ethanol/day) and women (≤15g ethanol/day); High-risk drinking: men (>25g ethanol/day) and women (>15g ethanol/day based on the 2016 Chinese Dietary Guide.

Table 5.3. Associations between genetic polymorphisms and stomach cancer

dbSNP no.	Cases, n(%)	Controls, n(%)	aOR*	sbOR*
		miRNA pathway		
IL15 (rs10519613)				
C:C	249 (31.6)	803 (33.5)	1.00	1.00
C:A	301 (38.2)	1022 (42.6)	0.89 (0.71, 1.12)	0.90 (0.72, 1.13)
A:A	117 (14.8)	422 (17.6)	0.85 (0.64, 1.14)	0.87 (0.66, 1.15)
Log-Additive			0.92 (0.80, 1.06)	0.93 (0.80, 1.06)
Dominant			0.88 (0.71, 1.09)	0.89 (0.73, 1.10)
Recessive			0.90 (0.70, 1.18)	0.92 (0.71, 1.19)
miR-196a2 (rs11614913)				
T:T	218 (27.7)	693 (28.9)	1.00	1.00
C:T	283 (35.9)	1035 (43.2)	0.86 (0.68, 1.09)	0.89 (0.71, 1.12)
C:C	164 (20.8)	467 (19.5)	0.97 (0.73, 1.28)	1.00 (0.76, 1.31)
Log-Additive			0.97 (0.84, 1.12)	0.99 (0.86, 1.14)
Dominant			0.89 (0.72, 1.11)	0.92 (0.74, 1.14)
Recessive			1.06 (0.83, 1.35)	1.07 (0.84, 1.36)
WWOX (rs12828)				
G:G	257 (32.6)	922 (38.4)	1.00	1.00
A:G	269 (34.1)	960 (40.0)	1.08 (0.86, 1.36)	1.10 (0.88, 1.37)
A:A	135 (17.1)	320 (13.3)	**1.49 (1.12, 1.99)**	**1.47 (1.11, 1.95)**
Log-Additive			**1.20 (1.04, 1.38)**	**1.20 (1.04, 1.38)**
Dominant			1.19 (0.96, 1.47)	1.20 (0.98, 1.48)
Recessive			**1.43 (1.10, 1.86)**	**1.40 (1.09, 1.81)**
Ran (rs14035)				
C:C	458 (58.1)	1421 (59.3)	1.00	1.00
C:T	186 (23.6)	617 (25.7)	0.97 (0.77, 1.23)	0.97 (0.77, 1.21)
T:T	29 (3.7)	95 (4.0)	1.17 (0.72, 1.92)	1.13 (0.71, 1.80)
Log-Additive			1.02 (0.85, 1.23)	1.01 (0.85, 1.21)
Dominant			1.00 (0.80, 1.25)	0.99 (0.80, 1.23)
Recessive			1.18 (0.72, 1.93)	1.14 (0.72, 1.81)
CXCL12 (rs1804429)				
T:T	597 (75.8)	1969 (82.1)	1.00	1.00
G:T	66 (8.4)	275 (11.5)	0.85 (0.61, 1.18)	0.82 (0.59, 1.12)
G:G	6 (0.8)	12 (0.5)	1.07 (0.27, 4.20)	1.24 (0.48, 3.16)
Log-Additive			0.88 (0.65, 1.19)	0.88 (0.66, 1.18)
Dominant			0.86 (0.62, 1.18)	0.84 (0.62, 1.15)
Recessive			1.09 (0.28, 4.27)	1.25 (0.49, 3.20)
Gemin3 (rs197412)				
T:T	322 (40.9)	1011 (42.2)	1.00	1.00
T:C	263 (33.4)	972 (40.5)	0.81 (0.65, 1.01)	0.82 (0.67, 1.02)
C:C	89 (11.3)	247 (10.3)	1.27 (0.93, 1.74)	1.24 (0.91, 1.68)
Log-Additive			1.03 (0.88, 1.19)	1.02 (0.88, 1.18)
Dominant			0.90 (0.73, 1.10)	0.91 (0.74, 1.11)
Recessive			**1.41 (1.05, 1.90)**	**1.35 (1.01, 1.80)**
E2F2 (rs2075993)				
G:G	283 (35.9)	814 (33.9)	1.00	1.00
G:A	262 (33.2)	999 (41.7)	**0.78 (0.62, 0.97)**	**0.79 (0.63, 0.98)**
A:A	120 (15.2)	365 (15.2)	0.89 (0.66, 1.19)	0.89 (0.67, 1.19)
Log-Additive			0.91 (0.78, 1.05)	0.91 (0.79, 1.05)
Dominant			**0.81 (0.66, 0.99)**	**0.81 (0.66, 1.00)**
Recessive			1.01 (0.77, 1.32)	1.00 (0.77, 1.31)
THBS1 (rs2292305)				
T:T	307 (39.0)	1014 (42.3)	1.00	1.00
C:T	236 (29.9)	935 (39.0)	0.89 (0.71, 1.11)	0.86 (0.69, 1.07)

C:C	74 (9.4)	268 (11.2)	1.00 (0.72, 1.40)	0.98 (0.72, 1.35)
Log-Additive			0.97 (0.83, 1.13)	0.95 (0.82, 1.10)
Dominant			0.92 (0.74, 1.13)	0.88 (0.72, 1.08)
Recessive			1.06 (0.78, 1.45)	1.05 (0.77, 1.42)
pre-miR-146a (rs2910164)				
C:C	224 (28.4)	826 (34.4)	1.00	1.00
G:C	324 (41.1)	1040 (43.4)	1.16 (0.93, 1.46)	1.17 (0.94, 1.46)
G:G	109 (13.8)	394 (16.4)	0.95 (0.70, 1.28)	0.96 (0.71, 1.29)
Log-Additive			1.00 (0.87, 1.16)	1.01 (0.88, 1.16)
Dominant			1.10 (0.89, 1.36)	1.11 (0.90, 1.37)
Recessive			0.87 (0.66, 1.14)	0.88 (0.67, 1.15)
CTNNB1 (rs2953)				
T:T	384 (48.7)	1267 (52.8)	1.00	1.00
G:T	233 (29.6)	836 (34.9)	0.86 (0.69, 1.07)	0.89 (0.72, 1.10)
G:G	51 (6.5)	164 (6.8)	0.89 (0.60, 1.34)	0.90 (0.61, 1.32)
Log-Additive			0.91 (0.77, 1.07)	0.92 (0.78, 1.07)
Dominant			0.87 (0.71, 1.07)	0.89 (0.72, 1.08)
Recessive			0.95 (0.64, 1.40)	0.94 (0.64, 1.36)
DOCK4 (rs3801790)				
A:A	281 (35.7)	856 (35.7)	1.00	1.00
A:G	277 (35.2)	994 (41.5)	0.86 (0.69, 1.07)	0.87 (0.70, 1.09)
G:G	115 (14.6)	368 (15.3)	0.95 (0.71, 1.28)	0.98 (0.74, 1.31)
Log-Additive			0.95 (0.82, 1.10)	0.96 (0.84, 1.11)
Dominant			0.88 (0.72, 1.09)	0.90 (0.74, 1.11)
Recessive			1.03 (0.78, 1.36)	1.05 (0.81, 1.37)
Rbl2 (rs3929)				
G:G	440 (55.8)	1531 (63.8)	1.00	1.00
C:G	214 (27.2)	673 (28.1)	1.13 (0.90, 1.40)	1.10 (0.89, 1.37)
C:C	29 (3.7)	92 (3.8)	1.02 (0.61, 1.71)	1.05 (0.65, 1.69)
Log-Additive			1.08 (0.90, 1.28)	1.07 (0.90, 1.27)
Dominant			1.11 (0.90, 1.37)	1.10 (0.89, 1.35)
Recessive			0.99 (0.59, 1.64)	1.02 (0.64, 1.64)
IL6R (rs4072391)				
C:C	556 (70.6)	1870 (78.0)	1.00	1.00
C:T	95 (12.1)	364 (15.2)	0.94 (0.71, 1.26)	0.92 (0.70, 1.22)
T:T	19 (2.4)	32 (1.3)	1.89 (0.95, 3.79)	1.65 (0.88, 3.10)
Log-Additive			1.09 (0.86, 1.37)	1.07 (0.85, 1.34)
Dominant			1.02 (0.78, 1.34)	1.00 (0.77, 1.31)
Recessive			1.91 (0.96, 3.82)	1.67 (0.89, 3.13)
CDK6 (rs42031)				
A:A	605 (76.8)	2061 (85.9)	1.00	1.00
A:T	68 (8.6)	200 (8.3)	1.20 (0.85, 1.68)	1.15 (0.83, 1.60)
T:T	6 (0.8)	13 (0.5)	1.21 (0.34, 4.35)	1.31 (0.53, 3.28)
Log-Additive			1.17 (0.87, 1.59)	1.18 (0.88, 1.57)
Dominant			1.20 (0.86, 1.66)	1.17 (0.85, 1.62)
Recessive			1.19 (0.33, 4.27)	1.30 (0.52, 3.25)
Ago2 (rs4961280)				
C:C	535 (67.9)	1685 (70.3)	1.00	1.00
C:A	116 (14.7)	462 (19.3)	0.78 (0.60, 1.01)	0.79 (0.61, 1.01)
A:A	19 (2.4)	45 (1.9)	1.29 (0.66, 2.52)	1.23 (0.67, 2.25)
Log-Additive			0.89 (0.71, 1.10)	0.89 (0.72, 1.10)
Dominant			0.82 (0.64, 1.06)	0.83 (0.65, 1.05)
Recessive			1.36 (0.70, 2.64)	1.27 (0.70, 2.33)
miR-26a1 (rs7372209)				
C:C	364 (46.2)	1131 (47.2)	1.00	1.00

C:T	265 (33.6)	908 (37.9)	0.98 (0.79, 1.20)	0.95 (0.77, 1.17)
T:T	50 (6.3)	215 (9.0)	0.67 (0.45, 1.00)	**0.65 (0.44, 0.95)**
Log-Additive			0.89 (0.76, 1.04)	0.86 (0.74, 1.01)
Dominant			0.92 (0.75, 1.12)	0.89 (0.73, 1.08)
Recessive			0.68 (0.46, 1.00)	**0.66 (0.46, 0.96)**
Gemin4 (rs7813)				
T:T	333 (42.3)	1124 (46.9)	1.00	1.00
C:T	247 (31.3)	845 (35.2)	1.05 (0.84, 1.30)	1.05 (0.84, 1.30)
C:C	74 (9.4)	215 (9.0)	1.02 (0.72, 1.43)	1.02 (0.73, 1.42)
Log-Additive			1.02 (0.88, 1.19)	1.02 (0.88, 1.19)
Dominant			1.04 (0.85, 1.28)	1.04 (0.85, 1.27)
Recessive			1.00 (0.71, 1.39)	1.00 (0.72, 1.38)
KARS (rs9266)				
C:C	440 (55.8)	1428 (59.5)	1.00	1.00
C:T	189 (24.0)	710 (29.6)	**0.80 (0.63, 1.00)**	0.81 (0.65, 1.01)
T:T	43 (5.5)	116 (4.8)	0.99 (0.64, 1.54)	1.01 (0.67, 1.53)
Log-Additive			0.89 (0.75, 1.06)	0.90 (0.76, 1.07)
Dominant			0.83 (0.67, 1.02)	0.84 (0.68, 1.03)
Recessive			1.07 (0.69, 1.64)	1.07 (0.71, 1.61)
		Stem cell pathway		
HEY1 (rs1046472)				
C:C	411 (52.2)	1423 (59.3)	1.00	1.00
A:C	218 (27.7)	728 (30.4)	1.09 (0.87, 1.35)	1.08 (0.87, 1.34)
A:A	52 (6.6)	108 (4.5)	1.42 (0.93, 2.17)	1.38 (0.92, 2.07)
Log-Additive			1.14 (0.97, 1.35)	1.14 (0.96, 1.34)
Dominant			1.13 (0.92, 1.39)	1.13 (0.92, 1.38)
Recessive			1.38 (0.91, 2.09)	1.34 (0.90, 2.00)
Oct4 (rs13409)				
C:C	242 (30.7)	818 (34.1)	1.00	1.00
C:T	291 (36.9)	1013 (42.2)	0.90 (0.72, 1.13)	0.92 (0.73, 1.14)
T:T	133 (16.9)	421 (17.6)	0.91 (0.68, 1.21)	0.91 (0.69, 1.20)
Log-Additive			0.94 (0.82, 1.09)	0.95 (0.82, 1.09)
Dominant			0.90 (0.73, 1.11)	0.91 (0.74, 1.12)
Recessive			0.96 (0.74, 1.24)	0.95 (0.74, 1.22)
AXIN1 (rs1981492)				
G:G	364 (46.2)	1148 (47.9)	1.00	1.00
A:G	234 (29.7)	864 (36.0)	**0.79 (0.63, 0.98)**	**0.80 (0.65, 1.00)**
A:A	87 (11.0)	217 (9.0)	0.98 (0.70, 1.37)	0.99 (0.72, 1.37)
Log-Additive			0.92 (0.79, 1.07)	0.92 (0.80, 1.07)
Dominant			0.83 (0.68, 1.01)	0.84 (0.69, 1.03)
Recessive			1.08 (0.78, 1.49)	1.08 (0.79, 1.48)
DVL2 (rs222851)				
A:A	260 (33.0)	886 (36.9)	1.00	1.00
A:G	304 (38.6)	1001 (41.7)	1.14 (0.91, 1.42)	1.14 (0.92, 1.42)
G:G	93 (11.8)	327 (13.6)	1.03 (0.75, 1.43)	1.06 (0.77, 1.44)
Log-Additive			1.05 (0.90, 1.21)	1.06 (0.91, 1.22)
Dominant			1.11 (0.90, 1.37)	1.12 (0.91, 1.38)
Recessive			0.97 (0.72, 1.30)	0.99 (0.74, 1.31)
FZD3 (rs2241802)				
G:G	227 (28.8)	712 (29.7)	1.00	1.00
A:G	288 (36.5)	995 (41.5)	0.99 (0.78, 1.26)	0.98 (0.78, 1.24)
A:A	123 (15.6)	433 (18.1)	1.04 (0.77, 1.40)	1.04 (0.79, 1.39)
Log-Additive			1.02 (0.88, 1.18)	1.02 (0.88, 1.18)
Dominant			1.01 (0.80, 1.26)	1.00 (0.80, 1.25)
Recessive			1.05 (0.81, 1.36)	1.06 (0.82, 1.36)

Dec1 (rs2269700)				
T:T	493 (62.6)	1519 (63.3)	1.00	1.00
C:T	181 (23.0)	652 (27.2)	0.88 (0.70, 1.10)	0.89 (0.71, 1.10)
C:C	11 (1.4)	90 (3.8)	0.61 (0.31, 1.21)	0.64 (0.35, 1.17)
Log-Additive			0.85 (0.70, 1.03)	0.84 (0.70, 1.02)
Dominant			0.85 (0.68, 1.06)	0.85 (0.69, 1.06)
Recessive			0.63 (0.32, 1.25)	0.66 (0.36, 1.20)
Oct4 (rs3130932)				
T:T	353 (44.8)	1043 (43.5)	1.00	1.00
G:T	246 (31.2)	957 (39.9)	0.87 (0.70, 1.08)	0.86 (0.70, 1.07)
G:G	79 (10.0)	256 (10.7)	1.03 (0.74, 1.42)	1.01 (0.74, 1.39)
Log-Additive			0.96 (0.83, 1.12)	0.96 (0.83, 1.11)
Dominant			0.90 (0.74, 1.10)	0.89 (0.73, 1.09)
Recessive			1.09 (0.80, 1.49)	1.08 (0.79, 1.46)
WNT2 (rs3729629)				
G:G	337 (42.8)	1019 (42.5)	1.00	1.00
C:G	273 (34.6)	987 (41.2)	0.86 (0.70, 1.07)	0.88 (0.71, 1.08)
C:C	65 (8.2)	248 (10.3)	0.81 (0.57, 1.16)	0.83 (0.59, 1.16)
Log-Additive			0.89 (0.76, 1.03)	0.90 (0.77, 1.04)
Dominant			0.85 (0.70, 1.04)	0.87 (0.71, 1.06)
Recessive			0.87 (0.62, 1.22)	0.88 (0.63, 1.21)
HEY2 (rs3734637)				
A:A	414 (52.5)	1339 (55.8)	1.00	1.00
A:C	217 (27.5)	756 (31.5)	0.92 (0.73, 1.14)	0.94 (0.75, 1.16)
C:C	30 (3.8)	156 (6.5)	**0.57 (0.36, 0.91)**	**0.60 (0.39, 0.93)**
Log-Additive			**0.83 (0.70, 0.99)**	**0.84 (0.71, 0.99)**
Dominant			0.85 (0.69, 1.05)	0.87 (0.70, 1.06)
Recessive			**0.59 (0.37, 0.93)**	**0.61 (0.40, 0.94)**
Ctbp2 (rs3740535)				
G:G	364 (46.2)	1233 (51.4)	1.00	1.00
A:G	228 (28.9)	844 (35.2)	0.91 (0.73, 1.14)	0.92 (0.74, 1.14)
A:A	72 (9.1)	175 (7.3)	1.22 (0.85, 1.74)	1.21 (0.86, 1.70)
Log-Additive			1.03 (0.88, 1.20)	1.03 (0.88, 1.20)
Dominant			0.97 (0.79, 1.19)	0.98 (0.80, 1.19)
Recessive			1.26 (0.89, 1.78)	1.24 (0.89, 1.74)
WNT2 (rs4730775)				
C:C	393 (49.9)	1282 (53.5)	1.00	1.00
C:T	228 (28.9)	794 (33.1)	0.86 (0.69, 1.07)	0.90 (0.72, 1.11)
T:T	35 (4.4)	152 (6.3)	0.92 (0.60, 1.42)	0.93 (0.62, 1.40)
Log-Additive			0.91 (0.77, 1.08)	0.93 (0.79, 1.10)
Dominant			0.87 (0.71, 1.07)	0.90 (0.73, 1.11)
Recessive			0.97 (0.64, 1.49)	0.97 (0.64, 1.45)
WNT8A (rs4835761)				
A:A	263 (33.4)	751 (31.3)	1.00	1.00
A:G	268 (34.0)	1029 (42.9)	**0.74 (0.59, 0.93)**	**0.74 (0.59, 0.92)**
G:G	133 (16.9)	403 (16.8)	0.97 (0.74, 1.29)	0.98 (0.74, 1.28)
Log-Additive			0.95 (0.82, 1.09)	0.94 (0.82, 1.09)
Dominant			**0.81 (0.65, 1.00)**	**0.80 (0.65, 0.99)**
Recessive			1.14 (0.89, 1.48)	1.14 (0.89, 1.47)
Notch4 (rs520692)				
A:A	485 (61.5)	1724 (71.9)	1.00	1.00
A:G	151 (19.2)	504 (21.0)	0.96 (0.75, 1.21)	0.95 (0.75, 1.21)
G:G	7 (0.9)	42 (1.8)	0.71 (0.31, 1.65)	0.78 (0.38, 1.57)
Log-Additive			0.93 (0.75, 1.15)	0.93 (0.75, 1.14)
Dominant			0.94 (0.74, 1.18)	0.94 (0.74, 1.18)

Recessive			0.72 (0.31, 1.66)	0.78 (0.39, 1.58)
Rex1 (rs6815391)				
T:T	302 (38.3)	971 (40.5)	1.00	1.00
C:T	254 (32.2)	925 (38.6)	0.93 (0.74, 1.16)	0.93 (0.74, 1.16)
C:C	99 (12.6)	297 (12.4)	1.09 (0.81, 1.48)	1.07 (0.79, 1.43)
Log-Additive			1.02 (0.88, 1.18)	1.01 (0.87, 1.16)
Dominant			0.97 (0.79, 1.19)	0.96 (0.79, 1.18)
Recessive			1.13 (0.85, 1.51)	1.10 (0.84, 1.46)
HES2 (rs8708)				
A:A	463 (58.8)	1515 (63.2)	1.00	1.00
A:G	169 (21.4)	625 (26.1)	1.02 (0.81, 1.28)	1.01 (0.80, 1.26)
G:G	18 (2.3)	92 (3.8)	0.85 (0.48, 1.51)	0.86 (0.51, 1.46)
Log-Additive			0.98 (0.81, 1.18)	0.97 (0.81, 1.17)
Dominant			1.00 (0.80, 1.24)	0.99 (0.79, 1.23)
Recessive			0.85 (0.48, 1.50)	0.86 (0.51, 1.45)
Notch4 (rs915894)				
C:C	224 (28.4)	661 (27.6)	1.00	1.00
A:C	291 (36.9)	1055 (44.0)	0.83 (0.66, 1.05)	0.85 (0.68, 1.07)
A:A	157 (19.9)	506 (21.1)	0.95 (0.72, 1.25)	0.98 (0.75, 1.28)
Log-Additive			0.96 (0.84, 1.11)	0.98 (0.85, 1.12)
Dominant			0.87 (0.70, 1.08)	0.89 (0.72, 1.11)
Recessive			1.06 (0.83, 1.34)	1.07 (0.85, 1.36)
		NF-κB pathway		
miR-300 (rs12894467)				
T:T	361 (45.8)	1360 (56.7)	1.00	1.00
C:T	224 (28.4)	714 (29.8)	**1.38 (1.10, 1.73)**	**1.37 (1.10, 1.71)**
C:C	59 (7.5)	126 (5.3)	**1.54 (1.03, 2.31)**	**1.55 (1.05, 2.27)**
Log-Additive			**1.30 (1.10, 1.53)**	**1.31 (1.12, 1.54)**
Dominant			**1.41 (1.14, 1.74)**	**1.41 (1.15, 1.74)**
Recessive			1.37 (0.92, 2.03)	1.39 (0.95, 2.02)
IKBKAP (rs1538660)				
C:C	324 (41.1)	1038 (43.3)	1.00	1.00
C:T	269 (34.1)	931 (38.8)	0.84 (0.67, 1.04)	0.85 (0.68, 1.05)
T:T	83 (10.5)	259 (10.8)	1.06 (0.76, 1.47)	1.10 (0.81, 1.51)
Log-Additive			0.96 (0.83, 1.12)	0.98 (0.85, 1.14)
Dominant			0.88 (0.72, 1.08)	0.90 (0.74, 1.10)
Recessive			1.15 (0.84, 1.57)	1.19 (0.88, 1.60)
IKBKAP (rs2230793)				
A:A	339 (43.0)	1076 (44.9)	1.00	1.00
A:C	249 (31.6)	933 (38.9)	0.86 (0.69, 1.07)	0.87 (0.70, 1.07)
C:C	90 (11.4)	233 (9.7)	**1.44 (1.05, 1.99)**	**1.39 (1.02, 1.90)**
Log-Additive			1.08 (0.93, 1.26)	1.08 (0.93, 1.25)
Dominant			0.97 (0.79, 1.18)	0.97 (0.80, 1.18)
Recessive			**1.54 (1.13, 2.10)**	**1.48 (1.10, 1.99)**
IKBKAP (rs3204145)				
T:T	328 (41.6)	1054 (44.0)	1.00	1.00
A:T	281 (35.7)	959 (40.0)	0.82 (0.67, 1.02)	0.83 (0.67, 1.02)
A:A	72 (9.1)	250 (10.4)	0.94 (0.67, 1.32)	0.99 (0.71, 1.37)
Log-Additive			0.91 (0.79, 1.06)	0.93 (0.80, 1.08)
Dominant			0.85 (0.69, 1.03)	0.86 (0.70, 1.04)
Recessive			1.03 (0.74, 1.42)	1.07 (0.78, 1.46)
		GWAS		
RUNX1 (rs2014300)				
G:G	515 (65.4)	1740 (72.6)	1.00	1.00
A:G	132 (16.8)	478 (19.9)	1.00 (0.77, 1.29)	1.01 (0.79, 1.29)

A:A	23 (2.9)	51 (2.1)	1.33 (0.73, 2.44)	1.26 (0.72, 2.21)
Log-Additive			1.06 (0.86, 1.30)	1.06 (0.87, 1.30)
Dominant			1.03 (0.81, 1.32)	1.04 (0.82, 1.32)
Recessive			1.33 (0.73, 2.44)	1.26 (0.72, 2.20)
PLCE1 (rs2274223)				
A:A	346 (43.9)	1402 (58.5)	1.00	1.00
A:G	225 (28.6)	705 (29.4)	1.25 (1.00, 1.58)	1.24 (0.99, 1.56)
G:G	28 (3.6)	97 (4.0)	1.40 (0.86, 2.27)	1.33 (0.84, 2.11)
Log-Additive			**1.22 (1.02, 1.46)**	**1.21 (1.02, 1.45)**
Dominant			**1.27 (1.02, 1.59)**	**1.26 (1.02, 1.57)**
Recessive			1.29 (0.80, 2.08)	1.24 (0.79, 1.96)
GPC5 (rs2352028)				
C:C	446 (56.6)	1430 (59.6)	1.00	1.00
C:T	221 (28.0)	717 (29.9)	0.96 (0.77, 1.19)	0.97 (0.78, 1.20)
T:T	35 (4.4)	124 (5.2)	0.76 (0.47, 1.23)	0.76 (0.48, 1.19)
Log-Additive			0.92 (0.77, 1.09)	0.92 (0.78, 1.09)
Dominant			0.93 (0.76, 1.14)	0.93 (0.76, 1.14)
Recessive			0.77 (0.48, 1.24)	0.76 (0.49, 1.19)
TERT (rs2736100)				
T:T	268 (34.0)	713 (29.7)	1.00	1.00
G:T	281 (35.7)	1014 (42.3)	**0.70 (0.56, 0.88)**	**0.71 (0.57, 0.89)**
G:G	111 (14.1)	406 (16.9)	**0.65 (0.48, 0.88)**	**0.67 (0.50, 0.89)**
Log-Additive			**0.79 (0.68, 0.91)**	**0.79 (0.68, 0.91)**
Dominant			**0.69 (0.55, 0.85)**	**0.69 (0.56, 0.86)**
Recessive			0.79 (0.60, 1.04)	0.80 (0.61, 1.04)
CRPP1 -CRP (rs2808630)				
T:T	504 (64.0)	1675 (69.8)	1.00	1.00
C:T	129 (16.4)	504 (21.0)	0.94 (0.73, 1.21)	0.95 (0.74, 1.22)
C:C	31 (3.9)	65 (2.7)	1.62 (0.97, 2.71)	1.57 (0.97, 2.54)
Log-Additive			1.08 (0.89, 1.31)	1.10 (0.91, 1.32)
Dominant			1.02 (0.81, 1.29)	1.04 (0.82, 1.31)
Recessive			1.64 (0.98, 2.74)	1.58 (0.98, 2.56)
PLCE1 (rs3781264)				
T:T	486 (61.7)	1541 (64.3)	1.00	1.00
C:T	160 (20.3)	537 (22.4)	0.97 (0.77, 1.24)	0.97 (0.76, 1.22)
C:C	23 (2.9)	52 (2.2)	1.42 (0.81, 2.49)	1.35 (0.80, 2.28)
Log-Additive			1.06 (0.87, 1.28)	1.05 (0.87, 1.27)
Dominant			1.02 (0.81, 1.28)	1.01 (0.81, 1.27)
Recessive			1.43 (0.82, 2.50)	1.36 (0.81, 2.29)
CLPTM1L (rs401681)				
C:C	323 (41.0)	1010 (42.1)	1.00	1.00
C:T	257 (32.6)	940 (39.2)	0.84 (0.67, 1.04)	0.83 (0.67, 1.03)
T:T	84 (10.7)	245 (10.2)	1.10 (0.79, 1.53)	1.09 (0.79, 1.50)
Log-Additive			0.97 (0.84, 1.13)	0.97 (0.84, 1.13)
Dominant			0.89 (0.72, 1.09)	0.89 (0.72, 1.08)
Recessive			1.19 (0.87, 1.63)	1.18 (0.87, 1.61)
GKN2 -GKN1 (rs4254535)				
T:T	382 (48.5)	1267 (52.8)	1.00	1.00
C:T	214 (27.2)	792 (33.0)	0.90 (0.72, 1.12)	0.91 (0.73, 1.13)
C:C	68 (8.6)	181 (7.5)	1.37 (0.96, 1.94)	1.34 (0.96, 1.88)
Log-Additive			1.06 (0.91, 1.24)	1.07 (0.91, 1.24)
Dominant			0.98 (0.80, 1.20)	0.99 (0.81, 1.21)
Recessive			**1.42 (1.01, 2.01)**	1.39 (1.00, 1.93)
CCR4 -GLB1 (rs4678680)				
T:T	627 (79.6)	2046 (85.3)	1.00	1.00

G:T	74 (9.4)	249 (10.4)	1.02 (0.74, 1.41)	1.01 (0.74, 1.38)
G:G	8 (1.0)	11 (0.5)	2.17 (0.74, 6.37)	1.87 (0.80, 4.38)
Log-Additive			1.11 (0.84, 1.48)	1.14 (0.87, 1.50)
Dominant			1.07 (0.79, 1.46)	1.08 (0.80, 1.46)
Recessive			2.16 (0.74, 6.36)	1.87 (0.80, 4.38)
TERT -CLPTM1L (rs4975616)				
A:A	499 (63.3)	1606 (67.0)	1.00	1.00
A:G	147 (18.7)	570 (23.8)	0.93 (0.73, 1.18)	0.92 (0.73, 1.16)
G:G	32 (4.1)	67 (2.8)	1.62 (0.96, 2.73)	1.52 (0.93, 2.48)
Log-Additive			1.06 (0.88, 1.28)	1.05 (0.87, 1.27)
Dominant			1.00 (0.80, 1.25)	0.99 (0.79, 1.24)
Recessive			1.65 (0.98, 2.77)	1.54 (0.95, 2.51)
CHEK2 (rs738722)				
C:C	338 (42.9)	1220 (50.9)	1.00	1.00
C:T	249 (31.6)	806 (33.6)	1.17 (0.94, 1.46)	1.14 (0.92, 1.41)
T:T	74 (9.4)	179 (7.5)	**1.52 (1.08, 2.15)**	**1.47 (1.06, 2.06)**
Log-Additive			**1.21 (1.04, 1.41)**	**1.20 (1.03, 1.39)**
Dominant			**1.24 (1.01, 1.52)**	1.21 (0.99, 1.48)
Recessive			**1.43 (1.02, 1.99)**	**1.40 (1.01, 1.94)**
TGM5 (rs748404)				
T:T	607 (77.0)	2027 (84.5)	1.00	1.00
C:T	59 (7.5)	215 (9.0)	1.01 (0.72, 1.42)	0.99 (0.71, 1.38)
C:C	6 (0.8)	12 (0.5)	0.65 (0.16, 2.70)	0.80 (0.30, 2.12)
Log-Additive			0.97 (0.71, 1.32)	0.95 (0.70, 1.28)
Dominant			0.99 (0.70, 1.38)	0.96 (0.70, 1.33)
Recessive			0.65 (0.16, 2.69)	0.80 (0.30, 2.12)
IL1RAP (rs7626795)				
A:A	461 (58.5)	1481 (61.8)	1.00	1.00
A:G	188 (23.9)	666 (27.8)	0.91 (0.73, 1.15)	0.92 (0.73, 1.14)
G:G	34 (4.3)	101 (4.2)	0.88 (0.54, 1.42)	0.92 (0.59, 1.45)
Log-Additive			0.92 (0.77, 1.10)	0.93 (0.79, 1.11)
Dominant			0.91 (0.73, 1.13)	0.92 (0.74, 1.13)
Recessive			0.90 (0.56, 1.45)	0.95 (0.61, 1.48)
CHRNA3 (rs8042374)				
G:G	342 (43.4)	1097 (45.7)	1.00	1.00
A:G	240 (30.5)	899 (37.5)	**0.80 (0.64, 0.99)**	**0.80 (0.65, 1.00)**
A:A	72 (9.1)	190 (7.9)	1.29 (0.91, 1.84)	1.22 (0.87, 1.72)
Log-Additive			0.99 (0.85, 1.17)	0.98 (0.84, 1.15)
Dominant			0.88 (0.71, 1.08)	0.87 (0.71, 1.07)
Recessive			**1.43 (1.01, 2.01)**	1.33 (0.96, 1.86)
FTO (rs8050136)				
C:C	514 (65.2)	1791 (74.7)	1.00	1.00
A:C	155 (19.7)	427 (17.8)	**1.32 (1.03, 1.69)**	**1.30 (1.02, 1.66)**
A:A	5 (0.6)	49 (2.0)	**0.23 (0.07, 0.78)**	**0.40 (0.18, 0.90)**
Log-Additive			1.05 (0.84, 1.30)	1.04 (0.84, 1.29)
Dominant			1.19 (0.93, 1.52)	1.17 (0.92, 1.49)
Recessive			**0.22 (0.07, 0.74)**	**0.39 (0.18, 0.87)**
ZBTB12-C2 (rs9267673)				
C:C	474 (60.2)	1610 (67.1)	1.00	1.00
C:T	165 (20.9)	568 (23.7)	0.90 (0.71, 1.15)	0.89 (0.70, 1.12)
T:T	36 (4.6)	70 (2.9)	1.51 (0.91, 2.51)	1.48 (0.92, 2.37)
Log-Additive			1.04 (0.86, 1.25)	1.03 (0.86, 1.24)
Dominant			0.97 (0.78, 1.22)	0.96 (0.77, 1.20)
Recessive			1.56 (0.94, 2.57)	1.52 (0.95, 2.43)
HLA-DQB1- HLA-DQA2 (rs9275572)				

G:G	349 (44.3)	1186 (49.5)	1.00	1.00
A:G	241 (30.6)	851 (35.5)	0.89 (0.71, 1.10)	0.91 (0.73, 1.12)
A:A	67 (8.5)	210 (8.8)	1.20 (0.85, 1.71)	1.18 (0.84, 1.66)
Log-Additive			1.02 (0.87, 1.19)	1.02 (0.88, 1.19)
Dominant			0.94 (0.77, 1.16)	0.96 (0.78, 1.17)
Recessive			1.27 (0.90, 1.77)	1.23 (0.89, 1.71)
SEMA5B (rs9868873)				
G:G	459 (58.2)	1509 (62.9)	1.00	1.00
A:G	173 (22.0)	661 (27.6)	0.86 (0.68, 1.08)	0.89 (0.71, 1.11)
A:A	52 (6.6)	92 (3.8)	**1.71 (1.12, 2.60)**	**1.65 (1.10, 2.46)**
Log-Additive			1.07 (0.91, 1.27)	1.09 (0.92, 1.29)
Dominant			0.97 (0.78, 1.20)	1.00 (0.81, 1.23)
Recessive			**1.79 (1.18, 2.70)**	**1.70 (1.14, 2.53)**
		HIF pathway		
HIF1A (rs2057482)				
C:C	454 (57.6)	1453 (60.6)	1.00	1.00
T:C	224 (28.4)	676 (28.2)	1.04 (0.84, 1.29)	1.07 (0.86, 1.32)
T:T	31 (3.9)	100 (4.2)	1.03 (0.63, 1.68)	1.05 (0.67, 1.67)
Log-Additive			1.03 (0.87, 1.22)	1.05 (0.89, 1.25)
Dominant			1.04 (0.84, 1.28)	1.06 (0.87, 1.31)
Recessive			1.01 (0.62, 1.65)	1.03 (0.66, 1.63)
HIF1AN (rs2295778)				
C:C	383 (48.6)	1203 (50.2)	1.00	1.00
C:G	267 (33.9)	728 (30.4)	1.15 (0.92, 1.43)	1.14 (0.92, 1.41)
G:G	36 (4.6)	129 (5.4)	0.96 (0.61, 1.51)	0.96 (0.62, 1.47)
Log-Additive			1.06 (0.89, 1.26)	1.06 (0.89, 1.25)
Dominant			1.12 (0.90, 1.38)	1.11 (0.90, 1.37)
Recessive			0.91 (0.59, 1.42)	0.91 (0.60, 1.39)
		Beta-carotene metabolism-related pathway		
R267S (rs12934922)				
A:A	520 (66.0)	1671 (69.7)	1.00	1.00
A:T	144 (18.3)	525 (21.9)	0.90 (0.70, 1.15)	0.90 (0.71, 1.15)
T:T	22 (2.8)	50 (2.1)	**1.84 (1.04, 3.28)**	1.68 (0.98, 2.88)
Log-Additive			1.05 (0.86, 1.28)	1.05 (0.87, 1.28)
Dominant			0.97 (0.77, 1.23)	0.98 (0.78, 1.23)
Recessive			**1.89 (1.07, 3.35)**	**1.72 (1.01, 2.93)**
A379V (rs7501331)				
C:C	541 (68.7)	1713 (71.4)	1.00	1.00
C:T	122 (15.5)	502 (20.9)	0.82 (0.64, 1.07)	0.83 (0.65, 1.07)
T:T	27 (3.4)	63 (2.6)	1.63 (0.97, 2.72)	1.49 (0.92, 2.43)
Log-Additive			1.01 (0.83, 1.23)	1.00 (0.83, 1.22)
Dominant			0.92 (0.72, 1.16)	0.92 (0.73, 1.16)
Recessive			**1.69 (1.01, 2.83)**	1.54 (0.95, 2.50)

Notes: aOR: adjusted odds ratios; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), and body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28kg/m^2).

Table 5.4. Associations between selected SNPs related to the miRNA pathway and stomach cancer by dietary intake of total fatty acids

	Low Fatty Acids				High Fatty acids			
dbSNP no.	Ca, n(%)	Co, n(%)	aOR*	sbOR*	Ca, n(%)	Co, n(%)	aOR*	sbOR*
IL15(rs10519613)								
C:C	117 (34.9)	400 (34.1)	1.00	1.00	125 (29.2)	394 (33.1)	1.00	1.00
C:A	130 (38.8)	493 (42.0)	0.82 (0.59, 1.15)	0.86 (0.63, 1.18)	163 (38.1)	512 (43.0)	0.98 (0.72, 1.34)	0.99 (0.74, 1.33)
A:A	43 (12.8)	209 (17.8)	0.63 (0.40, 1.01)	0.72 (0.47, 1.08)	65 (15.2)	211 (17.7)	0.92 (0.62, 1.37)	0.94 (0.66, 1.35)
Log-Additive			0.80 (0.64, 1.00)	0.82 (0.66, 1.02)			0.96 (0.80, 1.17)	0.97 (0.80, 1.17)
Dominant			0.77 (0.56, 1.05)	0.80 (0.59, 1.07)			0.96 (0.72, 1.29)	0.97 (0.74, 1.28)
Recessive			0.70 (0.46, 1.09)	0.77 (0.52, 1.13)			0.93 (0.66, 1.33)	0.94 (0.68, 1.31)
miR-196a2 (rs11614913)								
T:T	80 (23.9)	347 (29.6)	1.00	1.00	131 (30.6)	339 (28.5)	1.00	1.00
C:T	138 (41.2)	490 (41.7)	1.25 (0.87, 1.80)	1.23 (0.88, 1.71)	135 (31.5)	528 (44.4)	**0.63 (0.45, 0.87)**	**0.68 (0.50, 0.92)**
C:C	71 (21.2)	237 (20.2)	1.02 (0.66, 1.58)	1.01 (0.68, 1.50)	85 (19.9)	224 (18.8)	0.96 (0.66, 1.41)	1.01 (0.71, 1.44)
Log-Additive			1.03 (0.83, 1.27)	1.03 (0.84, 1.27)			0.94 (0.77, 1.14)	0.96 (0.79, 1.16)
Dominant			1.17 (0.83, 1.65)	1.16 (0.85, 1.60)			**0.72 (0.54, 0.97)**	0.77 (0.58, 1.02)
Recessive			0.89 (0.61, 1.30)	0.91 (0.64, 1.28)			1.26 (0.90, 1.77)	1.24 (0.90, 1.70)
WWOX (rs12828)								
G:G	122 (36.4)	463 (39.4)	1.00	1.00	130 (30.4)	447 (37.6)	1.00	1.00
A:G	120 (35.8)	470 (40.0)	1.09 (0.77, 1.53)	1.06 (0.77, 1.46)	134 (31.3)	476 (40.0)	1.03 (0.75, 1.41)	1.04 (0.77, 1.40)
A:A	54 (16.1)	146 (12.4)	1.45 (0.93, 2.26)	1.36 (0.91, 2.04)	77 (18.0)	170 (14.3)	1.47 (0.99, 2.17)	1.40 (0.98, 2.01)
Log-Additive			1.18 (0.95, 1.47)	1.18 (0.95, 1.45)			1.18 (0.97, 1.44)	1.19 (0.98, 1.43)
Dominant			1.18 (0.86, 1.62)	1.16 (0.86, 1.57)			1.15 (0.86, 1.53)	1.16 (0.88, 1.53)
Recessive			1.39 (0.92, 2.08)	1.33 (0.91, 1.93)			**1.45 (1.02, 2.06)**	1.38 (0.99, 1.92)
Ran (rs14035)								
C:C	190 (56.7)	688 (58.6)	1.00	1.00	251 (58.6)	717 (60.3)	1.00	1.00
C:T	99 (29.6)	298 (25.4)	1.23 (0.88, 1.72)	1.20 (0.87, 1.64)	83 (19.4)	309 (26.0)	0.82 (0.59, 1.15)	0.83 (0.60, 1.13)
T:T	10 (3.0)	50 (4.3)	0.73 (0.32, 1.65)	0.81 (0.44, 1.49)	16 (3.7)	45 (3.8)	1.65 (0.85, 3.20)	1.39 (0.80, 2.42)
Log-Additive			1.06 (0.81, 1.38)	1.04 (0.80, 1.34)			1.02 (0.79, 1.32)	1.01 (0.79, 1.29)
Dominant			1.16 (0.84, 1.60)	1.12 (0.83, 1.52)			0.91 (0.67, 1.25)	0.91 (0.68, 1.23)
Recessive			0.68 (0.30, 1.53)	0.78 (0.42, 1.43)			1.75 (0.91, 3.36)	1.45 (0.83, 2.51)
CXCL12 (rs1804429)								
T:T	261 (77.9)	967 (82.4)	1.00	1.00	314 (73.4)	979 (82.3)	1.00	1.00
G:T	37 (11.0)	130 (11.1)	1.01 (0.64, 1.61)	0.96 (0.63, 1.46)	27 (6.3)	139 (11.7)	0.67 (0.41, 1.09)	0.70 (0.46, 1.08)
G:G	1 (0.3)	5 (0.4)	0.78 (0.07, 8.21)	0.96 (0.39, 2.35)	4 (0.9)	7 (0.6)	0.68 (0.07, 6.23)	1.08 (0.46, 2.55)
Log-Additive			1.00 (0.65, 1.53)	0.95 (0.64, 1.41)			0.69 (0.44, 1.09)	0.77 (0.52, 1.14)
Dominant			1.01 (0.64, 1.59)	0.96 (0.63, 1.44)			0.67 (0.41, 1.08)	0.73 (0.48, 1.11)
Recessive			0.78 (0.07, 8.18)	0.96 (0.39, 2.35)			0.71 (0.08, 6.49)	1.09 (0.46, 2.58)

Gemin3 (rs197412)								
T:T	141 (42.1)	514 (43.8)	1.00	1.00	170 (39.7)	478 (40.2)	1.00	1.00
T:C	118 (35.2)	463 (39.4)	0.89 (0.64, 1.24)	0.90 (0.66, 1.23)	135 (31.5)	501 (42.1)	0.74 (0.55, 1.00)	0.77 (0.58, 1.02)
C:C	41 (12.2)	125 (10.6)	1.47 (0.93, 2.32)	1.34 (0.89, 2.03)	46 (10.7)	117 (9.8)	1.15 (0.73, 1.80)	1.13 (0.75, 1.70)
Log-Additive			1.12 (0.90, 1.40)	1.10 (0.89, 1.37)			0.96 (0.77, 1.18)	0.96 (0.78, 1.18)
Dominant			1.01 (0.75, 1.37)	1.01 (0.76, 1.35)			0.82 (0.61, 1.08)	0.84 (0.64, 1.10)
Recessive			**1.55 (1.01, 2.39)**	1.39 (0.94, 2.07)			1.33 (0.87, 2.04)	1.26 (0.85, 1.86)
E2F2 (rs2075993)								
G:G	127 (37.9)	426 (36.3)	1.00	1.00	146 (34.1)	374 (31.4)	1.00	1.00
G:A	120 (35.8)	448 (38.2)	0.84 (0.60, 1.17)	0.86 (0.63, 1.17)	132 (30.8)	540 (45.4)	**0.70 (0.51, 0.96)**	**0.73 (0.54, 0.98)**
A:A	48 (14.3)	186 (15.8)	0.80 (0.51, 1.25)	0.82 (0.55, 1.23)	68 (15.9)	175 (14.7)	0.96 (0.64, 1.44)	0.97 (0.67, 1.41)
Log-Additive			0.88 (0.71, 1.09)	0.88 (0.71, 1.08)			0.92 (0.75, 1.12)	0.92 (0.76, 1.12)
Dominant			0.82 (0.60, 1.12)	0.83 (0.62, 1.12)			0.77 (0.57, 1.02)	0.78 (0.60, 1.03)
Recessive			0.87 (0.57, 1.32)	0.87 (0.60, 1.28)			1.16 (0.80, 1.68)	1.13 (0.80, 1.59)
THBS1 (rs2292305)								
T:T	133 (39.7)	478 (40.7)	1.00	1.00	162 (37.9)	525 (44.1)	1.00	1.00
C:T	106 (31.6)	457 (38.9)	0.85 (0.61, 1.19)	0.83 (0.60, 1.13)	124 (29.0)	464 (39.0)	0.98 (0.72, 1.33)	0.95 (0.71, 1.27)
C:C	34 (10.1)	154 (13.1)	0.86 (0.54, 1.39)	0.86 (0.56, 1.32)	37 (8.6)	110 (9.2)	1.22 (0.76, 1.95)	1.16 (0.76, 1.78)
Log-Additive			0.91 (0.73, 1.13)	0.88 (0.71, 1.10)			1.06 (0.86, 1.31)	1.04 (0.85, 1.29)
Dominant			0.85 (0.62, 1.17)	0.82 (0.61, 1.11)			1.03 (0.77, 1.37)	1.00 (0.76, 1.32)
Recessive			0.93 (0.59, 1.46)	0.93 (0.62, 1.40)			1.23 (0.78, 1.93)	1.18 (0.78, 1.78)
pre-miR-146a (rs2910164)								
C:C	105 (31.3)	419 (35.7)	1.00	1.00	114 (26.6)	398 (33.4)	1.00	1.00
G:C	141 (42.1)	501 (42.7)	1.22 (0.87, 1.70)	1.19 (0.87, 1.63)	171 (40.0)	522 (43.9)	1.07 (0.78, 1.48)	1.09 (0.81, 1.47)
G:G	46 (13.7)	191 (16.3)	0.80 (0.50, 1.30)	0.82 (0.54, 1.26)	57 (13.3)	198 (16.6)	1.03 (0.68, 1.55)	1.05 (0.72, 1.53)
Log-Additive			0.96 (0.77, 1.19)	0.96 (0.77, 1.18)			1.02 (0.84, 1.25)	1.04 (0.86, 1.27)
Dominant			1.10 (0.80, 1.52)	1.08 (0.80, 1.46)			1.06 (0.79, 1.43)	1.09 (0.82, 1.45)
Recessive			0.72 (0.46, 1.12)	0.76 (0.51, 1.12)			0.98 (0.68, 1.42)	1.01 (0.71, 1.42)
CTNNB1 (rs2953)								
T:T	178 (53.1)	639 (54.4)	1.00	1.00	193 (45.1)	611 (51.3)	1.00	1.00
G:T	98 (29.3)	395 (33.6)	0.91 (0.65, 1.27)	0.94 (0.69, 1.28)	125 (29.2)	431 (36.2)	0.79 (0.58, 1.06)	0.82 (0.62, 1.09)
G:G	27 (8.1)	80 (6.8)	1.13 (0.63, 2.01)	1.07 (0.65, 1.77)	23 (5.4)	81 (6.8)	0.71 (0.40, 1.27)	0.78 (0.48, 1.28)
Log-Additive			0.99 (0.78, 1.27)	1.00 (0.79, 1.26)			0.82 (0.65, 1.03)	0.83 (0.67, 1.04)
Dominant			0.95 (0.69, 1.29)	0.97 (0.72, 1.29)			0.77 (0.58, 1.03)	0.80 (0.61, 1.05)
Recessive			1.17 (0.66, 2.05)	1.09 (0.67, 1.79)			0.78 (0.44, 1.38)	0.83 (0.51, 1.35)
DOCK4 (rs3801790)								
A:A	116 (34.6)	431 (36.7)	1.00	1.00	153 (35.7)	412 (34.6)	1.00	1.00
A:G	132 (39.4)	478 (40.7)	1.05 (0.75, 1.47)	1.05 (0.77, 1.43)	135 (31.5)	508 (42.7)	**0.71 (0.52, 0.97)**	0.76 (0.56, 1.01)
G:G	52 (15.5)	177 (15.1)	1.04 (0.66, 1.63)	1.09 (0.73, 1.62)	60 (14.0)	182 (15.3)	0.93 (0.62, 1.40)	0.96 (0.66, 1.39)

Log-Additive			1.02 (0.82, 1.27)	1.05 (0.85, 1.29)			0.91 (0.74, 1.11)	0.92 (0.75, 1.12)
Dominant			1.04 (0.76, 1.43)	1.06 (0.79, 1.43)			0.77 (0.58, 1.02)	0.80 (0.61, 1.05)
Recessive			1.01 (0.67, 1.53)	1.06 (0.73, 1.55)			1.11 (0.76, 1.62)	1.09 (0.76, 1.55)
Rbl2 (rs3929)								
G:G	201 (60.0)	738 (62.9)	1.00	1.00	224 (52.3)	772 (64.9)	1.00	1.00
C:G	90 (26.9)	337 (28.7)	0.94 (0.67, 1.31)	0.94 (0.69, 1.29)	116 (27.1)	330 (27.7)	1.29 (0.96, 1.74)	1.23 (0.92, 1.63)
C:C	10 (3.0)	48 (4.1)	0.68 (0.30, 1.53)	0.78 (0.42, 1.44)	17 (4.0)	42 (3.5)	1.49 (0.75, 2.94)	1.30 (0.74, 2.30)
Log-Additive			0.89 (0.68, 1.17)	0.89 (0.69, 1.15)			1.26 (0.99, 1.60)	1.23 (0.97, 1.55)
Dominant			0.91 (0.66, 1.25)	0.90 (0.67, 1.22)			1.31 (0.98, 1.75)	1.26 (0.96, 1.66)
Recessive			0.69 (0.31, 1.55)	0.79 (0.43, 1.46)			1.37 (0.70, 2.69)	1.25 (0.71, 2.19)
IL6R (rs4072391)								
C:C	250 (74.6)	907 (77.3)	1.00	1.00	284 (66.4)	938 (78.8)	1.00	1.00
C:T	38 (11.3)	193 (16.4)	0.70 (0.44, 1.12)	0.72 (0.48, 1.09)	54 (12.6)	164 (13.8)	1.17 (0.79, 1.72)	1.13 (0.79, 1.61)
T:T	8 (2.4)	13 (1.1)	2.79 (0.98, 8.00)	1.58 (0.75, 3.31)	11 (2.6)	19 (1.6)	1.50 (0.58, 3.88)	1.23 (0.61, 2.46)
Log-Additive			0.98 (0.68, 1.41)	0.96 (0.68, 1.34)			1.19 (0.87, 1.62)	1.16 (0.87, 1.56)
Dominant			0.83 (0.54, 1.28)	0.84 (0.57, 1.23)			1.20 (0.84, 1.73)	1.17 (0.83, 1.64)
Recessive			**2.93 (1.02, 8.39)**	1.61 (0.77, 3.37)			1.46 (0.57, 3.78)	1.22 (0.61, 2.44)
CDK6 (rs42031)								
A:A	268 (80.0)	1015 (86.5)	1.00	1.00	316 (73.8)	1021 (85.8)	1.00	1.00
A:T	28 (8.4)	95 (8.1)	1.13 (0.67, 1.89)	1.08 (0.68, 1.71)	37 (8.6)	101 (8.5)	1.27 (0.79, 2.04)	1.17 (0.76, 1.79)
T:T	1 (0.3)	6 (0.5)	NA	0.79 (0.32, 1.96)	5 (1.2)	7 (0.6)	2.34 (0.58, 9.36)	1.47 (0.66, 3.28)
Log-Additive			0.97 (0.59, 1.58)	0.96 (0.62, 1.49)			1.34 (0.90, 2.00)	1.31 (0.91, 1.88)
Dominant			1.04 (0.62, 1.74)	1.02 (0.65, 1.60)			1.34 (0.86, 2.10)	1.27 (0.85, 1.91)
Recessive			NA	0.79 (0.32, 1.95)			2.30 (0.57, 9.17)	1.46 (0.66, 3.26)
Ago2 (rs4961280)								
C:C	242 (72.2)	831 (70.8)	1.00	1.00	273 (63.8)	834 (70.1)	1.00	1.00
C:A	46 (13.7)	226 (19.3)	0.71 (0.48, 1.07)	0.74 (0.51, 1.07)	66 (15.4)	226 (19.0)	0.83 (0.58, 1.19)	0.85 (0.61, 1.19)
A:A	8 (2.4)	17 (1.4)	1.69 (0.55, 5.21)	1.25 (0.59, 2.65)	11 (2.6)	28 (2.4)	1.06 (0.45, 2.50)	1.04 (0.54, 1.98)
Log-Additive			0.85 (0.60, 1.20)	0.86 (0.63, 1.19)			0.90 (0.67, 1.21)	0.91 (0.69, 1.21)
Dominant			0.77 (0.52, 1.13)	0.79 (0.56, 1.13)			0.86 (0.61, 1.21)	0.88 (0.64, 1.20)
Recessive			1.81 (0.59, 5.55)	1.28 (0.60, 2.72)			1.10 (0.46, 2.59)	1.05 (0.55, 2.02)
miR-26a1 (rs7372209)								
C:C	157 (46.9)	565 (48.1)	1.00	1.00	196 (45.8)	550 (46.2)	1.00	1.00
C:T	119 (35.5)	436 (37.1)	1.02 (0.74, 1.41)	1.00 (0.74, 1.35)	132 (30.8)	462 (38.8)	0.90 (0.67, 1.20)	0.89 (0.67, 1.17)
T:T	21 (6.3)	111 (9.5)	0.72 (0.39, 1.34)	0.75 (0.45, 1.24)	29 (6.8)	100 (8.4)	0.70 (0.41, 1.21)	0.74 (0.46, 1.18)
Log-Additive			0.93 (0.73, 1.18)	0.90 (0.71, 1.13)			0.86 (0.69, 1.07)	0.85 (0.69, 1.05)
Dominant			0.97 (0.71, 1.32)	0.93 (0.70, 1.25)			0.86 (0.65, 1.14)	0.84 (0.65, 1.10)
Recessive			0.71 (0.39, 1.30)	0.75 (0.45, 1.23)			0.73 (0.43, 1.25)	0.77 (0.48, 1.22)
Gemin4 (rs7813)								

T:T	147 (43.9)	530 (45.1)	1.00	1.00	170 (39.7)	582 (48.9)	1.00	1.00
C:T	109 (32.5)	419 (35.7)	0.98 (0.70, 1.37)	1.01 (0.74, 1.37)	130 (30.4)	414 (34.8)	1.13 (0.83, 1.53)	1.10 (0.83, 1.47)
C:C	36 (10.7)	112 (9.5)	0.84 (0.50, 1.42)	0.88 (0.56, 1.39)	37 (8.6)	98 (8.2)	1.30 (0.81, 2.09)	1.24 (0.81, 1.90)
Log-Additive			0.94 (0.75, 1.18)	0.95 (0.76, 1.18)			1.14 (0.92, 1.40)	1.13 (0.92, 1.39)
Dominant			0.95 (0.70, 1.29)	0.97 (0.72, 1.30)			1.16 (0.88, 1.55)	1.15 (0.87, 1.50)
Recessive			0.85 (0.52, 1.40)	0.88 (0.57, 1.37)			1.24 (0.78, 1.95)	1.20 (0.79, 1.81)
KARS (rs9266)								
C:C	202 (60.3)	706 (60.1)	1.00	1.00	224 (52.3)	702 (59.0)	1.00	1.00
C:T	83 (24.8)	350 (29.8)	0.76 (0.54, 1.07)	0.79 (0.58, 1.09)	98 (22.9)	350 (29.4)	0.79 (0.58, 1.09)	0.82 (0.61, 1.10)
T:T	12 (3.6)	45 (3.8)	0.77 (0.34, 1.73)	0.89 (0.49, 1.63)	28 (6.5)	70 (5.9)	1.01 (0.58, 1.75)	1.01 (0.63, 1.64)
Log-Additive			0.80 (0.60, 1.06)	0.83 (0.64, 1.08)			0.90 (0.72, 1.14)	0.92 (0.73, 1.14)
Dominant			0.76 (0.55, 1.05)	0.79 (0.58, 1.08)			0.83 (0.62, 1.11)	0.85 (0.65, 1.13)
Recessive			0.84 (0.37, 1.87)	0.93 (0.51, 1.71)			1.08 (0.63, 1.87)	1.06 (0.66, 1.71)

Notes: aOR: adjusted odds ratios; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Ca: Cases; Co: Controls; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income 10 years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28), and total energy intake (continuous, kcal/day).

Table 5.5. Associations between selected SNPs related to the stem cell pathway and stomach cancer by dietary intake of total fatty acids

	Low Fatty Acids				High Fatty acids			
dbSNP no.	Ca, n(%)	Co, n(%)	aOR*	sbOR*	Ca, n(%)	Co, n(%)	aOR*	sbOR*
HEY1 (rs1046472)								
C:C	190 (56.7)	710 (60.5)	1.00	1.00	205 (47.9)	693 (58.2)	1.00	1.00
A:C	94 (28.1)	342 (29.1)	1.11 (0.80, 1.55)	1.12 (0.82, 1.52)	118 (27.6)	375 (31.5)	1.06 (0.78, 1.43)	1.03 (0.77, 1.37)
A:A	19 (5.7)	57 (4.9)	1.18 (0.61, 2.26)	1.11 (0.64, 1.92)	31 (7.2)	51 (4.3)	1.71 (0.97, 3.02)	1.49 (0.91, 2.45)
Log-Additive			1.10 (0.85, 1.41)	1.10 (0.86, 1.40)			1.18 (0.94, 1.49)	1.16 (0.93, 1.45)
Dominant			1.12 (0.82, 1.54)	1.13 (0.84, 1.51)			1.14 (0.86, 1.51)	1.11 (0.85, 1.46)
Recessive			1.14 (0.60, 2.16)	1.08 (0.63, 1.86)			1.67 (0.96, 2.92)	1.48 (0.90, 2.42)
Oct4 (rs13409)								
C:C	103 (30.7)	404 (34.4)	1.00	1.00	129 (30.1)	402 (33.8)	1.00	1.00
C:T	135 (40.3)	480 (40.9)	1.00 (0.71, 1.42)	1.06 (0.77, 1.45)	145 (33.9)	522 (43.9)	0.77 (0.57, 1.06)	0.78 (0.58, 1.05)
T:T	59 (17.6)	221 (18.8)	0.89 (0.58, 1.36)	0.88 (0.60, 1.28)	71 (16.6)	193 (16.2)	0.98 (0.66, 1.45)	1.02 (0.71, 1.46)
Log-Additive			0.95 (0.77, 1.17)	0.94 (0.77, 1.15)			0.95 (0.78, 1.16)	0.96 (0.79, 1.17)
Dominant			0.96 (0.70, 1.32)	0.99 (0.73, 1.33)			0.83 (0.62, 1.11)	0.84 (0.64, 1.11)
Recessive			0.89 (0.61, 1.30)	0.85 (0.60, 1.21)			1.12 (0.78, 1.61)	1.15 (0.82, 1.60)
AXIN1 (rs1981492)								
G:G	152 (45.4)	561 (47.8)	1.00	1.00	200 (46.7)	567 (47.6)	1.00	1.00
A:G	114 (34.0)	421 (35.9)	0.88 (0.63, 1.22)	0.92 (0.68, 1.25)	110 (25.7)	436 (36.6)	**0.70 (0.51, 0.95)**	**0.72 (0.54, 0.96)**
A:A	35 (10.4)	111 (9.5)	0.79 (0.47, 1.33)	0.85 (0.54, 1.34)	49 (11.4)	104 (8.7)	1.14 (0.72, 1.78)	1.11 (0.74, 1.68)
Log-Additive			0.89 (0.70, 1.11)	0.91 (0.73, 1.13)			0.93 (0.75, 1.15)	0.93 (0.76, 1.14)
Dominant			0.86 (0.63, 1.17)	0.89 (0.67, 1.19)			0.79 (0.59, 1.04)	0.80 (0.61, 1.05)
Recessive			0.84 (0.51, 1.38)	0.88 (0.57, 1.36)			1.31 (0.85, 2.02)	1.24 (0.83, 1.85)
DVL2 (rs222851)								
A:A	120 (35.8)	411 (35.0)	1.00	1.00	133 (31.1)	461 (38.7)	1.00	1.00
A:G	134 (40.0)	494 (42.1)	1.16 (0.83, 1.62)	1.15 (0.84, 1.57)	155 (36.2)	492 (41.3)	1.10 (0.81, 1.50)	1.09 (0.82, 1.46)
G:G	38 (11.3)	171 (14.6)	0.82 (0.50, 1.35)	0.86 (0.56, 1.32)	52 (12.1)	153 (12.9)	1.24 (0.80, 1.92)	1.20 (0.81, 1.78)
Log-Additive			0.96 (0.77, 1.21)	0.97 (0.78, 1.21)			1.11 (0.90, 1.37)	1.11 (0.91, 1.36)
Dominant			1.07 (0.78, 1.47)	1.07 (0.79, 1.44)			1.13 (0.85, 1.51)	1.13 (0.86, 1.49)
Recessive			0.76 (0.48, 1.20)	0.81 (0.54, 1.21)			1.17 (0.78, 1.76)	1.15 (0.79, 1.67)
FZD3 (rs2241802)								
G:G	103 (30.7)	339 (28.9)	1.00	1.00	122 (28.5)	365 (30.7)	1.00	1.00
A:G	131 (39.1)	492 (41.9)	0.91 (0.64, 1.29)	0.91 (0.66, 1.26)	141 (32.9)	487 (40.9)	1.03 (0.74, 1.44)	1.01 (0.74, 1.38)
A:A	56 (16.7)	211 (18.0)	0.81 (0.51, 1.27)	0.86 (0.58, 1.28)	62 (14.5)	220 (18.5)	1.23 (0.82, 1.84)	1.18 (0.82, 1.71)
Log-Additive			0.90 (0.72, 1.12)	0.91 (0.74, 1.13)			1.10 (0.90, 1.34)	1.09 (0.90, 1.33)
Dominant			0.88 (0.63, 1.22)	0.88 (0.65, 1.21)			1.09 (0.80, 1.49)	1.07 (0.80, 1.44)

Recessive			0.86 (0.57, 1.28)	0.90 (0.63, 1.30)			1.21 (0.85, 1.72)	1.18 (0.84, 1.64)
Dec1 (rs2269700)								
T:T	218 (65.1)	763 (65.0)	1.00	1.00	254 (59.3)	736 (61.8)	1.00	1.00
C:T	81 (24.2)	301 (25.6)	1.03 (0.74, 1.45)	1.02 (0.74, 1.41)	97 (22.7)	341 (28.7)	0.78 (0.57, 1.07)	0.82 (0.61, 1.10)
C:C	5 (1.5)	42 (3.6)	0.75 (0.28, 1.97)	0.85 (0.44, 1.67)	6 (1.4)	48 (4.0)	0.49 (0.18, 1.30)	0.65 (0.34, 1.25)
Log-Additive			0.97 (0.73, 1.29)	0.97 (0.74, 1.27)			0.76 (0.58, 1.00)	0.77 (0.59, 1.00)
Dominant			1.00 (0.72, 1.39)	0.99 (0.73, 1.35)			0.75 (0.55, 1.02)	0.77 (0.58, 1.03)
Recessive			0.74 (0.28, 1.95)	0.85 (0.43, 1.66)			0.52 (0.20, 1.39)	0.67 (0.35, 1.29)
Oct4 (rs3130932)								
T:T	159 (47.5)	539 (45.9)	1.00	1.00	181 (42.3)	495 (41.6)	1.00	1.00
G:T	109 (32.5)	457 (38.9)	0.95 (0.69, 1.31)	0.96 (0.71, 1.30)	127 (29.7)	484 (40.7)	0.79 (0.58, 1.07)	0.78 (0.59, 1.04)
G:G	35 (10.4)	115 (9.8)	1.23 (0.76, 2.01)	1.16 (0.75, 1.79)	42 (9.8)	137 (11.5)	0.89 (0.57, 1.40)	0.90 (0.60, 1.35)
Log-Additive			1.06 (0.84, 1.32)	1.05 (0.84, 1.30)			0.89 (0.72, 1.10)	0.88 (0.72, 1.08)
Dominant			1.01 (0.74, 1.36)	1.01 (0.76, 1.35)			0.81 (0.61, 1.08)	0.80 (0.61, 1.05)
Recessive			1.26 (0.79, 2.02)	1.17 (0.77, 1.80)			0.99 (0.64, 1.53)	0.99 (0.66, 1.46)
WNT2 (rs3729629)								
G:G	147 (43.9)	499 (42.5)	1.00	1.00	181 (42.3)	507 (42.6)	1.00	1.00
C:G	115 (34.3)	482 (41.1)	**0.70 (0.51, 0.97)**	0.75 (0.56, 1.02)	148 (34.6)	494 (41.5)	0.98 (0.73, 1.32)	1.01 (0.76, 1.33)
C:C	34 (10.1)	125 (10.6)	1.00 (0.60, 1.65)	1.00 (0.64, 1.56)	25 (5.8)	119 (10.0)	0.61 (0.36, 1.03)	0.68 (0.43, 1.07)
Log-Additive			0.88 (0.70, 1.11)	0.89 (0.72, 1.12)			0.86 (0.69, 1.06)	0.87 (0.70, 1.07)
Dominant			0.76 (0.56, 1.02)	0.79 (0.60, 1.06)			0.90 (0.68, 1.20)	0.92 (0.70, 1.20)
Recessive			1.17 (0.72, 1.90)	1.11 (0.72, 1.71)			0.61 (0.37, 1.02)	0.68 (0.43, 1.05)
HEY2 (rs3734637)								
A:A	189 (56.4)	643 (54.8)	1.00	1.00	207 (48.4)	681 (57.2)	1.00	1.00
A:C	98 (29.3)	376 (32.0)	0.95 (0.68, 1.31)	0.98 (0.72, 1.33)	113 (26.4)	367 (30.8)	0.94 (0.69, 1.28)	0.97 (0.72, 1.30)
C:C	13 (3.9)	80 (6.8)	**0.45 (0.21, 0.94)**	0.58 (0.33, 1.01)	17 (4.0)	74 (6.2)	0.77 (0.41, 1.43)	0.84 (0.50, 1.40)
Log-Additive			0.81 (0.63, 1.04)	0.82 (0.64, 1.04)			0.91 (0.72, 1.15)	0.92 (0.74, 1.16)
Dominant			0.85 (0.62, 1.16)	0.87 (0.65, 1.17)			0.91 (0.68, 1.22)	0.93 (0.71, 1.24)
Recessive			**0.45 (0.22, 0.94)**	0.58 (0.33, 1.01)			0.79 (0.43, 1.45)	0.84 (0.50, 1.41)
Ctbp2 (rs3740535)								
G:G	156 (46.6)	616 (52.5)	1.00	1.00	195 (45.6)	598 (50.3)	1.00	1.00
A:G	108 (32.2)	405 (34.5)	1.00 (0.72, 1.39)	1.00 (0.73, 1.36)	110 (25.7)	430 (36.1)	0.83 (0.61, 1.13)	0.85 (0.63, 1.13)
A:A	34 (10.1)	90 (7.7)	1.37 (0.83, 2.27)	1.28 (0.82, 2.00)	37 (8.6)	84 (7.1)	1.05 (0.63, 1.75)	1.04 (0.66, 1.63)
Log-Additive			1.11 (0.89, 1.39)	1.11 (0.89, 1.38)			0.94 (0.75, 1.17)	0.94 (0.76, 1.17)
Dominant			1.07 (0.79, 1.46)	1.07 (0.80, 1.43)			0.87 (0.65, 1.16)	0.88 (0.67, 1.16)
Recessive			1.37 (0.84, 2.23)	1.28 (0.83, 1.98)			1.13 (0.69, 1.86)	1.10 (0.70, 1.71)
WNT2 (rs4730775)								
C:C	170 (50.7)	632 (53.8)	1.00	1.00	214 (50.0)	633 (53.2)	1.00	1.00
C:T	106 (31.6)	390 (33.2)	0.81 (0.58, 1.13)	0.89 (0.66, 1.21)	110 (25.7)	395 (33.2)	0.85 (0.63, 1.15)	0.88 (0.66, 1.17)

T:T	16 (4.8)	71 (6.0)	1.09 (0.57, 2.07)	1.08 (0.63, 1.85)	16 (3.7)	78 (6.6)	0.72 (0.39, 1.35)	0.79 (0.47, 1.33)
Log-Additive			0.92 (0.71, 1.19)	0.96 (0.75, 1.23)			0.85 (0.67, 1.08)	0.86 (0.68, 1.08)
Dominant			0.85 (0.62, 1.16)	0.92 (0.68, 1.24)			0.83 (0.62, 1.11)	0.85 (0.64, 1.12)
Recessive			1.18 (0.63, 2.21)	1.11 (0.65, 1.90)			0.77 (0.41, 1.42)	0.82 (0.49, 1.37)
WNT8A (rs4835761)								
A:A	115 (34.3)	358 (30.5)	1.00	1.00	137 (32.0)	377 (31.7)	1.00	1.00
A:G	117 (34.9)	508 (43.3)	**0.66 (0.47, 0.94)**	**0.67 (0.49, 0.93)**	141 (32.9)	510 (42.9)	0.82 (0.60, 1.13)	0.85 (0.63, 1.14)
G:G	63 (18.8)	200 (17.0)	0.96 (0.63, 1.47)	0.99 (0.68, 1.45)	67 (15.7)	201 (16.9)	0.98 (0.66, 1.46)	0.99 (0.69, 1.42)
Log-Additive			0.93 (0.75, 1.15)	0.93 (0.75, 1.14)			0.96 (0.79, 1.17)	0.96 (0.80, 1.17)
Dominant			0.75 (0.54, 1.03)	0.75 (0.56, 1.01)			0.87 (0.65, 1.16)	0.88 (0.67, 1.17)
Recessive			1.20 (0.82, 1.76)	1.20 (0.84, 1.70)			1.09 (0.76, 1.56)	1.07 (0.77, 1.50)
Notch4 (rs520692)								
A:A	209 (62.4)	846 (72.1)	1.00	1.00	258 (60.3)	860 (72.3)	1.00	1.00
A:G	67 (20.0)	247 (21.0)	0.97 (0.67, 1.40)	0.99 (0.71, 1.39)	80 (18.7)	248 (20.8)	0.92 (0.66, 1.28)	0.92 (0.67, 1.26)
G:G	4 (1.2)	21 (1.8)	1.06 (0.34, 3.32)	1.02 (0.48, 2.14)	2 (0.5)	18 (1.5)	0.37 (0.08, 1.69)	0.71 (0.33, 1.53)
Log-Additive			0.99 (0.72, 1.36)	1.00 (0.74, 1.35)			0.85 (0.63, 1.15)	0.86 (0.64, 1.14)
Dominant			0.98 (0.68, 1.39)	1.00 (0.72, 1.38)			0.88 (0.64, 1.22)	0.88 (0.65, 1.20)
Recessive			1.07 (0.34, 3.33)	1.02 (0.48, 2.14)			0.38 (0.08, 1.72)	0.72 (0.33, 1.55)
Rex1 (rs6815391)								
T:T	125 (37.3)	479 (40.8)	1.00	1.00	167 (39.0)	481 (40.4)	1.00	1.00
C:T	121 (36.1)	459 (39.1)	1.12 (0.79, 1.57)	1.11 (0.81, 1.51)	123 (28.7)	452 (38.0)	0.82 (0.60, 1.12)	0.82 (0.61, 1.11)
C:C	50 (14.9)	143 (12.2)	**1.64 (1.05, 2.56)**	**1.51 (1.01, 2.26)**	45 (10.5)	149 (12.5)	0.76 (0.49, 1.19)	0.78 (0.52, 1.16)
Log-Additive			**1.25 (1.00, 1.55)**	**1.24 (1.01, 1.53)**			0.86 (0.70, 1.05)	0.85 (0.69, 1.04)
Dominant			1.24 (0.91, 1.70)	1.24 (0.92, 1.67)			0.80 (0.60, 1.07)	0.80 (0.60, 1.05)
Recessive			**1.56 (1.03, 2.35)**	1.45 (0.99, 2.12)			0.84 (0.55, 1.27)	0.84 (0.58, 1.23)
HES2 (rs8708)								
A:A	214 (63.9)	753 (64.1)	1.00	1.00	232 (54.2)	738 (62.0)	1.00	1.00
A:G	70 (20.9)	307 (26.1)	1.00 (0.70, 1.42)	0.99 (0.71, 1.37)	92 (21.5)	315 (26.5)	0.97 (0.71, 1.34)	0.97 (0.71, 1.31)
G:G	6 (1.8)	43 (3.7)	0.80 (0.32, 2.00)	0.87 (0.45, 1.67)	12 (2.8)	46 (3.9)	0.93 (0.44, 1.96)	0.96 (0.53, 1.73)
Log-Additive			0.96 (0.72, 1.28)	0.95 (0.72, 1.25)			0.97 (0.75, 1.25)	0.96 (0.75, 1.24)
Dominant			0.97 (0.69, 1.37)	0.96 (0.70, 1.32)			0.97 (0.71, 1.31)	0.96 (0.72, 1.28)
Recessive			0.80 (0.32, 1.99)	0.87 (0.45, 1.67)			0.94 (0.44, 1.97)	0.96 (0.53, 1.74)
Notch4 (rs915894)								
C:C	109 (32.5)	319 (27.2)	1.00	1.00	107 (25.0)	331 (27.8)	1.00	1.00
A:C	131 (39.1)	525 (44.7)	0.77 (0.55, 1.09)	0.83 (0.60, 1.14)	145 (33.9)	521 (43.8)	0.87 (0.62, 1.22)	0.88 (0.65, 1.21)
A:A	58 (17.3)	245 (20.9)	0.71 (0.46, 1.09)	0.78 (0.53, 1.15)	97 (22.7)	250 (21.0)	1.22 (0.84, 1.77)	1.23 (0.87, 1.74)
Log-Additive			0.83 (0.67, 1.03)	0.86 (0.70, 1.05)			1.10 (0.91, 1.33)	1.11 (0.92, 1.34)
Dominant			0.75 (0.55, 1.04)	0.80 (0.59, 1.08)			0.98 (0.72, 1.34)	1.01 (0.75, 1.35)
Recessive			0.82 (0.56, 1.21)	0.86 (0.61, 1.23)			1.33 (0.96, 1.82)	1.32 (0.97, 1.78)

				NF-κB pathway				
miR-300 (rs12894467)								
T:T	166 (49.6)	652 (55.5)	1.00	1.00	182 (42.5)	691 (58.1)	1.00	1.00
C:T	99 (29.6)	364 (31.0)	1.17 (0.84, 1.64)	1.18 (0.86, 1.61)	115 (26.9)	338 (28.4)	**1.61 (1.18, 2.21)**	**1.49 (1.10, 2.00)**
C:C	25 (7.5)	66 (5.6)	1.11 (0.59, 2.07)	1.17 (0.70, 1.96)	33 (7.7)	59 (5.0)	**1.89 (1.09, 3.27)**	1.60 (0.99, 2.59)
Log-Additive			1.10 (0.86, 1.42)	1.15 (0.91, 1.46)			**1.47 (1.17, 1.84)**	**1.42 (1.14, 1.77)**
Dominant			1.16 (0.84, 1.59)	1.20 (0.89, 1.61)			**1.66 (1.24, 2.23)**	**1.56 (1.18, 2.07)**
Recessive			1.04 (0.57, 1.92)	1.12 (0.68, 1.86)			1.59 (0.94, 2.71)	1.44 (0.90, 2.30)
IKBKAP (rs1538660)								
C:C	140 (41.8)	494 (42.1)	1.00	1.00	172 (40.2)	528 (44.4)	1.00	1.00
C:T	126 (37.6)	473 (40.3)	0.79 (0.57, 1.09)	0.82 (0.60, 1.10)	132 (30.8)	447 (37.6)	0.88 (0.65, 1.20)	0.89 (0.67, 1.19)
T:T	35 (10.4)	120 (10.2)	1.02 (0.61, 1.69)	1.11 (0.71, 1.72)	47 (11.0)	135 (11.3)	1.09 (0.71, 1.69)	1.09 (0.73, 1.62)
Log-Additive			0.92 (0.73, 1.17)	0.97 (0.78, 1.21)			1.00 (0.81, 1.22)	1.00 (0.82, 1.22)
Dominant			0.83 (0.61, 1.12)	0.87 (0.65, 1.16)			0.93 (0.70, 1.24)	0.94 (0.72, 1.23)
Recessive			1.14 (0.70, 1.86)	1.20 (0.78, 1.84)			1.15 (0.76, 1.75)	1.14 (0.78, 1.66)
IKBKAP (rs2230793)								
A:A	141 (42.1)	534 (45.5)	1.00	1.00	184 (43.0)	532 (44.7)	1.00	1.00
A:C	114 (34.0)	460 (39.2)	0.89 (0.64, 1.23)	0.90 (0.66, 1.22)	127 (29.7)	461 (38.7)	0.87 (0.64, 1.17)	0.87 (0.66, 1.15)
C:C	43 (12.8)	111 (9.5)	**1.75 (1.09, 2.81)**	**1.54 (1.01, 2.35)**	45 (10.5)	114 (9.6)	1.34 (0.85, 2.12)	1.27 (0.84, 1.92)
Log-Additive			1.18 (0.94, 1.47)	1.16 (0.94, 1.44)			1.05 (0.85, 1.30)	1.05 (0.85, 1.28)
Dominant			1.04 (0.77, 1.41)	1.04 (0.78, 1.39)			0.95 (0.72, 1.26)	0.95 (0.73, 1.24)
Recessive			**1.85 (1.18, 2.89)**	**1.60 (1.06, 2.41)**			1.43 (0.92, 2.21)	1.34 (0.90, 2.00)
IKBKAP (rs3204145)								
T:T	138 (41.2)	509 (43.4)	1.00	1.00	178 (41.6)	531 (44.6)	1.00	1.00
A:T	130 (38.8)	488 (41.6)	0.82 (0.59, 1.13)	0.84 (0.62, 1.13)	140 (32.7)	460 (38.7)	0.84 (0.62, 1.13)	0.85 (0.64, 1.13)
A:A	34 (10.1)	120 (10.2)	1.02 (0.61, 1.70)	1.10 (0.71, 1.72)	37 (8.6)	126 (10.6)	0.89 (0.56, 1.42)	0.93 (0.61, 1.40)
Log-Additive			0.94 (0.74, 1.18)	0.97 (0.78, 1.21)			0.91 (0.74, 1.12)	0.91 (0.75, 1.12)
Dominant			0.85 (0.63, 1.15)	0.89 (0.67, 1.18)			0.85 (0.64, 1.12)	0.86 (0.66, 1.12)
Recessive			1.13 (0.69, 1.84)	1.18 (0.77, 1.82)			0.96 (0.61, 1.51)	0.98 (0.65, 1.47)

Notes: aOR: adjusted odds ratios; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Ca: Cases; Co: Controls; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28kg/m^2), and total energy intake (continuous, kcal/day).

Table 5.6. Associations between selected SNPs related to the GWAS and stomach cancer by dietary intake of total fatty acids

	Low Fatty Acids				High Fatty acids			
dbSNP no.	Ca, n(%)	Co, n(%)	aOR*	sbOR*	Ca, n(%)	Co, n(%)	aOR*	sbOR*
RUNX1 (rs2014300)								
G:G	236 (70.4)	858 (73.1)	1.00	1.00	259 (60.5)	860 (72.3)	1.00	1.00
A:G	55 (16.4)	237 (20.2)	0.97 (0.66, 1.42)	0.98 (0.69, 1.39)	73 (17.1)	235 (19.7)	1.06 (0.74, 1.50)	1.06 (0.76, 1.47)
A:A	8 (2.4)	23 (2.0)	1.07 (0.40, 2.85)	1.02 (0.51, 2.05)	14 (3.3)	27 (2.3)	1.51 (0.67, 3.42)	1.28 (0.67, 2.41)
Log-Additive			0.99 (0.73, 1.36)	0.99 (0.74, 1.34)			1.12 (0.85, 1.49)	1.12 (0.86, 1.47)
Dominant			0.98 (0.68, 1.41)	0.99 (0.70, 1.38)			1.10 (0.79, 1.54)	1.11 (0.81, 1.51)
Recessive			1.07 (0.40, 2.86)	1.02 (0.51, 2.05)			1.49 (0.66, 3.37)	1.27 (0.67, 2.39)
PLCE1 (rs2274223)								
A:A	163 (48.7)	692 (58.9)	1.00	1.00	169 (39.5)	688 (57.8)	1.00	1.00
A:G	95 (28.4)	346 (29.5)	1.04 (0.73, 1.47)	1.06 (0.77, 1.46)	119 (27.8)	354 (29.7)	**1.43 (1.03, 1.97)**	1.34 (0.99, 1.82)
G:G	13 (3.9)	43 (3.7)	1.43 (0.69, 2.97)	1.24 (0.69, 2.26)	15 (3.5)	51 (4.3)	1.46 (0.76, 2.83)	1.28 (0.74, 2.23)
Log-Additive			1.11 (0.84, 1.46)	1.12 (0.86, 1.45)			**1.31 (1.02, 1.69)**	**1.28 (1.01, 1.63)**
Dominant			1.08 (0.78, 1.51)	1.10 (0.81, 1.50)			**1.43 (1.05, 1.95)**	**1.36 (1.02, 1.83)**
Recessive			1.41 (0.68, 2.90)	1.23 (0.68, 2.22)			1.28 (0.67, 2.44)	1.19 (0.69, 2.04)
GPC5 (rs2352028)								
C:C	206 (61.5)	713 (60.7)	1.00	1.00	227 (53.0)	697 (58.6)	1.00	1.00
C:T	93 (27.8)	339 (28.9)	0.95 (0.68, 1.32)	0.98 (0.72, 1.33)	117 (27.3)	368 (30.9)	0.94 (0.70, 1.27)	0.95 (0.72, 1.26)
T:T	14 (4.2)	63 (5.4)	0.79 (0.39, 1.60)	0.83 (0.47, 1.47)	21 (4.9)	61 (5.1)	0.76 (0.39, 1.48)	0.82 (0.47, 1.41)
Log-Additive			0.92 (0.71, 1.19)	0.93 (0.73, 1.19)			0.91 (0.72, 1.15)	0.91 (0.73, 1.14)
Dominant			0.92 (0.67, 1.27)	0.94 (0.70, 1.27)			0.92 (0.69, 1.22)	0.92 (0.70, 1.21)
Recessive			0.80 (0.40, 1.61)	0.84 (0.48, 1.47)			0.77 (0.40, 1.50)	0.83 (0.48, 1.42)
TERT (rs2736100)								
T:T	118 (35.2)	325 (27.7)	1.00	1.00	139 (32.5)	376 (31.6)	1.00	1.00
G:T	132 (39.4)	513 (43.7)	**0.54 (0.38, 0.77)**	**0.60 (0.43, 0.83)**	145 (33.9)	493 (41.4)	0.89 (0.65, 1.23)	0.90 (0.67, 1.22)
G:G	46 (13.7)	206 (17.5)	**0.44 (0.28, 0.71)**	**0.52 (0.34, 0.79)**	56 (13.1)	194 (16.3)	0.78 (0.51, 1.19)	0.83 (0.57, 1.21)
Log-Additive			**0.64 (0.51, 0.81)**	**0.65 (0.52, 0.81)**			0.89 (0.72, 1.08)	0.90 (0.73, 1.09)
Dominant			**0.51 (0.37, 0.71)**	**0.54 (0.40, 0.74)**			0.86 (0.64, 1.16)	0.87 (0.66, 1.15)
Recessive			**0.64 (0.42, 0.98)**	**0.68 (0.46, 0.99)**			0.83 (0.56, 1.22)	0.87 (0.61, 1.24)
CRPP1 -CRP (rs2808630)								
T:T	229 (68.4)	825 (70.3)	1.00	1.00	256 (59.8)	825 (69.3)	1.00	1.00
C:T	55 (16.4)	244 (20.8)	0.90 (0.61, 1.31)	0.94 (0.66, 1.32)	71 (16.6)	255 (21.4)	1.01 (0.71, 1.43)	0.99 (0.71, 1.38)
C:C	13 (3.9)	32 (2.7)	1.39 (0.64, 3.02)	1.27 (0.69, 2.32)	16 (3.7)	33 (2.8)	1.77 (0.86, 3.64)	1.45 (0.80, 2.62)
Log-Additive			1.02 (0.76, 1.36)	1.05 (0.80, 1.38)			1.15 (0.88, 1.50)	1.13 (0.88, 1.46)
Dominant			0.96 (0.67, 1.37)	1.00 (0.72, 1.39)			1.10 (0.79, 1.52)	1.08 (0.79, 1.47)
Recessive			1.42 (0.66, 3.07)	1.28 (0.70, 2.34)			1.77 (0.86, 3.62)	1.45 (0.80, 2.61)
PLCE1 (rs3781264)								

T:T	220 (65.7)	748 (63.7)	1.00	1.00	246 (57.5)	772 (64.9)	1.00	1.00
C:T	67 (20.0)	260 (22.1)	0.88 (0.61, 1.27)	0.90 (0.64, 1.26)	90 (21.0)	273 (22.9)	1.08 (0.78, 1.50)	1.04 (0.76, 1.42)
C:C	10 (3.0)	26 (2.2)	1.50 (0.64, 3.49)	1.26 (0.65, 2.41)	12 (2.8)	24 (2.0)	1.57 (0.73, 3.41)	1.32 (0.71, 2.43)
Log-Additive			1.00 (0.74, 1.35)	1.01 (0.76, 1.34)			1.15 (0.88, 1.49)	1.12 (0.87, 1.44)
Dominant			0.94 (0.66, 1.33)	0.95 (0.69, 1.32)			1.13 (0.83, 1.54)	1.09 (0.81, 1.47)
Recessive			1.55 (0.67, 3.58)	1.27 (0.66, 2.45)			1.54 (0.71, 3.32)	1.31 (0.71, 2.41)
CLPTM1L (rs401681)								
C:C	139 (41.5)	504 (42.9)	1.00	1.00	173 (40.4)	497 (41.8)	1.00	1.00
C:T	119 (35.5)	453 (38.6)	0.97 (0.70, 1.34)	0.97 (0.71, 1.31)	127 (29.7)	468 (39.3)	0.75 (0.55, 1.02)	0.76 (0.57, 1.02)
T:T	39 (11.6)	118 (10.1)	1.30 (0.79, 2.14)	1.24 (0.80, 1.93)	42 (9.8)	125 (10.5)	0.99 (0.63, 1.56)	1.00 (0.66, 1.51)
Log-Additive			1.08 (0.86, 1.36)	1.08 (0.87, 1.35)			0.91 (0.73, 1.12)	0.91 (0.74, 1.12)
Dominant			1.03 (0.76, 1.40)	1.03 (0.77, 1.38)			0.80 (0.60, 1.06)	0.81 (0.62, 1.06)
Recessive			1.32 (0.82, 2.12)	1.26 (0.82, 1.92)			1.12 (0.73, 1.74)	1.11 (0.74, 1.65)
GKN2 -GKN1 (rs4254535)								
T:T	158 (47.2)	635 (54.1)	1.00	1.00	211 (49.3)	613 (51.5)	1.00	1.00
C:T	97 (29.0)	372 (31.7)	1.11 (0.79, 1.56)	1.11 (0.81, 1.51)	109 (25.5)	413 (34.7)	**0.70 (0.51, 0.95)**	**0.72 (0.54, 0.97)**
C:C	34 (10.1)	93 (7.9)	**1.86 (1.13, 3.06)**	**1.65 (1.06, 2.57)**	30 (7.0)	86 (7.2)	0.98 (0.58, 1.66)	0.96 (0.61, 1.53)
Log-Additive			**1.28 (1.02, 1.60)**	**1.28 (1.03, 1.59)**			0.85 (0.68, 1.07)	0.85 (0.68, 1.06)
Dominant			1.26 (0.92, 1.71)	1.26 (0.94, 1.68)			**0.74 (0.56, 0.99)**	0.76 (0.58, 1.00)
Recessive			**1.78 (1.10, 2.89)**	**1.60 (1.03, 2.46)**			1.12 (0.67, 1.88)	1.06 (0.67, 1.67)
CCR4 -GLB1 (rs4678680)								
T:T	272 (81.2)	1004 (85.5)	1.00	1.00	332 (77.6)	1011 (85.0)	1.00	1.00
G:T	32 (9.6)	118 (10.1)	1.00 (0.61, 1.66)	1.02 (0.65, 1.58)	40 (9.3)	130 (10.9)	0.97 (0.63, 1.49)	0.96 (0.65, 1.42)
G:G	4 (1.2)	5 (0.4)	2.61 (0.57, 11.86)	1.30 (0.56, 3.04)	4 (0.9)	6 (0.5)	1.78 (0.38, 8.40)	1.36 (0.59, 3.10)
Log-Additive			1.14 (0.74, 1.75)	1.13 (0.77, 1.67)			1.04 (0.70, 1.52)	1.08 (0.76, 1.54)
Dominant			1.08 (0.67, 1.75)	1.08 (0.71, 1.66)			1.00 (0.66, 1.52)	1.03 (0.70, 1.50)
Recessive			2.61 (0.57, 11.84)	1.30 (0.56, 3.03)			1.78 (0.38, 8.42)	1.36 (0.60, 3.11)
TERT -CLPTM1L (rs4975616)								
A:A	226 (67.5)	786 (67.0)	1.00	1.00	254 (59.3)	802 (67.4)	1.00	1.00
A:G	62 (18.5)	275 (23.4)	0.83 (0.57, 1.20)	0.83 (0.59, 1.17)	80 (18.7)	285 (23.9)	1.06 (0.77, 1.48)	1.05 (0.77, 1.43)
G:G	16 (4.8)	37 (3.2)	1.30 (0.61, 2.77)	1.16 (0.64, 2.13)	15 (3.5)	30 (2.5)	2.00 (0.96, 4.17)	1.56 (0.85, 2.83)
Log-Additive			0.96 (0.72, 1.27)	0.95 (0.72, 1.24)			1.20 (0.92, 1.56)	1.19 (0.92, 1.53)
Dominant			0.89 (0.63, 1.25)	0.88 (0.64, 1.22)			1.15 (0.84, 1.57)	1.14 (0.85, 1.53)
Recessive			1.36 (0.64, 2.88)	1.19 (0.65, 2.18)			1.97 (0.95, 4.08)	1.54 (0.85, 2.80)
CHEK2 (rs738722)								
C:C	140 (41.8)	582 (49.6)	1.00	1.00	183 (42.8)	620 (52.1)	1.00	1.00
C:T	112 (33.4)	420 (35.8)	1.14 (0.81, 1.59)	1.06 (0.77, 1.44)	130 (30.4)	376 (31.6)	1.25 (0.92, 1.68)	1.22 (0.92, 1.62)
T:T	39 (11.6)	81 (6.9)	**2.24 (1.35, 3.70)**	**1.86 (1.19, 2.91)**	32 (7.5)	96 (8.1)	1.07 (0.65, 1.76)	1.05 (0.67, 1.64)
Log-Additive			**1.37 (1.09, 1.73)**	**1.32 (1.06, 1.66)**			1.11 (0.90, 1.37)	1.10 (0.90, 1.35)

Dominant			1.32 (0.96, 1.80)	1.24 (0.93, 1.67)			1.21 (0.91, 1.60)	1.19 (0.91, 1.56)
Recessive			**2.11 (1.31, 3.42)**	**1.82 (1.18, 2.81)**			0.98 (0.60, 1.59)	0.99 (0.64, 1.52)
TGM5 (rs748404)								
T:T	270 (80.6)	1000 (85.2)	1.00	1.00	316 (73.8)	999 (83.9)	1.00	1.00
C:T	26 (7.8)	100 (8.5)	1.13 (0.67, 1.93)	1.06 (0.67, 1.69)	29 (6.8)	112 (9.4)	0.87 (0.54, 1.40)	0.88 (0.58, 1.36)
C:C	1 (0.3)	6 (0.5)	0.27 (0.03, 2.46)	0.76 (0.32, 1.78)	5 (1.2)	6 (0.5)	1.77 (0.28, 11.23)	1.13 (0.47, 2.72)
Log-Additive			0.94 (0.59, 1.51)	0.92 (0.60, 1.40)			0.94 (0.61, 1.45)	0.94 (0.64, 1.40)
Dominant			1.03 (0.61, 1.73)	0.98 (0.62, 1.55)			0.90 (0.56, 1.43)	0.91 (0.60, 1.39)
Recessive			0.27 (0.03, 2.43)	0.75 (0.32, 1.78)			1.79 (0.28, 11.35)	1.13 (0.47, 2.73)
IL1RAP (rs7626795)								
A:A	200 (59.7)	711 (60.6)	1.00	1.00	247 (57.7)	752 (63.2)	1.00	1.00
A:G	89 (26.6)	338 (28.8)	0.81 (0.57, 1.14)	0.87 (0.63, 1.19)	91 (21.3)	317 (26.6)	1.02 (0.74, 1.39)	0.98 (0.73, 1.32)
G:G	16 (4.8)	49 (4.2)	0.82 (0.41, 1.66)	0.94 (0.54, 1.65)	16 (3.7)	51 (4.3)	1.00 (0.50, 1.98)	0.98 (0.56, 1.71)
Log-Additive			0.85 (0.65, 1.11)	0.91 (0.71, 1.16)			1.01 (0.79, 1.29)	0.98 (0.77, 1.25)
Dominant			0.81 (0.58, 1.12)	0.87 (0.65, 1.18)			1.01 (0.75, 1.37)	0.98 (0.73, 1.30)
Recessive			0.87 (0.44, 1.75)	0.97 (0.56, 1.69)			0.99 (0.50, 1.95)	0.98 (0.56, 1.71)
CHRNA3 (rs8042374)								
G:G	147 (43.9)	538 (45.8)	1.00	1.00	182 (42.5)	548 (46.1)	1.00	1.00
A:G	111 (33.1)	435 (37.1)	0.88 (0.63, 1.23)	0.89 (0.65, 1.21)	123 (28.7)	449 (37.7)	0.78 (0.57, 1.05)	0.79 (0.59, 1.05)
A:A	29 (8.7)	95 (8.1)	1.28 (0.75, 2.19)	1.16 (0.73, 1.86)	38 (8.9)	93 (7.8)	1.44 (0.88, 2.36)	1.29 (0.83, 2.00)
Log-Additive			1.03 (0.81, 1.31)	1.01 (0.80, 1.27)			1.02 (0.81, 1.27)	1.00 (0.81, 1.24)
Dominant			0.95 (0.69, 1.29)	0.95 (0.71, 1.27)			0.87 (0.66, 1.16)	0.87 (0.67, 1.15)
Recessive			1.36 (0.81, 2.27)	1.21 (0.76, 1.91)			1.61 (1.00, 2.58)	1.41 (0.92, 2.16)
FTO (rs8050136)								
C:C	232 (69.3)	869 (74.0)	1.00	1.00	268 (62.6)	897 (75.4)	1.00	1.00
A:C	67 (20.0)	226 (19.3)	1.14 (0.78, 1.66)	1.14 (0.81, 1.61)	78 (18.2)	196 (16.5)	**1.43 (1.01, 2.05)**	1.36 (0.97, 1.89)
A:A	3 (0.9)	19 (1.6)	0.45 (0.10, 2.05)	0.76 (0.35, 1.66)	2 (0.5)	30 (2.5)	**0.12 (0.01, 0.89)**	0.52 (0.25, 1.10)
Log-Additive			1.01 (0.72, 1.40)	1.02 (0.75, 1.38)			1.03 (0.76, 1.39)	1.01 (0.76, 1.35)
Dominant			1.08 (0.75, 1.55)	1.08 (0.77, 1.51)			1.22 (0.87, 1.73)	1.17 (0.84, 1.62)
Recessive			0.44 (0.10, 1.99)	0.75 (0.35, 1.64)			**0.11 (0.01, 0.83)**	0.51 (0.24, 1.07)
ZBTB12-C2 (rs9267673)								
C:C	207 (61.8)	777 (66.2)	1.00	1.00	250 (58.4)	808 (67.9)	1.00	1.00
C:T	81 (24.2)	287 (24.4)	0.89 (0.62, 1.27)	0.89 (0.64, 1.23)	77 (18.0)	276 (23.2)	0.94 (0.67, 1.31)	0.91 (0.66, 1.25)
T:T	13 (3.9)	36 (3.1)	1.07 (0.47, 2.40)	1.03 (0.55, 1.93)	22 (5.1)	32 (2.7)	**2.34 (1.19, 4.61)**	**1.86 (1.07, 3.25)**
Log-Additive			0.94 (0.71, 1.26)	0.94 (0.71, 1.23)			1.18 (0.91, 1.53)	1.17 (0.92, 1.50)
Dominant			0.91 (0.65, 1.27)	0.90 (0.66, 1.24)			1.07 (0.78, 1.47)	1.06 (0.79, 1.42)
Recessive			1.10 (0.49, 2.46)	1.05 (0.56, 1.97)			**2.38 (1.22, 4.66)**	**1.89 (1.09, 3.30)**

HLA-DQB1- HLA-DQA2 (rs9275572)								
G:G	156 (46.6)	569 (48.5)	1.00	1.00	181 (42.3)	596 (50.1)	1.00	1.00
A:G	112 (33.4)	427 (36.4)	0.95 (0.68, 1.32)	0.98 (0.72, 1.32)	119 (27.8)	418 (35.1)	0.78 (0.57, 1.07)	0.81 (0.60, 1.09)
A:A	26 (7.8)	107 (9.1)	1.30 (0.76, 2.22)	1.20 (0.75, 1.91)	39 (9.1)	99 (8.3)	1.05 (0.65, 1.69)	1.07 (0.70, 1.64)
Log-Additive			1.07 (0.84, 1.35)	1.06 (0.85, 1.33)			0.93 (0.75, 1.16)	0.95 (0.77, 1.17)
Dominant			1.01 (0.74, 1.37)	1.03 (0.77, 1.37)			0.84 (0.63, 1.12)	0.86 (0.66, 1.14)
Recessive			1.33 (0.80, 2.22)	1.21 (0.76, 1.91)			1.16 (0.73, 1.84)	1.15 (0.76, 1.74)
SEMA5B (rs9868873)								
G:G	211 (63.0)	752 (64.1)	1.00	1.00	234 (54.7)	736 (61.8)	1.00	1.00
A:G	68 (20.3)	326 (27.8)	0.73 (0.51, 1.04)	0.78 (0.56, 1.08)	99 (23.1)	329 (27.6)	0.97 (0.71, 1.33)	0.99 (0.73, 1.33)
A:A	25 (7.5)	33 (2.8)	1.64 (0.83, 3.24)	1.42 (0.81, 2.49)	22 (5.1)	56 (4.7)	1.59 (0.90, 2.82)	1.41 (0.86, 2.33)
Log-Additive			0.96 (0.73, 1.26)	0.99 (0.77, 1.28)			1.12 (0.89, 1.41)	1.12 (0.90, 1.41)
Dominant			0.83 (0.60, 1.15)	0.88 (0.65, 1.20)			1.06 (0.79, 1.42)	1.07 (0.81, 1.42)
Recessive			1.79 (0.92, 3.51)	1.49 (0.85, 2.61)			1.61 (0.91, 2.83)	1.42 (0.86, 2.33)

Notes: aOR: adjusted odds ratios; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Ca: Cases; Co: Controls; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28kg/m^2), and total energy intake (continuous, kcal/day).

Table 5.7. Associations between selected SNPs related to the HIF and beta-carotene metabolism pathway and stomach cancer by dietary intake of total fatty acids

	Low Fatty Acids				High Fatty acids			
dbSNP no.	Ca, n(%)	Co, n(%)	aOR*	sbOR*	Ca, n(%)	Co, n(%)	aOR*	sbOR*
HIF pathway								
HIF1A (rs2057482)								
C:C	196 (58.5)	690 (58.8)	1.00	1.00	243 (56.8)	744 (62.5)	1.00	1.00
T:C	100 (29.9)	353 (30.1)	0.95 (0.68, 1.32)	1.01 (0.74, 1.37)	116 (27.1)	312 (26.2)	1.14 (0.84, 1.53)	1.12 (0.84, 1.49)
T:T	12 (3.6)	47 (4.0)	0.92 (0.41, 2.06)	1.00 (0.54, 1.84)	18 (4.2)	53 (4.5)	1.01 (0.53, 1.94)	1.01 (0.59, 1.74)
Log-Additive			0.95 (0.72, 1.25)	1.00 (0.78, 1.30)			1.07 (0.85, 1.35)	1.07 (0.86, 1.34)
Dominant			0.94 (0.68, 1.30)	1.01 (0.75, 1.36)			1.12 (0.84, 1.48)	1.11 (0.84, 1.46)
Recessive			0.93 (0.42, 2.08)	1.00 (0.54, 1.83)			0.97 (0.51, 1.85)	0.99 (0.58, 1.69)
HIF1AN (rs2295778)								
C:C	174 (51.9)	581 (49.5)	1.00	1.00	197 (46.0)	609 (51.2)	1.00	1.00
C:G	117 (34.9)	363 (30.9)	1.07 (0.77, 1.49)	1.05 (0.77, 1.43)	138 (32.2)	357 (30.0)	1.17 (0.86, 1.59)	1.18 (0.88, 1.57)
G:G	17 (5.1)	60 (5.1)	1.17 (0.59, 2.31)	1.09 (0.62, 1.91)	18 (4.2)	67 (5.6)	0.79 (0.42, 1.46)	0.85 (0.50, 1.42)
Log-Additive			1.08 (0.83, 1.40)	1.06 (0.82, 1.36)			1.01 (0.80, 1.28)	1.02 (0.82, 1.28)
Dominant			1.08 (0.79, 1.49)	1.06 (0.78, 1.43)			1.10 (0.82, 1.48)	1.11 (0.84, 1.47)
Recessive			1.14 (0.58, 2.22)	1.08 (0.62, 1.88)			0.74 (0.40, 1.36)	0.81 (0.48, 1.34)
Beta-carotene metabolism related								
R267S (rs12934922)								
A:A	233 (69.6)	831 (70.8)	1.00	1.00	267 (62.4)	819 (68.8)	1.00	1.00
A:T	66 (19.7)	252 (21.5)	1.03 (0.71, 1.49)	1.05 (0.75, 1.46)	74 (17.3)	264 (22.2)	0.80 (0.57, 1.13)	0.81 (0.59, 1.12)
T:T	7 (2.1)	18 (1.5)	1.49 (0.49, 4.50)	1.18 (0.56, 2.49)	14 (3.3)	32 (2.7)	1.88 (0.93, 3.82)	1.52 (0.85, 2.73)
Log-Additive			1.08 (0.79, 1.49)	1.09 (0.81, 1.47)			1.02 (0.78, 1.33)	1.01 (0.79, 1.31)
Dominant			1.06 (0.74, 1.51)	1.07 (0.77, 1.49)			0.91 (0.66, 1.25)	0.91 (0.67, 1.23)
Recessive			1.48 (0.49, 4.45)	1.17 (0.56, 2.48)			1.98 (0.98, 4.00)	1.57 (0.88, 2.82)
A379V (rs7501331)								
C:C	241 (71.9)	834 (71.0)	1.00	1.00	283 (66.1)	856 (71.9)	1.00	1.00
C:T	52 (15.5)	252 (21.5)	0.79 (0.53, 1.17)	0.81 (0.57, 1.16)	65 (15.2)	244 (20.5)	0.87 (0.61, 1.24)	0.88 (0.63, 1.22)
T:T	10 (3.0)	35 (3.0)	1.50 (0.69, 3.26)	1.25 (0.67, 2.31)	15 (3.5)	28 (2.4)	1.48 (0.70, 3.09)	1.28 (0.71, 2.33)
Log-Additive			0.97 (0.72, 1.30)	0.96 (0.72, 1.27)			1.01 (0.77, 1.33)	1.01 (0.78, 1.31)
Dominant			0.87 (0.61, 1.25)	0.88 (0.63, 1.23)			0.94 (0.68, 1.31)	0.95 (0.70, 1.29)
Recessive			1.58 (0.73, 3.41)	1.28 (0.69, 2.38)			1.52 (0.72, 3.17)	1.30 (0.72, 2.37)

Notes: aOR: adjusted odds ratios; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Ca: Cases; Co: Controls; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income 10 years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28), and total energy intake (continuous, kcal/day).

Table 5.8. Associations between selected SNPs related to the miRNA pathway and stomach cancer by dietary intake of total cholesterol

	Low Cholesterol				High Cholesterol			
dbSNP no.	Ca, n(%)	Co, n(%)	aOR*	sbOR*	Cas, n(%)	Co, n(%)	aOR*	sbOR*
IL15(rs10519613)								
C:C	112 (32.3)	474 (34.3)	1.00	1.00	130 (31.3)	320 (32.6)	1.00	1.00
C:A	137 (39.5)	583 (42.2)	0.91 (0.66, 1.26)	0.94 (0.69, 1.27)	156 (37.5)	422 (43.0)	0.91 (0.66, 1.26)	0.93 (0.69, 1.26)
A:A	50 (14.4)	240 (17.4)	0.86 (0.56, 1.31)	0.90 (0.61, 1.32)	58 (13.9)	180 (18.3)	0.78 (0.51, 1.19)	0.82 (0.56, 1.20)
Log-Additive			0.92 (0.75, 1.13)	0.94 (0.77, 1.14)			0.89 (0.72, 1.09)	0.90 (0.73, 1.09)
Dominant			0.89 (0.66, 1.21)	0.92 (0.69, 1.23)			0.87 (0.64, 1.18)	0.88 (0.66, 1.18)
Recessive			0.90 (0.61, 1.33)	0.92 (0.64, 1.32)			0.82 (0.56, 1.20)	0.85 (0.60, 1.21)
miR-196a2 (rs11614913)								
T:T	87 (25.1)	419 (30.3)	1.00	1.00	124 (29.8)	267 (27.2)	1.00	1.00
C:T	134 (38.6)	601 (43.5)	1.00 (0.71, 1.41)	1.01 (0.74, 1.39)	139 (33.4)	417 (42.5)	0.72 (0.51, 1.01)	0.78 (0.57, 1.07)
C:C	72 (20.7)	263 (19.0)	1.05 (0.70, 1.58)	1.08 (0.74, 1.56)	84 (20.2)	198 (20.2)	0.86 (0.58, 1.29)	0.90 (0.63, 1.31)
Log-Additive			1.02 (0.83, 1.25)	1.04 (0.86, 1.27)			0.91 (0.74, 1.11)	0.92 (0.75, 1.12)
Dominant			1.02 (0.74, 1.40)	1.04 (0.77, 1.41)			0.76 (0.56, 1.05)	0.81 (0.60, 1.09)
Recessive			1.05 (0.74, 1.49)	1.07 (0.77, 1.49)			1.05 (0.74, 1.49)	1.03 (0.74, 1.43)
WWOX (rs12828)								
G:G	122 (35.2)	527 (38.1)	1.00	1.00	130 (31.3)	383 (39.0)	1.00	1.00
A:G	123 (35.4)	567 (41.0)	1.10 (0.79, 1.52)	1.08 (0.80, 1.47)	131 (31.5)	379 (38.6)	1.05 (0.75, 1.46)	1.06 (0.78, 1.44)
A:A	53 (15.3)	183 (13.2)	1.38 (0.90, 2.12)	1.34 (0.91, 1.97)	78 (18.8)	133 (13.5)	**1.60 (1.07, 2.40)**	**1.49 (1.03, 2.15)**
Log-Additive			1.16 (0.94, 1.43)	1.17 (0.95, 1.43)			**1.23 (1.01, 1.51)**	**1.23 (1.01, 1.49)**
Dominant			1.17 (0.86, 1.59)	1.17 (0.88, 1.56)			1.20 (0.89, 1.63)	1.20 (0.90, 1.61)
Recessive			1.32 (0.89, 1.94)	1.29 (0.90, 1.85)			**1.56 (1.08, 2.25)**	**1.45 (1.03, 2.05)**
Ran (rs14035)								
C:C	194 (55.9)	837 (60.6)	1.00	1.00	247 (59.4)	568 (57.8)	1.00	1.00
C:T	97 (28.0)	358 (25.9)	1.12 (0.81, 1.54)	1.09 (0.80, 1.48)	85 (20.4)	249 (25.4)	0.86 (0.61, 1.22)	0.87 (0.63, 1.21)
T:T	11 (3.2)	58 (4.2)	0.82 (0.39, 1.74)	0.86 (0.48, 1.55)	15 (3.6)	37 (3.8)	1.42 (0.71, 2.85)	1.26 (0.71, 2.24)
Log-Additive			1.02 (0.79, 1.32)	1.00 (0.78, 1.28)			1.00 (0.77, 1.31)	1.01 (0.78, 1.30)
Dominant			1.07 (0.79, 1.47)	1.04 (0.78, 1.40)			0.93 (0.67, 1.28)	0.94 (0.69, 1.27)
Recessive			0.79 (0.38, 1.67)	0.85 (0.47, 1.52)			1.49 (0.75, 2.96)	1.30 (0.73, 2.29)
CXCL12 (rs1804429)								
T:T	271 (78.1)	1135 (82.1)	1.00	1.00	304 (73.1)	811 (82.6)	1.00	1.00
G:T	27 (7.8)	157 (11.4)	0.68 (0.42, 1.12)	0.71 (0.46, 1.09)	37 (8.9)	112 (11.4)	0.93 (0.59, 1.48)	0.92 (0.60, 1.39)
G:G	2 (0.6)	6 (0.4)	0.87 (0.09, 8.77)	0.98 (0.40, 2.39)	3 (0.7)	6 (0.6)	0.69 (0.07, 6.43)	1.09 (0.46, 2.58)
Log-Additive			0.71 (0.45, 1.13)	0.73 (0.48, 1.10)			0.92 (0.60, 1.41)	0.96 (0.65, 1.41)
Dominant			0.69 (0.43, 1.12)	0.71 (0.46, 1.09)			0.92 (0.59, 1.45)	0.94 (0.62, 1.41)
Recessive			0.89 (0.09, 9.03)	0.98 (0.40, 2.40)			0.70 (0.08, 6.48)	1.09 (0.46, 2.59)

Gemin3 (rs197412)								
T:T	149 (42.9)	594 (43.0)	1.00	1.00	162 (38.9)	398 (40.5)	1.00	1.00
T:C	108 (31.1)	560 (40.5)	0.72 (0.52, 1.00)	0.74 (0.55, 1.00)	145 (34.9)	404 (41.1)	0.89 (0.65, 1.22)	0.91 (0.68, 1.23)
C:C	47 (13.5)	138 (10.0)	1.55 (1.00, 2.39)	1.42 (0.95, 2.11)	40 (9.6)	104 (10.6)	1.06 (0.67, 1.69)	1.05 (0.69, 1.60)
Log-Additive			1.08 (0.87, 1.34)	1.06 (0.86, 1.31)			0.99 (0.79, 1.22)	0.99 (0.80, 1.22)
Dominant			0.88 (0.65, 1.18)	0.89 (0.67, 1.17)			0.92 (0.69, 1.24)	0.94 (0.71, 1.25)
Recessive			**1.79 (1.19, 2.71)**	**1.59 (1.08, 2.33)**			1.12 (0.72, 1.75)	1.09 (0.73, 1.63)
E2F2 (rs2075993)								
G:G	119 (34.3)	495 (35.8)	1.00	1.00	154 (37.0)	305 (31.1)	1.00	1.00
G:A	124 (35.7)	558 (40.4)	0.96 (0.69, 1.32)	0.95 (0.70, 1.28)	128 (30.8)	430 (43.8)	**0.58 (0.42, 0.80)**	**0.64 (0.47, 0.86)**
A:A	56 (16.1)	208 (15.1)	1.14 (0.76, 1.73)	1.12 (0.77, 1.63)	60 (14.4)	153 (15.6)	**0.64 (0.41, 0.99)**	0.69 (0.47, 1.03)
Log-Additive			1.05 (0.86, 1.28)	1.04 (0.86, 1.27)			**0.74 (0.60, 0.92)**	**0.75 (0.61, 0.92)**
Dominant			1.01 (0.75, 1.36)	1.00 (0.75, 1.33)			**0.60 (0.44, 0.81)**	**0.63 (0.47, 0.84)**
Recessive			1.17 (0.80, 1.71)	1.15 (0.80, 1.63)			0.84 (0.56, 1.27)	0.85 (0.58, 1.23)
THBS1 (rs2292305)								
T:T	154 (44.4)	579 (41.9)	1.00	1.00	141 (33.9)	424 (43.2)	1.00	1.00
C:T	103 (29.7)	537 (38.9)	0.73 (0.53, 1.00)	**0.73 (0.54, 0.99)**	127 (30.5)	384 (39.1)	1.15 (0.83, 1.59)	1.08 (0.80, 1.46)
C:C	32 (9.2)	164 (11.9)	0.79 (0.49, 1.27)	0.83 (0.54, 1.26)	39 (9.4)	100 (10.2)	1.26 (0.78, 2.05)	1.17 (0.76, 1.80)
Log-Additive			0.84 (0.67, 1.04)	0.83 (0.67, 1.03)			1.13 (0.91, 1.41)	1.10 (0.89, 1.36)
Dominant			**0.74 (0.55, 1.00)**	**0.74 (0.56, 0.98)**			1.18 (0.87, 1.59)	1.11 (0.84, 1.49)
Recessive			0.91 (0.58, 1.43)	0.93 (0.61, 1.39)			1.18 (0.75, 1.87)	1.14 (0.75, 1.72)
pre-miR-146a (rs2910164)								
C:C	101 (29.1)	488 (35.3)	1.00	1.00	118 (28.4)	329 (33.5)	1.00	1.00
G:C	145 (41.8)	594 (43.0)	1.37 (0.99, 1.91)	1.31 (0.97, 1.78)	167 (40.1)	429 (43.7)	0.98 (0.71, 1.36)	1.01 (0.75, 1.38)
G:G	49 (14.1)	232 (16.8)	0.96 (0.61, 1.49)	0.95 (0.64, 1.41)	54 (13.0)	157 (16.0)	0.89 (0.57, 1.39)	0.93 (0.62, 1.38)
Log-Additive			1.04 (0.84, 1.27)	1.03 (0.85, 1.26)			0.95 (0.77, 1.18)	0.97 (0.79, 1.19)
Dominant			1.24 (0.91, 1.70)	1.21 (0.90, 1.62)			0.96 (0.70, 1.30)	0.99 (0.74, 1.32)
Recessive			0.80 (0.54, 1.19)	0.83 (0.58, 1.20)			0.90 (0.60, 1.35)	0.92 (0.64, 1.33)
CTNNB1 (rs2953)								
T:T	173 (49.9)	743 (53.8)	1.00	1.00	198 (47.6)	507 (51.6)	1.00	1.00
G:T	108 (31.1)	480 (34.7)	0.96 (0.70, 1.32)	0.99 (0.74, 1.33)	115 (27.6)	346 (35.2)	0.77 (0.56, 1.06)	0.81 (0.60, 1.09)
G:G	21 (6.1)	90 (6.5)	0.98 (0.54, 1.80)	0.98 (0.59, 1.64)	29 (7.0)	71 (7.2)	0.84 (0.48, 1.45)	0.87 (0.54, 1.40)
Log-Additive			0.98 (0.77, 1.24)	0.99 (0.78, 1.24)			0.85 (0.67, 1.07)	0.86 (0.69, 1.08)
Dominant			0.97 (0.72, 1.30)	0.99 (0.74, 1.31)			0.78 (0.58, 1.05)	0.81 (0.61, 1.07)
Recessive			1.00 (0.55, 1.80)	0.98 (0.59, 1.63)			0.92 (0.54, 1.58)	0.92 (0.57, 1.48)
DOCK4 (rs3801790)								
A:A	124 (35.7)	498 (36.0)	1.00	1.00	145 (34.9)	345 (35.1)	1.00	1.00
A:G	126 (36.3)	574 (41.5)	0.84 (0.61, 1.16)	0.87 (0.65, 1.18)	141 (33.9)	412 (42.0)	0.87 (0.63, 1.20)	0.90 (0.66, 1.21)
G:G	49 (14.1)	209 (15.1)	0.87 (0.56, 1.35)	0.94 (0.63, 1.38)	63 (15.1)	150 (15.3)	1.07 (0.70, 1.63)	1.07 (0.73, 1.58)

Log-Additive			0.91 (0.74, 1.13)	0.94 (0.77, 1.15)			1.00 (0.81, 1.23)	1.01 (0.83, 1.23)
Dominant			0.85 (0.63, 1.15)	0.88 (0.66, 1.18)			0.92 (0.68, 1.24)	0.94 (0.71, 1.25)
Recessive			0.95 (0.64, 1.43)	0.99 (0.69, 1.44)			1.15 (0.78, 1.70)	1.13 (0.79, 1.62)
Rbl2 (rs3929)								
G:G	202 (58.2)	878 (63.5)	1.00	1.00	223 (53.6)	632 (64.4)	1.00	1.00
C:G	90 (25.9)	392 (28.4)	0.99 (0.72, 1.36)	0.98 (0.72, 1.33)	116 (27.9)	275 (28.0)	1.23 (0.90, 1.68)	1.18 (0.88, 1.59)
C:C	10 (2.9)	55 (4.0)	0.53 (0.23, 1.23)	0.69 (0.37, 1.26)	17 (4.1)	35 (3.6)	1.62 (0.81, 3.23)	1.37 (0.77, 2.42)
Log-Additive			0.88 (0.68, 1.14)	0.87 (0.68, 1.13)			1.25 (0.97, 1.60)	1.22 (0.96, 1.55)
Dominant			0.92 (0.68, 1.26)	0.91 (0.68, 1.22)			1.27 (0.95, 1.71)	1.23 (0.93, 1.64)
Recessive			0.54 (0.24, 1.22)	0.69 (0.38, 1.27)			1.51 (0.77, 2.99)	1.32 (0.75, 2.32)
IL6R (rs4072391)								
C:C	252 (72.6)	1067 (77.2)	1.00	1.00	282 (67.8)	778 (79.2)	1.00	1.00
C:T	38 (11.0)	225 (16.3)	0.68 (0.43, 1.08)	0.71 (0.48, 1.07)	54 (13.0)	132 (13.4)	1.24 (0.83, 1.85)	1.19 (0.82, 1.72)
T:T	10 (2.9)	19 (1.4)	2.11 (0.87, 5.12)	1.50 (0.77, 2.93)	9 (2.2)	13 (1.3)	1.26 (0.38, 4.18)	1.09 (0.51, 2.35)
Log-Additive			0.97 (0.70, 1.35)	0.96 (0.70, 1.31)			1.20 (0.86, 1.69)	1.17 (0.85, 1.61)
Dominant			0.82 (0.55, 1.24)	0.83 (0.58, 1.21)			1.24 (0.84, 1.82)	1.20 (0.84, 1.71)
Recessive			2.23 (0.92, 5.40)	1.54 (0.78, 3.00)			1.22 (0.37, 4.02)	1.08 (0.50, 2.32)
CDK6 (rs42031)								
A:A	274 (79.0)	1197 (86.6)	1.00	1.00	310 (74.5)	839 (85.4)	1.00	1.00
A:T	28 (8.1)	114 (8.2)	1.02 (0.61, 1.69)	0.98 (0.63, 1.54)	37 (8.9)	82 (8.4)	1.33 (0.82, 2.16)	1.24 (0.80, 1.92)
T:T	0	6 (0.4)	NA	0.83 (0.33, 2.08)	6 (1.4)	7 (0.7)	1.90 (0.48, 7.53)	1.37 (0.62, 3.04)
Log-Additive			0.92 (0.57, 1.50)	0.91 (0.59, 1.40)			1.34 (0.90, 2.01)	1.34 (0.93, 1.93)
Dominant			0.97 (0.58, 1.60)	0.94 (0.60, 1.47)			1.38 (0.87, 2.18)	1.33 (0.87, 2.01)
Recessive			NA	0.83 (0.33, 2.08)			1.86 (0.47, 7.37)	1.37 (0.62, 3.02)
Ago2 (rs4961280)								
C:C	233 (67.1)	961 (69.5)	1.00	1.00	282 (67.8)	704 (71.7)	1.00	1.00
C:A	57 (16.4)	274 (19.8)	0.85 (0.59, 1.24)	0.87 (0.62, 1.23)	55 (13.2)	178 (18.1)	0.71 (0.48, 1.05)	0.75 (0.53, 1.07)
A:A	8 (2.3)	27 (2.0)	1.27 (0.50, 3.23)	1.14 (0.57, 2.26)	11 (2.6)	18 (1.8)	1.24 (0.47, 3.25)	1.11 (0.55, 2.22)
Log-Additive			0.94 (0.69, 1.28)	0.95 (0.71, 1.27)			0.84 (0.61, 1.15)	0.85 (0.63, 1.14)
Dominant			0.89 (0.62, 1.27)	0.90 (0.65, 1.26)			0.76 (0.52, 1.10)	0.79 (0.56, 1.10)
Recessive			1.31 (0.52, 3.33)	1.16 (0.58, 2.30)			1.32 (0.50, 3.46)	1.14 (0.57, 2.29)
miR-26a1 (rs7372209)								
C:C	158 (45.5)	645 (46.7)	1.00	1.00	195 (46.9)	470 (47.9)	1.00	1.00
C:T	124 (35.7)	533 (38.6)	1.00 (0.74, 1.36)	1.01 (0.76, 1.35)	127 (30.5)	365 (37.2)	0.93 (0.69, 1.26)	0.89 (0.67, 1.19)
T:T	18 (5.2)	129 (9.3)	0.53 (0.27, 1.01)	0.61 (0.36, 1.03)	32 (7.7)	82 (8.4)	0.93 (0.54, 1.57)	0.89 (0.56, 1.42)
Log-Additive			0.85 (0.68, 1.08)	0.85 (0.68, 1.06)			0.95 (0.76, 1.19)	0.91 (0.73, 1.13)
Dominant			0.91 (0.68, 1.23)	0.91 (0.69, 1.20)			0.93 (0.70, 1.24)	0.88 (0.67, 1.16)
Recessive			**0.53 (0.28, 0.99)**	0.61 (0.36, 1.01)			0.95 (0.57, 1.60)	0.92 (0.59, 1.46)
Gemin4 (rs7813)								

T:T	153 (44.1)	627 (45.4)	1.00	1.00	164 (39.4)	485 (49.4)	1.00	1.00
C:T	108 (31.1)	501 (36.3)	0.88 (0.64, 1.21)	0.92 (0.68, 1.23)	131 (31.5)	332 (33.8)	1.31 (0.95, 1.81)	1.25 (0.93, 1.69)
C:C	34 (9.8)	131 (9.5)	0.85 (0.52, 1.40)	0.90 (0.58, 1.39)	39 (9.4)	79 (8.0)	1.33 (0.81, 2.19)	1.23 (0.79, 1.91)
Log-Additive			0.91 (0.73, 1.13)	0.93 (0.75, 1.15)			1.20 (0.97, 1.50)	1.18 (0.95, 1.46)
Dominant			0.87 (0.65, 1.18)	0.90 (0.68, 1.20)			1.32 (0.98, 1.78)	1.27 (0.95, 1.68)
Recessive			0.90 (0.56, 1.45)	0.93 (0.60, 1.42)			1.19 (0.73, 1.92)	1.14 (0.74, 1.75)
KARS (rs9266)								
C:C	209 (60.2)	822 (59.5)	1.00	1.00	217 (52.2)	586 (59.7)	1.00	1.00
C:T	81 (23.3)	422 (30.5)	0.74 (0.53, 1.03)	0.76 (0.55, 1.03)	100 (24.0)	278 (28.3)	0.84 (0.60, 1.16)	0.89 (0.66, 1.21)
T:T	12 (3.5)	54 (3.9)	0.96 (0.48, 1.94)	0.97 (0.55, 1.71)	28 (6.7)	61 (6.2)	0.93 (0.51, 1.69)	0.98 (0.59, 1.61)
Log-Additive			0.84 (0.65, 1.09)	0.84 (0.65, 1.08)			0.91 (0.71, 1.15)	0.94 (0.75, 1.18)
Dominant			0.77 (0.56, 1.05)	0.78 (0.58, 1.04)			0.85 (0.63, 1.16)	0.90 (0.68, 1.20)
Recessive			1.05 (0.53, 2.11)	1.03 (0.58, 1.81)			0.98 (0.55, 1.77)	1.01 (0.61, 1.65)

Notes: aOR: adjusted odds ratios; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Ca: Cases; Co: Controls; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28 kg/m^2), and total energy intake (continuous, kcal/day).

Table 5.9. Associations between selected SNPs related to the Stem cell pathway and stomach cancer by dietary intake of total cholesterol

	Low Cholesterol				High Cholesterol			
dbSNP no.	Ca, n(%)	Co, n(%)	aOR*	sbOR*	Ca, n(%)	Co, n(%)	aOR*	sbOR*
HEY1 (rs1046472)								
C:C	189 (54.5)	814 (58.9)	1.00	1.00	206 (49.5)	589 (60.0)	1.00	1.00
A:C	101 (29.1)	424 (30.7)	1.08 (0.79, 1.48)	1.07 (0.80, 1.44)	111 (26.7)	293 (29.8)	1.11 (0.81, 1.52)	1.08 (0.80, 1.45)
A:A	19 (5.5)	65 (4.7)	1.33 (0.72, 2.45)	1.22 (0.73, 2.07)	31 (7.5)	43 (4.4)	1.58 (0.87, 2.86)	1.38 (0.83, 2.30)
Log-Additive			1.12 (0.88, 1.42)	1.11 (0.88, 1.40)			1.18 (0.93, 1.50)	1.16 (0.93, 1.47)
Dominant			1.11 (0.83, 1.50)	1.11 (0.84, 1.48)			1.17 (0.87, 1.58)	1.15 (0.86, 1.52)
Recessive			1.30 (0.71, 2.36)	1.20 (0.72, 2.02)			1.52 (0.85, 2.73)	1.35 (0.82, 2.24)
Oct4 (rs13409)								
C:C	103 (29.7)	491 (35.5)	1.00	1.00	129 (31.0)	315 (32.1)	1.00	1.00
C:T	139 (40.1)	560 (40.5)	1.17 (0.84, 1.63)	1.19 (0.88, 1.61)	141 (33.9)	442 (45.0)	**0.66 (0.48, 0.92)**	**0.69 (0.51, 0.93)**
T:T	55 (15.9)	249 (18.0)	0.92 (0.61, 1.40)	0.91 (0.62, 1.33)	75 (18.0)	165 (16.8)	0.95 (0.63, 1.42)	0.98 (0.68, 1.41)
Log-Additive			0.99 (0.81, 1.20)	0.98 (0.81, 1.19)			0.92 (0.75, 1.13)	0.93 (0.76, 1.13)
Dominant			1.09 (0.80, 1.47)	1.09 (0.82, 1.46)			**0.74 (0.55, 1.00)**	0.76 (0.57, 1.01)
Recessive			0.85 (0.58, 1.23)	0.84 (0.59, 1.19)			1.19 (0.83, 1.72)	1.17 (0.83, 1.64)
AXIN1 (rs1981492)								
G:G	163 (47.0)	670 (48.5)	1.00	1.00	189 (45.4)	458 (46.6)	1.00	1.00
A:G	111 (32.0)	492 (35.6)	0.83 (0.61, 1.14)	0.86 (0.64, 1.15)	113 (27.2)	365 (37.2)	**0.70 (0.51, 0.96)**	**0.73 (0.54, 0.99)**
A:A	32 (9.2)	124 (9.0)	0.70 (0.41, 1.19)	0.79 (0.50, 1.24)	52 (12.5)	91 (9.3)	1.21 (0.77, 1.91)	1.18 (0.78, 1.78)
Log-Additive			0.84 (0.67, 1.05)	0.86 (0.69, 1.06)			0.96 (0.78, 1.19)	0.97 (0.78, 1.19)
Dominant			0.80 (0.60, 1.08)	0.83 (0.63, 1.10)			0.80 (0.60, 1.07)	0.83 (0.62, 1.09)
Recessive			0.76 (0.45, 1.26)	0.83 (0.53, 1.30)			1.41 (0.91, 2.18)	1.32 (0.88, 1.97)
DVL2 (rs222851)								
A:A	113 (32.6)	493 (35.7)	1.00	1.00	140 (33.7)	379 (38.6)	1.00	1.00
A:G	134 (38.6)	588 (42.5)	1.27 (0.91, 1.75)	1.23 (0.91, 1.67)	155 (37.3)	398 (40.5)	1.05 (0.76, 1.44)	1.06 (0.79, 1.43)
G:G	45 (13.0)	189 (13.7)	1.25 (0.80, 1.96)	1.20 (0.80, 1.80)	45 (10.8)	135 (13.7)	0.84 (0.52, 1.37)	0.87 (0.57, 1.34)
Log-Additive			1.15 (0.93, 1.42)	1.15 (0.93, 1.41)			0.95 (0.77, 1.19)	0.96 (0.78, 1.19)
Dominant			1.26 (0.93, 1.72)	1.24 (0.93, 1.67)			1.00 (0.74, 1.35)	1.01 (0.76, 1.34)
Recessive			1.10 (0.73, 1.65)	1.09 (0.75, 1.58)			0.82 (0.52, 1.29)	0.85 (0.57, 1.28)
FZD3 (rs2241802)								
G:G	108 (31.1)	414 (30.0)	1.00	1.00	117 (28.1)	290 (29.5)	1.00	1.00
A:G	130 (37.5)	593 (42.9)	0.91 (0.65, 1.27)	0.90 (0.66, 1.22)	142 (34.1)	386 (39.3)	1.04 (0.73, 1.48)	1.05 (0.76, 1.45)
A:A	53 (15.3)	265 (19.2)	0.92 (0.60, 1.39)	0.92 (0.63, 1.35)	65 (15.6)	166 (16.9)	1.09 (0.71, 1.67)	1.11 (0.75, 1.62)
Log-Additive			0.95 (0.77, 1.17)	0.94 (0.77, 1.15)			1.04 (0.85, 1.29)	1.06 (0.86, 1.30)
Dominant			0.91 (0.67, 1.25)	0.90 (0.67, 1.20)			1.06 (0.76, 1.46)	1.07 (0.79, 1.46)

Recessive			0.97 (0.66, 1.41)	0.97 (0.68, 1.38)			1.06 (0.73, 1.55)	1.08 (0.76, 1.53)
Dec1 (rs2269700)								
T:T	220 (63.4)	890 (64.4)	1.00	1.00	252 (60.6)	609 (62.0)	1.00	1.00
C:T	79 (22.8)	358 (25.9)	1.06 (0.76, 1.47)	1.07 (0.78, 1.46)	99 (23.8)	284 (28.9)	0.78 (0.57, 1.08)	0.80 (0.59, 1.08)
C:C	5 (1.4)	59 (4.3)	0.43 (0.15, 1.22)	0.65 (0.33, 1.26)	6 (1.4)	31 (3.2)	0.89 (0.34, 2.32)	0.88 (0.45, 1.73)
Log-Additive			0.91 (0.69, 1.19)	0.91 (0.70, 1.19)			0.82 (0.62, 1.09)	0.82 (0.63, 1.07)
Dominant			0.97 (0.71, 1.34)	0.98 (0.72, 1.32)			0.79 (0.58, 1.08)	0.80 (0.59, 1.07)
Recessive			0.42 (0.15, 1.20)	0.64 (0.33, 1.24)			0.95 (0.37, 2.47)	0.91 (0.46, 1.79)
Oct4 (rs3130932)								
T:T	155 (44.7)	625 (45.2)	1.00	1.00	185 (44.5)	409 (41.6)	1.00	1.00
G:T	113 (32.6)	532 (38.5)	0.96 (0.70, 1.32)	0.97 (0.72, 1.30)	123 (29.6)	409 (41.6)	0.77 (0.56, 1.05)	0.77 (0.58, 1.03)
G:G	31 (8.9)	149 (10.8)	0.94 (0.58, 1.54)	0.94 (0.61, 1.45)	46 (11.1)	103 (10.5)	1.13 (0.72, 1.80)	1.10 (0.72, 1.66)
Log-Additive			0.97 (0.78, 1.20)	0.96 (0.78, 1.19)			0.96 (0.78, 1.19)	0.95 (0.77, 1.17)
Dominant			0.96 (0.71, 1.29)	0.96 (0.72, 1.27)			0.84 (0.63, 1.12)	0.84 (0.64, 1.10)
Recessive			0.96 (0.60, 1.53)	0.95 (0.62, 1.45)			1.28 (0.82, 1.98)	1.21 (0.81, 1.81)
WNT2 (rs3729629)								
G:G	150 (43.2)	601 (43.5)	1.00	1.00	178 (42.8)	405 (41.2)	1.00	1.00
C:G	119 (34.3)	565 (40.9)	0.79 (0.58, 1.07)	0.82 (0.61, 1.09)	144 (34.6)	411 (41.9)	0.92 (0.68, 1.25)	0.96 (0.72, 1.28)
C:C	34 (9.8)	135 (9.8)	0.97 (0.59, 1.60)	0.99 (0.64, 1.54)	25 (6.0)	109 (11.1)	0.61 (0.35, 1.04)	0.67 (0.43, 1.07)
Log-Additive			0.91 (0.73, 1.14)	0.92 (0.74, 1.14)			0.83 (0.66, 1.04)	0.84 (0.68, 1.04)
Dominant			0.82 (0.61, 1.10)	0.85 (0.64, 1.12)			0.85 (0.63, 1.14)	0.87 (0.66, 1.15)
Recessive			1.09 (0.68, 1.75)	1.07 (0.70, 1.64)			0.63 (0.38, 1.06)	0.69 (0.44, 1.07)
HEY2 (rs3734637)								
A:A	186 (53.6)	769 (55.6)	1.00	1.00	210 (50.5)	555 (56.5)	1.00	1.00
A:C	101 (29.1)	432 (31.3)	1.01 (0.74, 1.38)	1.04 (0.77, 1.39)	110 (26.4)	311 (31.7)	0.87 (0.63, 1.21)	0.92 (0.68, 1.25)
C:C	11 (3.2)	94 (6.8)	**0.45 (0.21, 0.98)**	0.60 (0.34, 1.06)	19 (4.6)	60 (6.1)	0.73 (0.40, 1.35)	0.80 (0.48, 1.33)
Log-Additive			0.85 (0.66, 1.09)	0.86 (0.68, 1.09)			0.86 (0.68, 1.10)	0.88 (0.70, 1.11)
Dominant			0.92 (0.68, 1.24)	0.93 (0.70, 1.23)			0.85 (0.62, 1.15)	0.88 (0.66, 1.17)
Recessive			**0.45 (0.21, 0.97)**	0.59 (0.34, 1.04)			0.76 (0.42, 1.40)	0.81 (0.49, 1.35)
Ctbp2 (rs3740535)								
G:G	168 (48.4)	720 (52.1)	1.00	1.00	183 (44.0)	494 (50.3)	1.00	1.00
A:G	99 (28.5)	486 (35.2)	0.99 (0.72, 1.36)	0.97 (0.72, 1.31)	119 (28.6)	349 (35.5)	0.84 (0.61, 1.15)	0.87 (0.65, 1.17)
A:A	32 (9.2)	105 (7.6)	1.14 (0.68, 1.89)	1.12 (0.72, 1.75)	39 (9.4)	69 (7.0)	1.24 (0.74, 2.08)	1.17 (0.74, 1.85)
Log-Additive			1.04 (0.83, 1.29)	1.04 (0.84, 1.28)			1.00 (0.80, 1.25)	1.00 (0.80, 1.25)
Dominant			1.02 (0.76, 1.37)	1.01 (0.76, 1.34)			0.91 (0.68, 1.22)	0.93 (0.70, 1.23)
Recessive			1.14 (0.70, 1.87)	1.13 (0.73, 1.75)			1.33 (0.80, 2.20)	1.22 (0.78, 1.91)
WNT2 (rs4730775)								
C:C	178 (51.3)	756 (54.7)	1.00	1.00	206 (49.5)	509 (51.8)	1.00	1.00
C:T	101 (29.1)	456 (33.0)	0.90 (0.65, 1.23)	0.94 (0.70, 1.27)	115 (27.6)	329 (33.5)	0.76 (0.55, 1.05)	0.82 (0.61, 1.10)

T:T	16 (4.6)	80 (5.8)	0.95 (0.51, 1.79)	0.98 (0.58, 1.66)	16 (3.8)	69 (7.0)	0.73 (0.39, 1.38)	0.80 (0.47, 1.35)
Log-Additive			0.94 (0.73, 1.20)	0.96 (0.76, 1.22)			0.81 (0.63, 1.03)	0.83 (0.66, 1.05)
Dominant			0.91 (0.67, 1.22)	0.94 (0.71, 1.25)			0.76 (0.56, 1.02)	0.80 (0.60, 1.06)
Recessive			0.99 (0.53, 1.84)	0.99 (0.59, 1.68)			0.81 (0.43, 1.51)	0.84 (0.50, 1.42)
WNT8A (rs4835761)								
A:A	121 (34.9)	415 (30.0)	1.00	1.00	131 (31.5)	320 (32.6)	1.00	1.00
A:G	126 (36.3)	608 (44.0)	**0.71 (0.51, 0.99)**	**0.73 (0.54, 0.99)**	132 (31.7)	410 (41.8)	0.76 (0.55, 1.06)	0.78 (0.57, 1.06)
G:G	51 (14.7)	238 (17.2)	0.73 (0.48, 1.12)	0.80 (0.55, 1.17)	79 (19.0)	163 (16.6)	1.24 (0.83, 1.83)	1.19 (0.83, 1.70)
Log-Additive			0.83 (0.67, 1.02)	0.84 (0.69, 1.03)			1.06 (0.87, 1.30)	1.05 (0.86, 1.27)
Dominant			**0.72 (0.53, 0.97)**	**0.73 (0.55, 0.98)**			0.90 (0.66, 1.21)	0.90 (0.67, 1.19)
Recessive			0.89 (0.60, 1.30)	0.93 (0.65, 1.32)			1.42 (1.00, 2.03)	1.33 (0.95, 1.86)
Notch4 (rs520692)								
A:A	223 (64.3)	1007 (72.9)	1.00	1.00	244 (58.7)	699 (71.2)	1.00	1.00
A:G	72 (20.7)	282 (20.4)	0.92 (0.65, 1.31)	0.93 (0.67, 1.29)	75 (18.0)	213 (21.7)	0.96 (0.68, 1.35)	0.96 (0.70, 1.32)
G:G	5 (1.4)	26 (1.9)	1.12 (0.40, 3.11)	1.05 (0.52, 2.14)	1 (0.2)	13 (1.3)	0.25 (0.03, 2.02)	0.71 (0.31, 1.60)
Log-Additive			0.96 (0.71, 1.30)	0.97 (0.73, 1.28)			0.88 (0.64, 1.21)	0.88 (0.65, 1.19)
Dominant			0.93 (0.66, 1.31)	0.95 (0.69, 1.30)			0.92 (0.65, 1.29)	0.91 (0.67, 1.26)
Recessive			1.14 (0.41, 3.16)	1.06 (0.52, 2.15)			0.26 (0.03, 2.04)	0.71 (0.32, 1.61)
Rex1 (rs6815391)								
T:T	137 (39.5)	581 (42.0)	1.00	1.00	155 (37.3)	379 (38.6)	1.00	1.00
C:T	116 (33.4)	530 (38.4)	1.02 (0.74, 1.41)	1.03 (0.76, 1.39)	128 (30.8)	381 (38.8)	0.86 (0.62, 1.19)	0.86 (0.64, 1.17)
C:C	41 (11.8)	169 (12.2)	1.00 (0.63, 1.58)	0.96 (0.64, 1.45)	54 (13.0)	123 (12.5)	1.16 (0.75, 1.79)	1.14 (0.77, 1.68)
Log-Additive			1.01 (0.81, 1.24)	0.99 (0.81, 1.22)			1.03 (0.83, 1.26)	1.02 (0.83, 1.25)
Dominant			1.02 (0.75, 1.37)	1.01 (0.76, 1.34)			0.94 (0.69, 1.26)	0.94 (0.70, 1.24)
Recessive			0.99 (0.64, 1.52)	0.95 (0.64, 1.41)			1.25 (0.83, 1.87)	1.21 (0.83, 1.75)
HES2 (rs8708)								
A:A	208 (59.9)	866 (62.7)	1.00	1.00	238 (57.2)	625 (63.6)	1.00	1.00
A:G	75 (21.6)	372 (26.9)	1.03 (0.74, 1.43)	1.04 (0.76, 1.42)	87 (20.9)	250 (25.5)	0.93 (0.66, 1.31)	0.92 (0.67, 1.27)
G:G	10 (2.9)	48 (3.5)	1.09 (0.50, 2.38)	1.04 (0.56, 1.92)	8 (1.9)	41 (4.2)	0.69 (0.29, 1.63)	0.80 (0.43, 1.51)
Log-Additive			1.04 (0.79, 1.35)	1.04 (0.80, 1.34)			0.89 (0.68, 1.18)	0.88 (0.68, 1.15)
Dominant			1.04 (0.76, 1.42)	1.04 (0.77, 1.40)			0.90 (0.65, 1.25)	0.89 (0.65, 1.21)
Recessive			1.08 (0.50, 2.35)	1.03 (0.56, 1.90)			0.70 (0.30, 1.66)	0.81 (0.43, 1.53)
Notch4 (rs915894)								
C:C	107 (30.8)	352 (25.5)	1.00	1.00	109 (26.2)	298 (30.3)	1.00	1.00
A:C	127 (36.6)	642 (46.5)	**0.64 (0.45, 0.89)**	**0.69 (0.51, 0.95)**	149 (35.8)	404 (41.1)	1.08 (0.77, 1.52)	1.07 (0.78, 1.47)
A:A	64 (18.4)	288 (20.8)	0.75 (0.50, 1.12)	0.81 (0.56, 1.17)	91 (21.9)	207 (21.1)	1.26 (0.85, 1.87)	1.27 (0.89, 1.81)
Log-Additive			0.84 (0.68, 1.03)	0.86 (0.70, 1.05)			1.12 (0.92, 1.37)	1.14 (0.94, 1.38)
Dominant			**0.67 (0.49, 0.92)**	**0.71 (0.53, 0.96)**			1.14 (0.83, 1.57)	1.16 (0.86, 1.56)

Recessive			0.98 (0.69, 1.40)	0.99 (0.71, 1.37)			1.21 (0.86, 1.69)	1.22 (0.89, 1.68)
NF-κB pathway								
miR-300 (rs12894467)								
T:T	168 (48.4)	764 (55.3)	1.00	1.00	180 (43.3)	579 (59.0)	1.00	1.00
C:T	106 (30.5)	447 (32.3)	1.20 (0.88, 1.65)	1.20 (0.89, 1.62)	108 (26.0)	255 (26.0)	**1.59 (1.13, 2.22)**	**1.47 (1.08, 2.02)**
C:C	15 (4.3)	63 (4.6)	0.89 (0.44, 1.79)	0.95 (0.54, 1.67)	43 (10.3)	62 (6.3)	**1.99 (1.19, 3.34)**	**1.75 (1.11, 2.76)**
Log-Additive			1.08 (0.84, 1.38)	1.09 (0.86, 1.39)			**1.47 (1.17, 1.84)**	**1.45 (1.17, 1.81)**
Dominant			1.16 (0.85, 1.57)	1.16 (0.87, 1.55)			**1.67 (1.23, 2.28)**	**1.61 (1.20, 2.15)**
Recessive			0.83 (0.42, 1.65)	0.91 (0.52, 1.58)			**1.70 (1.03, 2.80)**	**1.57 (1.01, 2.45)**
IKBKAP (rs1538660)								
C:C	145 (41.8)	580 (42.0)	1.00	1.00	167 (40.1)	442 (45.0)	1.00	1.00
C:T	124 (35.7)	558 (40.4)	**0.70 (0.51, 0.96)**	**0.72 (0.54, 0.97)**	134 (32.2)	362 (36.9)	0.99 (0.72, 1.36)	1.00 (0.75, 1.34)
T:T	36 (10.4)	143 (10.3)	0.98 (0.61, 1.57)	1.03 (0.68, 1.57)	46 (11.1)	112 (11.4)	1.11 (0.69, 1.77)	1.12 (0.74, 1.70)
Log-Additive			0.88 (0.71, 1.10)	0.91 (0.73, 1.12)			1.03 (0.84, 1.28)	1.05 (0.85, 1.29)
Dominant			0.75 (0.56, 1.01)	0.78 (0.59, 1.03)			1.02 (0.76, 1.37)	1.03 (0.78, 1.37)
Recessive			1.15 (0.73, 1.81)	1.17 (0.78, 1.75)			1.11 (0.71, 1.74)	1.12 (0.75, 1.68)
IKBKAP (rs2230793)								
A:A	148 (42.7)	609 (44.1)	1.00	1.00	177 (42.5)	457 (46.5)	1.00	1.00
A:C	111 (32.0)	558 (40.4)	0.77 (0.56, 1.06)	0.79 (0.59, 1.07)	130 (31.3)	363 (37.0)	0.99 (0.73, 1.35)	0.98 (0.73, 1.31)
C:C	41 (11.8)	132 (9.6)	1.43 (0.91, 2.27)	1.37 (0.90, 2.07)	47 (11.3)	93 (9.5)	**1.70 (1.06, 2.73)**	1.47 (0.96, 2.25)
Log-Additive			1.05 (0.84, 1.30)	1.05 (0.85, 1.30)			1.19 (0.96, 1.48)	1.16 (0.94, 1.43)
Dominant			0.89 (0.66, 1.19)	0.91 (0.69, 1.20)			1.11 (0.83, 1.48)	1.09 (0.83, 1.44)
Recessive			**1.61 (1.04, 2.49)**	**1.49 (1.00, 2.23)**			**1.71 (1.08, 2.69)**	1.49 (0.99, 2.24)
IKBKAP (rs3204145)								
T:T	144 (41.5)	592 (42.8)	1.00	1.00	172 (41.3)	448 (45.6)	1.00	1.00
A:T	125 (36.0)	580 (42.0)	**0.69 (0.51, 0.95)**	**0.71 (0.53, 0.96)**	145 (34.9)	368 (37.5)	0.99 (0.73, 1.35)	1.00 (0.75, 1.34)
A:A	34 (9.8)	141 (10.2)	0.94 (0.58, 1.52)	1.00 (0.66, 1.52)	37 (8.9)	105 (10.7)	0.94 (0.57, 1.55)	0.98 (0.63, 1.53)
Log-Additive			0.86 (0.69, 1.08)	0.89 (0.72, 1.10)			0.98 (0.79, 1.21)	0.99 (0.81, 1.23)
Dominant			**0.74 (0.55, 0.99)**	0.76 (0.58, 1.01)			0.98 (0.74, 1.31)	1.00 (0.76, 1.31)
Recessive			1.12 (0.71, 1.77)	1.14 (0.76, 1.72)			0.94 (0.58, 1.53)	0.98 (0.64, 1.51)

Notes: aOR: adjusted odds ratios; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Ca: Cases; Co: Controls; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28 kg/m^2), and total energy intake (continuous, kcal/day).

Table 5.10. Associations between selected SNPs related to the GWAS and stomach cancer by dietary intake of total cholesterol

	Low Cholesterol				High Cholesterol			
dbSNP no.	Ca, n(%)	Co, n(%)	aOR*	sbOR*	Ca, n(%)	Co, n(%)	aOR*	sbOR*
RUNX1 (rs2014300)								
G:G	241 (69.5)	1021 (73.9)	1.00	1.00	254 (61.1)	697 (71.0)	1.00	1.00
A:G	55 (15.9)	273 (19.8)	0.88 (0.61, 1.28)	0.91 (0.65, 1.29)	73 (17.5)	199 (20.3)	1.15 (0.80, 1.65)	1.13 (0.81, 1.58)
A:A	7 (2.0)	24 (1.7)	0.81 (0.28, 2.39)	0.91 (0.45, 1.87)	15 (3.6)	26 (2.6)	1.69 (0.77, 3.73)	1.35 (0.73, 2.52)
Log-Additive			0.89 (0.65, 1.22)	0.91 (0.68, 1.23)			1.21 (0.92, 1.60)	1.20 (0.91, 1.56)
Dominant			0.88 (0.61, 1.25)	0.90 (0.65, 1.26)			1.21 (0.86, 1.70)	1.19 (0.87, 1.64)
Recessive			0.83 (0.28, 2.44)	0.92 (0.45, 1.89)			1.64 (0.75, 3.61)	1.33 (0.72, 2.48)
PLCE1 (rs2274223)								
A:A	157 (45.2)	811 (58.7)	1.00	1.00	175 (42.1)	569 (57.9)	1.00	1.00
A:G	87 (25.1)	399 (28.9)	1.16 (0.82, 1.63)	1.14 (0.83, 1.57)	127 (30.5)	301 (30.7)	1.32 (0.95, 1.83)	1.27 (0.94, 1.72)
G:G	18 (5.2)	62 (4.5)	1.60 (0.86, 2.97)	1.39 (0.82, 2.37)	10 (2.4)	32 (3.3)	1.27 (0.57, 2.85)	1.14 (0.61, 2.13)
Log-Additive			1.22 (0.94, 1.56)	1.21 (0.95, 1.54)			1.24 (0.95, 1.63)	1.22 (0.94, 1.58)
Dominant			1.22 (0.89, 1.69)	1.21 (0.90, 1.64)			1.32 (0.96, 1.81)	1.27 (0.94, 1.72)
Recessive			1.52 (0.83, 2.80)	1.35 (0.80, 2.28)			1.14 (0.51, 2.52)	1.07 (0.58, 1.99)
GPC5 (rs2352028)								
C:C	210 (60.5)	825 (59.7)	1.00	1.00	223 (53.6)	585 (59.6)	1.00	1.00
C:T	90 (25.9)	418 (30.2)	0.80 (0.58, 1.11)	0.85 (0.63, 1.15)	120 (28.8)	289 (29.4)	1.15 (0.85, 1.55)	1.13 (0.85, 1.51)
T:T	15 (4.3)	74 (5.4)	0.66 (0.33, 1.34)	0.74 (0.42, 1.29)	20 (4.8)	50 (5.1)	0.87 (0.44, 1.70)	0.90 (0.52, 1.56)
Log-Additive			0.81 (0.63, 1.04)	0.82 (0.64, 1.05)			1.04 (0.82, 1.32)	1.04 (0.82, 1.31)
Dominant			0.78 (0.57, 1.07)	0.81 (0.61, 1.09)			1.10 (0.83, 1.48)	1.09 (0.83, 1.44)
Recessive			0.71 (0.35, 1.43)	0.77 (0.44, 1.33)			0.83 (0.42, 1.61)	0.87 (0.50, 1.50)
TERT (rs2736100)								
T:T	125 (36.0)	406 (29.4)	1.00	1.00	132 (31.7)	295 (30.0)	1.00	1.00
G:T	130 (37.5)	601 (43.5)	**0.61 (0.44, 0.85)**	**0.65 (0.48, 0.88)**	147 (35.3)	405 (41.2)	0.81 (0.58, 1.14)	0.85 (0.62, 1.16)
G:G	46 (13.3)	245 (17.7)	**0.54 (0.35, 0.84)**	**0.60 (0.41, 0.89)**	56 (13.5)	155 (15.8)	0.68 (0.44, 1.07)	0.75 (0.50, 1.11)
Log-Additive			**0.71 (0.57, 0.88)**	**0.71 (0.58, 0.88)**			0.82 (0.66, 1.02)	0.84 (0.68, 1.03)
Dominant			**0.59 (0.43, 0.80)**	**0.61 (0.45, 0.82)**			0.78 (0.57, 1.06)	0.80 (0.60, 1.08)
Recessive			0.72 (0.48, 1.07)	0.74 (0.51, 1.07)			0.77 (0.51, 1.15)	0.81 (0.56, 1.17)
CRPP1 -CRP (rs2808630)								
T:T	222 (64.0)	967 (70.0)	1.00	1.00	263 (63.2)	683 (69.6)	1.00	1.00
C:T	61 (17.6)	293 (21.2)	1.13 (0.79, 1.61)	1.14 (0.82, 1.59)	65 (15.6)	206 (21.0)	0.79 (0.54, 1.14)	0.80 (0.57, 1.13)
C:C	16 (4.6)	37 (2.7)	**2.07 (1.03, 4.16)**	1.62 (0.91, 2.88)	13 (3.1)	28 (2.9)	1.07 (0.47, 2.44)	1.10 (0.59, 2.04)
Log-Additive			1.27 (0.97, 1.66)	1.28 (0.99, 1.65)			0.88 (0.66, 1.18)	0.90 (0.68, 1.19)
Dominant			1.24 (0.89, 1.72)	1.26 (0.92, 1.71)			0.82 (0.58, 1.16)	0.84 (0.61, 1.17)
Recessive			**2.01 (1.01, 4.02)**	1.58 (0.89, 2.82)			1.12 (0.49, 2.55)	1.12 (0.60, 2.10)
PLCE1 (rs3781264)								

T:T	220 (63.4)	909 (65.8)	1.00	1.00	246 (59.1)	611 (62.2)	1.00	1.00
C:T	67 (19.3)	306 (22.1)	0.96 (0.67, 1.37)	0.97 (0.70, 1.35)	90 (21.6)	227 (23.1)	1.01 (0.72, 1.42)	0.97 (0.71, 1.34)
C:C	11 (3.2)	39 (2.8)	1.18 (0.56, 2.51)	1.12 (0.61, 2.04)	11 (2.6)	11 (1.1)	**2.70 (1.04, 6.99)**	1.66 (0.84, 3.29)
Log-Additive			1.02 (0.77, 1.34)	1.02 (0.78, 1.33)			1.18 (0.88, 1.57)	1.14 (0.87, 1.50)
Dominant			0.99 (0.71, 1.38)	1.00 (0.73, 1.36)			1.10 (0.79, 1.52)	1.06 (0.78, 1.45)
Recessive			1.19 (0.56, 2.53)	1.12 (0.61, 2.05)			**2.69 (1.05, 6.93)**	1.66 (0.84, 3.29)
CLPTM1L (rs401681)								
C:C	143 (41.2)	603 (43.6)	1.00	1.00	169 (40.6)	398 (40.5)	1.00	1.00
C:T	122 (35.2)	532 (38.5)	0.99 (0.73, 1.35)	1.00 (0.75, 1.33)	124 (29.8)	389 (39.6)	**0.70 (0.50, 0.96)**	**0.71 (0.53, 0.97)**
T:T	35 (10.1)	135 (9.8)	0.94 (0.56, 1.57)	0.97 (0.62, 1.52)	46 (11.1)	108 (11.0)	1.25 (0.80, 1.95)	1.20 (0.80, 1.80)
Log-Additive			0.98 (0.78, 1.22)	0.99 (0.80, 1.23)			0.98 (0.79, 1.21)	0.97 (0.79, 1.20)
Dominant			0.98 (0.73, 1.32)	0.99 (0.75, 1.31)			0.81 (0.60, 1.09)	0.82 (0.62, 1.08)
Recessive			0.94 (0.58, 1.55)	0.97 (0.63, 1.51)			1.46 (0.95, 2.24)	1.36 (0.92, 2.01)
GKN2 -GKN1 (rs4254535)								
T:T	170 (49.0)	757 (54.8)	1.00	1.00	199 (47.8)	491 (50.0)	1.00	1.00
C:T	97 (28.0)	430 (31.1)	1.02 (0.74, 1.41)	1.01 (0.74, 1.36)	109 (26.2)	355 (36.2)	0.73 (0.53, 1.00)	0.77 (0.57, 1.04)
C:C	29 (8.4)	111 (8.0)	1.48 (0.91, 2.43)	1.42 (0.91, 2.20)	35 (8.4)	68 (6.9)	1.22 (0.72, 2.07)	1.10 (0.69, 1.75)
Log-Additive			1.15 (0.92, 1.43)	1.15 (0.93, 1.43)			0.93 (0.74, 1.18)	0.93 (0.74, 1.16)
Dominant			1.11 (0.83, 1.49)	1.11 (0.84, 1.47)			0.81 (0.60, 1.09)	0.83 (0.63, 1.10)
Recessive			1.47 (0.91, 2.37)	1.42 (0.92, 2.18)			1.38 (0.82, 2.30)	1.19 (0.76, 1.88)
CCR4 -GLB1 (rs4678680)								
T:T	280 (80.7)	1178 (85.2)	1.00	1.00	324 (77.9)	837 (85.2)	1.00	1.00
G:T	29 (8.4)	148 (10.7)	0.90 (0.56, 1.45)	0.92 (0.60, 1.41)	43 (10.3)	100 (10.2)	1.12 (0.71, 1.76)	1.08 (0.72, 1.63)
G:G	4 (1.2)	6 (0.4)	2.30 (0.55, 9.64)	1.28 (0.55, 2.96)	4 (1.0)	5 (0.5)	2.14 (0.45, 10.28)	1.43 (0.62, 3.28)
Log-Additive			1.03 (0.68, 1.56)	1.03 (0.71, 1.51)			1.19 (0.80, 1.78)	1.22 (0.85, 1.76)
Dominant			0.97 (0.61, 1.53)	0.98 (0.65, 1.48)			1.17 (0.75, 1.81)	1.17 (0.78, 1.74)
Recessive			2.33 (0.56, 9.74)	1.28 (0.56, 2.96)			2.11 (0.44, 10.13)	1.42 (0.62, 3.27)
TERT -CLPTM1L (rs4975616)								
A:A	235 (67.7)	942 (68.2)	1.00	1.00	245 (58.9)	646 (65.8)	1.00	1.00
A:G	60 (17.3)	312 (22.6)	0.81 (0.56, 1.15)	0.82 (0.58, 1.14)	82 (19.7)	248 (25.3)	1.09 (0.78, 1.53)	1.07 (0.78, 1.46)
G:G	9 (2.6)	39 (2.8)	0.99 (0.43, 2.29)	0.99 (0.52, 1.87)	22 (5.3)	28 (2.9)	**2.49 (1.24, 5.03)**	**1.81 (1.01, 3.24)**
Log-Additive			0.88 (0.66, 1.17)	0.88 (0.66, 1.15)			1.29 (1.00, 1.68)	1.27 (0.99, 1.63)
Dominant			0.83 (0.59, 1.16)	0.83 (0.61, 1.15)			1.22 (0.89, 1.68)	1.20 (0.89, 1.62)
Recessive			1.04 (0.45, 2.39)	1.02 (0.54, 1.92)			**2.43 (1.21, 4.87)**	**1.79 (1.01, 3.19)**
CHEK2 (rs738722)								
C:C	144 (41.5)	709 (51.3)	1.00	1.00	179 (43.0)	493 (50.2)	1.00	1.00
C:T	115 (33.1)	480 (34.7)	1.26 (0.91, 1.73)	1.16 (0.86, 1.56)	127 (30.5)	316 (32.2)	1.11 (0.81, 1.52)	1.09 (0.81, 1.47)
T:T	32 (9.2)	88 (6.4)	**2.19 (1.30, 3.68)**	**1.80 (1.13, 2.86)**	39 (9.4)	89 (9.1)	1.17 (0.73, 1.88)	1.14 (0.75, 1.74)
Log-Additive			**1.39 (1.11, 1.76)**	**1.34 (1.07, 1.68)**			1.09 (0.88, 1.35)	1.09 (0.89, 1.34)

Dominant			**1.39 (1.03, 1.88)**	1.31 (0.98, 1.74)			1.12 (0.84, 1.50)	1.11 (0.84, 1.47)
Recessive			**1.98 (1.20, 3.26)**	**1.71 (1.09, 2.69)**			1.12 (0.71, 1.77)	1.11 (0.73, 1.67)
TGM5 (rs748404)								
T:T	272 (78.4)	1189 (86.0)	1.00	1.00	314 (75.5)	810 (82.5)	1.00	1.00
C:T	26 (7.5)	111 (8.0)	1.28 (0.77, 2.13)	1.17 (0.74, 1.84)	29 (7.0)	101 (10.3)	0.76 (0.47, 1.25)	0.80 (0.52, 1.24)
C:C	1 (0.3)	7 (0.5)	0.56 (0.06, 5.50)	0.90 (0.37, 2.18)	5 (1.2)	5 (0.5)	0.77 (0.12, 4.75)	0.94 (0.40, 2.21)
Log-Additive			1.15 (0.73, 1.82)	1.09 (0.71, 1.65)			0.79 (0.51, 1.22)	0.81 (0.55, 1.21)
Dominant			1.22 (0.74, 2.02)	1.13 (0.72, 1.77)			0.76 (0.47, 1.23)	0.80 (0.52, 1.22)
Recessive			0.55 (0.06, 5.38)	0.90 (0.37, 2.17)			0.79 (0.13, 4.87)	0.94 (0.40, 2.22)
IL1RAP (rs7626795)								
A:A	209 (60.2)	845 (61.1)	1.00	1.00	238 (57.2)	618 (62.9)	1.00	1.00
A:G	87 (25.1)	394 (28.5)	0.83 (0.59, 1.15)	0.87 (0.64, 1.18)	93 (22.4)	261 (26.6)	1.03 (0.74, 1.44)	1.01 (0.74, 1.38)
G:G	13 (3.7)	58 (4.2)	0.62 (0.29, 1.33)	0.80 (0.45, 1.41)	19 (4.6)	42 (4.3)	1.18 (0.61, 2.26)	1.10 (0.64, 1.90)
Log-Additive			0.81 (0.62, 1.05)	0.85 (0.66, 1.09)			1.06 (0.83, 1.36)	1.04 (0.82, 1.32)
Dominant			0.80 (0.58, 1.09)	0.84 (0.62, 1.13)			1.06 (0.77, 1.44)	1.03 (0.77, 1.38)
Recessive			0.65 (0.31, 1.40)	0.82 (0.46, 1.45)			1.17 (0.61, 2.22)	1.10 (0.64, 1.88)
CHRNA3 (rs8042374)								
G:G	161 (46.4)	623 (45.1)	1.00	1.00	168 (40.4)	463 (47.1)	1.00	1.00
A:G	113 (32.6)	525 (38.0)	0.79 (0.57, 1.08)	0.81 (0.60, 1.09)	121 (29.1)	359 (36.6)	0.86 (0.62, 1.18)	0.85 (0.63, 1.15)
A:A	22 (6.3)	115 (8.3)	0.84 (0.47, 1.50)	0.87 (0.53, 1.42)	45 (10.8)	73 (7.4)	**1.97 (1.21, 3.20)**	**1.62 (1.05, 2.51)**
Log-Additive			0.85 (0.67, 1.08)	0.86 (0.68, 1.08)			1.19 (0.95, 1.49)	1.15 (0.93, 1.43)
Dominant			0.79 (0.59, 1.07)	0.81 (0.61, 1.08)			1.03 (0.76, 1.38)	1.00 (0.76, 1.33)
Recessive			0.93 (0.52, 1.63)	0.93 (0.57, 1.51)			**2.11 (1.32, 3.36)**	**1.72 (1.13, 2.62)**
FTO (rs8050136)								
C:C	228 (65.7)	1031 (74.6)	1.00	1.00	272 (65.4)	735 (74.8)	1.00	1.00
A:C	73 (21.0)	253 (18.3)	**1.44 (1.01, 2.05)**	**1.40 (1.00, 1.95)**	72 (17.3)	169 (17.2)	1.11 (0.76, 1.61)	1.09 (0.77, 1.54)
A:A	2 (0.6)	22 (1.6)	0.42 (0.08, 2.07)	0.75 (0.34, 1.66)	3 (0.7)	27 (2.7)	**0.12 (0.02, 0.88)**	0.51 (0.24, 1.07)
Log-Additive			1.21 (0.88, 1.65)	1.19 (0.89, 1.60)			0.84 (0.61, 1.16)	0.85 (0.63, 1.15)
Dominant			1.35 (0.95, 1.91)	1.31 (0.94, 1.81)			0.95 (0.66, 1.37)	0.94 (0.67, 1.32)
Recessive			0.39 (0.08, 1.91)	0.74 (0.34, 1.61)			**0.11 (0.01, 0.86)**	0.51 (0.24, 1.06)
ZBTB12-C2 (rs9267673)								
C:C	210 (60.5)	929 (67.2)	1.00	1.00	247 (59.4)	656 (66.8)	1.00	1.00
C:T	76 (21.9)	320 (23.2)	0.94 (0.66, 1.32)	0.94 (0.68, 1.30)	82 (19.7)	243 (24.7)	0.86 (0.61, 1.22)	0.83 (0.60, 1.15)
T:T	14 (4.0)	42 (3.0)	1.28 (0.60, 2.73)	1.15 (0.63, 2.09)	21 (5.0)	26 (2.6)	**2.09 (1.01, 4.31)**	1.72 (0.96, 3.08)
Log-Additive			1.01 (0.77, 1.33)	1.01 (0.78, 1.31)			1.09 (0.83, 1.42)	1.08 (0.83, 1.39)
Dominant			0.97 (0.70, 1.35)	0.97 (0.72, 1.32)			0.98 (0.71, 1.35)	0.96 (0.71, 1.30)
Recessive			1.30 (0.61, 2.76)	1.16 (0.63, 2.11)			**2.17 (1.06, 4.45)**	1.77 (0.99, 3.17)
HLA-DQB1- HLA-DQA2 (rs9275572)								
G:G	160 (46.1)	687 (49.7)	1.00	1.00	177 (42.5)	478 (48.7)	1.00	1.00

A:G	108 (31.1)	490 (35.5)	1.02 (0.74, 1.41)	1.02 (0.76, 1.38)	123 (29.6)	355 (36.2)	0.73 (0.53, 1.01)	0.79 (0.58, 1.06)
A:A	28 (8.1)	126 (9.1)	1.24 (0.76, 2.05)	1.18 (0.76, 1.85)	37 (8.9)	80 (8.1)	1.09 (0.65, 1.82)	1.08 (0.69, 1.69)
Log-Additive			1.08 (0.87, 1.35)	1.08 (0.87, 1.34)			0.91 (0.72, 1.15)	0.93 (0.75, 1.16)
Dominant			1.07 (0.79, 1.44)	1.07 (0.80, 1.41)			0.79 (0.59, 1.07)	0.84 (0.63, 1.11)
Recessive			1.23 (0.76, 1.99)	1.18 (0.76, 1.81)			1.23 (0.75, 2.03)	1.17 (0.75, 1.82)
SEMA5B (rs9868873)								
G:G	210 (60.5)	863 (62.4)	1.00	1.00	235 (56.5)	625 (63.6)	1.00	1.00
A:G	78 (22.5)	391 (28.3)	0.90 (0.65, 1.26)	0.94 (0.69, 1.28)	89 (21.4)	264 (26.9)	0.87 (0.62, 1.22)	0.90 (0.66, 1.23)
A:A	17 (4.9)	54 (3.9)	0.82 (0.41, 1.67)	0.88 (0.50, 1.56)	30 (7.2)	35 (3.6)	**2.86 (1.57, 5.21)**	**2.18 (1.31, 3.64)**
Log-Additive			0.91 (0.70, 1.17)	0.93 (0.72, 1.19)			1.25 (0.98, 1.59)	1.26 (1.00, 1.59)
Dominant			0.89 (0.65, 1.22)	0.92 (0.69, 1.24)			1.08 (0.79, 1.47)	1.11 (0.83, 1.49)
Recessive			0.85 (0.42, 1.71)	0.89 (0.51, 1.57)			**2.97 (1.65, 5.37)**	**2.23 (1.34, 3.70)**

Notes: aOR: adjusted odds ratios; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Ca: Cases; Co: Controls; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28kg/m^2), and total energy intake (continuous, kcal/day).

Table 5.11. Associations between selected SNPs related to the HIF and Beta-carotene metabolism pathway and stomach cancer by dietary intake of total cholesterol

	Low Cholesterol				High Cholesterol			
dbSNP no.	Ca, n(%)	Co, n(%)	aOR*	sbOR*	Ca, n(%)	Co, n(%)	aOR*	sbOR*
HIF pathway								
HIF1A (rs2057482)								
C:C	205 (59.1)	830 (60.1)	1.00	1.00	234 (56.3)	604 (61.5)	1.00	1.00
T:C	96 (27.7)	410 (29.7)	0.90 (0.65, 1.24)	0.95 (0.70, 1.28)	120 (28.8)	255 (26.0)	1.18 (0.87, 1.61)	1.18 (0.88, 1.58)
T:T	16 (4.6)	53 (3.8)	1.36 (0.69, 2.69)	1.25 (0.71, 2.19)	14 (3.4)	47 (4.8)	0.69 (0.32, 1.49)	0.82 (0.46, 1.47)
Log-Additive			1.01 (0.78, 1.30)	1.04 (0.81, 1.33)			1.02 (0.80, 1.31)	1.04 (0.82, 1.32)
Dominant			0.95 (0.70, 1.29)	1.00 (0.75, 1.33)			1.11 (0.83, 1.49)	1.12 (0.84, 1.48)
Recessive			1.41 (0.72, 2.76)	1.26 (0.72, 2.21)			0.66 (0.31, 1.40)	0.80 (0.45, 1.41)
HIF1AN (rs2295778)								
C:C	160 (46.1)	736 (53.3)	1.00	1.00	211 (50.7)	454 (46.2)	1.00	1.00
C:G	128 (36.9)	447 (32.3)	1.35 (0.99, 1.83)	1.30 (0.97, 1.74)	127 (30.5)	273 (27.8)	0.92 (0.66, 1.28)	0.94 (0.69, 1.28)
G:G	20 (5.8)	73 (5.3)	1.29 (0.69, 2.40)	1.18 (0.70, 2.00)	15 (3.6)	54 (5.5)	0.68 (0.35, 1.34)	0.77 (0.45, 1.33)
Log-Additive			1.23 (0.97, 1.56)	1.21 (0.96, 1.53)			0.87 (0.68, 1.12)	0.88 (0.69, 1.13)
Dominant			1.34 (0.99, 1.80)	1.30 (0.98, 1.72)			0.88 (0.64, 1.21)	0.89 (0.66, 1.20)
Recessive			1.14 (0.62, 2.09)	1.09 (0.65, 1.83)			0.71 (0.36, 1.37)	0.78 (0.46, 1.35)
Beta-carotene metabolism-related								
R267S (rs12934922)								
A:A	215 (62.0)	976 (70.6)	1.00	1.00	285 (68.5)	674 (68.6)	1.00	1.00
A:T	81 (23.3)	300 (21.7)	1.34 (0.96, 1.86)	1.31 (0.96, 1.79)	59 (14.2)	216 (22.0)	**0.59 (0.40, 0.87)**	**0.63 (0.44, 0.89)**
T:T	9 (2.6)	23 (1.7)	2.08 (0.84, 5.13)	1.46 (0.74, 2.90)	12 (2.9)	27 (2.7)	1.42 (0.65, 3.10)	1.24 (0.67, 2.29)
Log-Additive			**1.37 (1.04, 1.82)**	**1.36 (1.04, 1.77)**			0.80 (0.60, 1.08)	0.81 (0.61, 1.07)
Dominant			**1.39 (1.01, 1.91)**	**1.37 (1.01, 1.85)**			**0.67 (0.47, 0.96)**	**0.70 (0.50, 0.97)**
Recessive			1.92 (0.78, 4.71)	1.41 (0.71, 2.78)			1.57 (0.72, 3.42)	1.31 (0.70, 2.43)
A379V (rs7501331)								
C:C	238 (68.6)	987 (71.4)	1.00	1.00	286 (68.8)	703 (71.6)	1.00	1.00
C:T	58 (16.7)	299 (21.6)	0.85 (0.59, 1.23)	0.87 (0.62, 1.21)	59 (14.2)	197 (20.1)	0.82 (0.56, 1.20)	0.83 (0.59, 1.18)
T:T	13 (3.7)	36 (2.6)	1.94 (0.92, 4.09)	1.49 (0.81, 2.73)	12 (2.9)	27 (2.7)	1.22 (0.57, 2.63)	1.12 (0.61, 2.06)
Log-Additive			1.06 (0.80, 1.40)	1.05 (0.81, 1.38)			0.95 (0.71, 1.26)	0.94 (0.72, 1.23)
Dominant			0.96 (0.68, 1.34)	0.97 (0.70, 1.33)			0.88 (0.62, 1.25)	0.88 (0.63, 1.22)
Recessive			2.01 (0.95, 4.22)	1.52 (0.83, 2.78)			1.27 (0.59, 2.72)	1.15 (0.62, 2.10)

Notes: aOR: adjusted odds ratios; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Ca: Cases; Co: Controls; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28 kg/m^2), and total energy intake (continuous, kcal/day).

Table 5.12. Associations between selected SNPs related to the miRNA pathway and stomach cancer by dietary intake of total flavonoids

	Low Flavonoids				High Flavonoids			
dbSNP no.	Ca, n(%)	Co, n(%)	aOR*	sbOR*	Ca, n(%)	Co, n(%)	aOR*	sbOR*
IL15(rs10519613)								
C:C	110 (34.3)	376 (34.2)	1.00	1.00	132 (29.9)	418 (33.1)	1.00	1.00
C:A	121 (37.7)	466 (42.4)	0.89 (0.64, 1.25)	0.92 (0.67, 1.26)	172 (38.9)	539 (42.6)	0.90 (0.66, 1.23)	0.93 (0.70, 1.25)
A:A	37 (11.5)	197 (17.9)	0.66 (0.41, 1.06)	0.74 (0.49, 1.12)	71 (16.1)	223 (17.6)	0.94 (0.64, 1.38)	0.96 (0.67, 1.37)
Log-Additive			0.83 (0.67, 1.04)	0.85 (0.69, 1.05)			0.96 (0.79, 1.16)	0.97 (0.80, 1.17)
Dominant			0.82 (0.60, 1.13)	0.85 (0.63, 1.14)			0.91 (0.69, 1.22)	0.94 (0.71, 1.23)
Recessive			0.70 (0.45, 1.09)	0.77 (0.52, 1.13)			0.99 (0.70, 1.41)	0.99 (0.72, 1.38)
miR-196a2 (rs11614913)								
T:T	74 (23.1)	342 (31.1)	1.00	1.00	137 (31.0)	344 (27.2)	1.00	1.00
C:T	121 (37.7)	464 (42.2)	1.10 (0.76, 1.59)	1.09 (0.78, 1.53)	152 (34.4)	554 (43.8)	**0.70 (0.51, 0.97)**	0.75 (0.56, 1.01)
C:C	65 (20.2)	214 (19.5)	1.09 (0.70, 1.70)	1.08 (0.73, 1.60)	91 (20.6)	247 (19.5)	0.92 (0.63, 1.35)	0.96 (0.68, 1.37)
Log-Additive			1.05 (0.84, 1.30)	1.05 (0.85, 1.30)			0.93 (0.77, 1.13)	0.95 (0.78, 1.14)
Dominant			1.10 (0.77, 1.55)	1.10 (0.79, 1.52)			0.77 (0.57, 1.03)	0.81 (0.61, 1.07)
Recessive			1.03 (0.71, 1.51)	1.03 (0.73, 1.46)			1.13 (0.81, 1.58)	1.12 (0.82, 1.53)
WWOX (rs12828)								
G:G	102 (31.8)	434 (39.5)	1.00	1.00	150 (33.9)	476 (37.7)	1.00	1.00
A:G	116 (36.1)	444 (40.4)	1.23 (0.87, 1.73)	1.18 (0.86, 1.62)	138 (31.2)	502 (39.7)	0.93 (0.68, 1.27)	0.95 (0.71, 1.28)
A:A	51 (15.9)	143 (13.0)	1.39 (0.88, 2.19)	1.32 (0.88, 1.98)	80 (18.1)	173 (13.7)	**1.53 (1.04, 2.25)**	**1.44 (1.01, 2.06)**
Log-Additive			1.19 (0.96, 1.48)	1.19 (0.96, 1.46)			1.19 (0.98, 1.44)	1.18 (0.98, 1.43)
Dominant			1.27 (0.92, 1.75)	1.25 (0.92, 1.68)			1.09 (0.81, 1.45)	1.10 (0.84, 1.46)
Recessive			1.25 (0.83, 1.88)	1.22 (0.84, 1.79)			**1.59 (1.12, 2.26)**	**1.48 (1.06, 2.05)**
Ran (rs14035)								
C:C	179 (55.8)	679 (61.7)	1.00	1.00	262 (59.3)	726 (57.4)	1.00	1.00
C:T	86 (26.8)	258 (23.5)	1.39 (0.98, 1.96)	1.33 (0.96, 1.83)	96 (21.7)	349 (27.6)	0.75 (0.54, 1.05)	0.77 (0.57, 1.04)
T:T	8 (2.5)	57 (5.2)	0.61 (0.26, 1.44)	0.73 (0.39, 1.36)	18 (4.1)	38 (3.0)	1.87 (0.97, 3.61)	1.52 (0.88, 2.65)
Log-Additive			1.08 (0.83, 1.41)	1.06 (0.82, 1.37)			0.99 (0.77, 1.28)	0.99 (0.77, 1.26)
Dominant			1.25 (0.90, 1.74)	1.20 (0.88, 1.63)			0.86 (0.63, 1.17)	0.87 (0.65, 1.16)
Recessive			0.56 (0.24, 1.30)	0.70 (0.38, 1.29)			**2.02 (1.05, 3.89)**	1.60 (0.92, 2.78)
CXCL12 (rs1804429)								
T:T	239 (74.5)	912 (82.9)	1.00	1.00	336 (76.0)	1034 (81.8)	1.00	1.00
G:T	28 (8.7)	126 (11.5)	0.82 (0.50, 1.34)	0.82 (0.53, 1.27)	36 (8.1)	143 (11.3)	0.82 (0.52, 1.30)	0.81 (0.54, 1.22)
G:G	2 (0.6)	6 (0.5)	NA	0.95 (0.39, 2.31)	3 (0.7)	6 (0.5)	1.51 (0.25, 8.99)	1.09 (0.46, 2.61)
Log-Additive			0.76 (0.48, 1.22)	0.83 (0.55, 1.25)			0.88 (0.58, 1.34)	0.86 (0.59, 1.26)
Dominant			0.78 (0.48, 1.28)	0.82 (0.53, 1.26)			0.84 (0.54, 1.32)	0.83 (0.56, 1.25)

Recessive			NA	0.96 (0.39, 2.32)			1.54 (0.26, 9.18)	1.10 (0.46, 2.63)
Gemin3 (rs197412)								
T:T	123 (38.3)	476 (43.3)	1.00	1.00	188 (42.5)	516 (40.8)	1.00	1.00
T:C	104 (32.4)	450 (40.9)	0.91 (0.64, 1.28)	0.91 (0.66, 1.25)	149 (33.7)	514 (40.7)	0.75 (0.56, 1.01)	0.78 (0.59, 1.03)
C:C	46 (14.3)	113 (10.3)	**2.22 (1.40, 3.51)**	**1.93 (1.27, 2.93)**	41 (9.3)	129 (10.2)	0.80 (0.50, 1.26)	0.82 (0.55, 1.24)
Log-Additive			**1.33 (1.06, 1.66)**	**1.31 (1.06, 1.64)**			0.84 (0.68, 1.04)	0.84 (0.69, 1.03)
Dominant			1.14 (0.83, 1.56)	1.14 (0.85, 1.54)			0.76 (0.58, 1.01)	0.78 (0.59, 1.01)
Recessive			**2.33 (1.52, 3.57)**	**2.00 (1.35, 2.98)**			0.91 (0.59, 1.41)	0.91 (0.61, 1.35)
E2F2 (rs2075993)								
G:G	113 (35.2)	381 (34.6)	1.00	1.00	160 (36.2)	419 (33.1)	1.00	1.00
G:A	105 (32.7)	459 (41.7)	0.82 (0.58, 1.15)	0.85 (0.61, 1.16)	147 (33.3)	529 (41.9)	**0.73 (0.54, 0.99)**	0.75 (0.56, 1.00)
A:A	48 (15.0)	161 (14.6)	1.03 (0.66, 1.62)	1.02 (0.68, 1.53)	68 (15.4)	200 (15.8)	0.80 (0.53, 1.19)	0.83 (0.58, 1.20)
Log-Additive			0.97 (0.78, 1.21)	0.97 (0.78, 1.20)			0.86 (0.70, 1.04)	0.86 (0.71, 1.04)
Dominant			0.87 (0.63, 1.20)	0.89 (0.66, 1.20)			**0.75 (0.56, 0.99)**	0.76 (0.58, 1.00)
Recessive			1.15 (0.76, 1.74)	1.10 (0.75, 1.61)			0.93 (0.64, 1.36)	0.94 (0.67, 1.34)
THBS1 (rs2292305)								
T:T	125 (38.9)	457 (41.5)	1.00	1.00	170 (38.5)	546 (43.2)	1.00	1.00
C:T	101 (31.5)	439 (39.9)	0.95 (0.68, 1.33)	0.94 (0.69, 1.29)	129 (29.2)	482 (38.1)	0.87 (0.64, 1.18)	0.84 (0.63, 1.13)
C:C	24 (7.5)	130 (11.8)	0.86 (0.50, 1.45)	0.87 (0.55, 1.38)	47 (10.6)	134 (10.6)	1.11 (0.71, 1.72)	1.08 (0.72, 1.61)
Log-Additive			0.93 (0.74, 1.18)	0.92 (0.73, 1.16)			1.00 (0.81, 1.22)	0.98 (0.80, 1.20)
Dominant			0.93 (0.68, 1.28)	0.91 (0.68, 1.23)			0.92 (0.69, 1.23)	0.90 (0.68, 1.18)
Recessive			0.88 (0.53, 1.45)	0.89 (0.57, 1.39)			1.18 (0.78, 1.79)	1.15 (0.78, 1.69)
pre-miR-146a (rs2910164)								
C:C	101 (31.5)	387 (35.2)	1.00	1.00	118 (26.7)	430 (34.0)	1.00	1.00
G:C	126 (39.3)	457 (41.5)	1.07 (0.76, 1.50)	1.08 (0.79, 1.49)	186 (42.1)	566 (44.8)	1.20 (0.87, 1.64)	1.18 (0.88, 1.58)
G:G	39 (12.1)	203 (18.5)	0.67 (0.42, 1.08)	0.72 (0.47, 1.09)	64 (14.5)	186 (14.7)	1.20 (0.79, 1.82)	1.19 (0.81, 1.73)
Log-Additive			0.87 (0.70, 1.08)	0.87 (0.70, 1.08)			1.11 (0.91, 1.36)	1.12 (0.92, 1.36)
Dominant			0.94 (0.68, 1.31)	0.95 (0.70, 1.29)			1.20 (0.89, 1.61)	1.20 (0.90, 1.59)
Recessive			0.65 (0.42, 1.00)	0.69 (0.47, 1.02)			1.08 (0.74, 1.57)	1.09 (0.77, 1.54)
CTNNB1 (rs2953)								
T:T	161 (50.2)	578 (52.5)	1.00	1.00	210 (47.5)	672 (53.2)	1.00	1.00
G:T	94 (29.3)	392 (35.6)	0.82 (0.59, 1.15)	0.85 (0.62, 1.16)	129 (29.2)	434 (34.3)	0.86 (0.63, 1.15)	0.89 (0.67, 1.19)
G:G	19 (5.9)	81 (7.4)	0.76 (0.41, 1.40)	0.80 (0.48, 1.34)	31 (7.0)	80 (6.3)	1.04 (0.60, 1.80)	1.04 (0.65, 1.68)
Log-Additive			0.85 (0.66, 1.09)	0.85 (0.67, 1.08)			0.94 (0.75, 1.18)	0.96 (0.77, 1.19)
Dominant			0.81 (0.59, 1.11)	0.82 (0.61, 1.11)			0.88 (0.67, 1.17)	0.92 (0.70, 1.20)
Recessive			0.82 (0.45, 1.49)	0.83 (0.50, 1.39)			1.11 (0.65, 1.89)	1.08 (0.67, 1.72)
DOCK4 (rs3801790)								
A:A	106 (33.0)	409 (37.2)	1.00	1.00	163 (36.9)	434 (34.3)	1.00	1.00

A:G	111 (34.6)	454 (41.3)	1.00 (0.71, 1.41)	0.99 (0.72, 1.36)	156 (35.3)	532 (42.1)	0.77 (0.57, 1.04)	0.82 (0.62, 1.09)
G:G	54 (16.8)	171 (15.5)	1.14 (0.73, 1.79)	1.17 (0.79, 1.74)	58 (13.1)	188 (14.9)	0.87 (0.57, 1.31)	0.90 (0.62, 1.32)
Log-Additive			1.06 (0.85, 1.31)	1.08 (0.87, 1.33)			0.89 (0.73, 1.09)	0.91 (0.75, 1.10)
Dominant			1.04 (0.75, 1.43)	1.05 (0.78, 1.42)			0.79 (0.60, 1.05)	0.83 (0.64, 1.09)
Recessive			1.15 (0.76, 1.72)	1.18 (0.81, 1.70)			0.99 (0.68, 1.46)	0.99 (0.69, 1.41)
Rbl2 (rs3929)								
G:G	186 (57.9)	693 (63.0)	1.00	1.00	239 (54.1)	817 (64.6)	1.00	1.00
C:G	77 (24.0)	336 (30.5)	0.89 (0.63, 1.25)	0.89 (0.64, 1.22)	129 (29.2)	331 (26.2)	1.33 (0.99, 1.79)	1.27 (0.96, 1.69)
C:C	11 (3.4)	32 (2.9)	1.32 (0.58, 2.98)	1.17 (0.62, 2.20)	16 (3.6)	58 (4.6)	0.89 (0.46, 1.73)	0.92 (0.53, 1.59)
Log-Additive			0.98 (0.74, 1.30)	0.97 (0.74, 1.27)			1.13 (0.90, 1.43)	1.12 (0.89, 1.40)
Dominant			0.93 (0.67, 1.28)	0.92 (0.68, 1.26)			1.26 (0.95, 1.67)	1.22 (0.93, 1.60)
Recessive			1.37 (0.61, 3.08)	1.19 (0.63, 2.25)			0.81 (0.42, 1.56)	0.87 (0.51, 1.49)
IL6R (rs4072391)								
C:C	229 (71.3)	859 (78.1)	1.00	1.00	305 (69.0)	986 (78.0)	1.00	1.00
C:T	39 (12.1)	178 (16.2)	0.81 (0.52, 1.26)	0.82 (0.55, 1.22)	53 (12.0)	179 (14.2)	1.07 (0.71, 1.59)	1.03 (0.72, 1.49)
T:T	7 (2.2)	10 (0.9)	2.24 (0.69, 7.22)	1.36 (0.63, 2.96)	12 (2.7)	22 (1.7)	1.86 (0.77, 4.48)	1.41 (0.72, 2.75)
Log-Additive			0.98 (0.68, 1.42)	0.97 (0.69, 1.37)			1.19 (0.87, 1.62)	1.16 (0.86, 1.55)
Dominant			0.89 (0.58, 1.35)	0.89 (0.61, 1.31)			1.16 (0.80, 1.68)	1.12 (0.79, 1.58)
Recessive			2.31 (0.72, 7.45)	1.38 (0.63, 2.99)			1.84 (0.77, 4.43)	1.40 (0.72, 2.74)
CDK6 (rs42031)								
A:A	250 (77.9)	948 (86.2)	1.00	1.00	334 (75.6)	1088 (86.1)	1.00	1.00
A:T	24 (7.5)	90 (8.2)	0.98 (0.56, 1.70)	0.96 (0.59, 1.55)	41 (9.3)	106 (8.4)	1.39 (0.88, 2.19)	1.27 (0.84, 1.92)
T:T	3 (0.9)	7 (0.6)	1.69 (0.29, 10.02)	1.28 (0.55, 3.01)	3 (0.7)	6 (0.5)	1.12 (0.19, 6.80)	1.03 (0.43, 2.44)
Log-Additive			1.05 (0.65, 1.70)	1.09 (0.72, 1.66)			1.31 (0.87, 1.97)	1.23 (0.85, 1.80)
Dominant			1.02 (0.60, 1.73)	1.03 (0.65, 1.64)			1.37 (0.88, 2.14)	1.27 (0.85, 1.90)
Recessive			1.69 (0.29, 10.03)	1.28 (0.55, 3.01)			1.09 (0.18, 6.57)	1.02 (0.43, 2.42)
Ago2 (rs4961280)								
C:C	223 (69.5)	786 (71.5)	1.00	1.00	292 (66.1)	879 (69.5)	1.00	1.00
C:A	43 (13.4)	213 (19.4)	0.73 (0.48, 1.09)	0.77 (0.54, 1.12)	69 (15.6)	239 (18.9)	0.83 (0.58, 1.19)	0.83 (0.60, 1.16)
A:A	5 (1.6)	13 (1.2)	1.05 (0.29, 3.79)	1.01 (0.46, 2.20)	14 (3.2)	32 (2.5)	1.37 (0.61, 3.04)	1.20 (0.64, 2.25)
Log-Additive			0.79 (0.56, 1.14)	0.82 (0.59, 1.14)			0.96 (0.72, 1.27)	0.95 (0.72, 1.25)
Dominant			0.75 (0.50, 1.11)	0.79 (0.55, 1.13)			0.89 (0.64, 1.24)	0.89 (0.65, 1.22)
Recessive			1.12 (0.31, 4.02)	1.03 (0.47, 2.25)			1.42 (0.64, 3.14)	1.23 (0.66, 2.30)
miR-26a1 (rs7372209)								
C:C	143 (44.5)	518 (47.1)	1.00	1.00	210 (47.5)	597 (47.2)	1.00	1.00
C:T	113 (35.2)	430 (39.1)	1.06 (0.77, 1.46)	1.03 (0.76, 1.39)	138 (31.2)	468 (37.0)	0.90 (0.67, 1.20)	0.89 (0.67, 1.17)
T:T	20 (6.2)	105 (9.5)	0.62 (0.33, 1.17)	0.68 (0.40, 1.14)	30 (6.8)	106 (8.4)	0.77 (0.45, 1.31)	0.78 (0.49, 1.24)

Log-Additive			0.90 (0.71, 1.15)	0.88 (0.70, 1.11)			0.89 (0.71, 1.10)	0.87 (0.70, 1.07)
Dominant			0.97 (0.72, 1.33)	0.94 (0.70, 1.26)			0.87 (0.66, 1.15)	0.85 (0.66, 1.11)
Recessive			0.60 (0.32, 1.12)	0.67 (0.40, 1.12)			0.81 (0.48, 1.36)	0.81 (0.52, 1.28)
Gemin4 (rs7813)								
T:T	133 (41.4)	506 (46.0)	1.00	1.00	184 (41.6)	606 (47.9)	1.00	1.00
C:T	104 (32.4)	392 (35.6)	1.01 (0.73, 1.41)	1.04 (0.76, 1.42)	135 (30.5)	441 (34.9)	1.08 (0.80, 1.47)	1.06 (0.79, 1.41)
C:C	27 (8.4)	112 (10.2)	0.67 (0.38, 1.16)	0.74 (0.46, 1.18)	46 (10.4)	98 (7.8)	1.53 (0.97, 2.43)	1.42 (0.94, 2.16)
Log-Additive			0.88 (0.70, 1.11)	0.89 (0.71, 1.12)			1.19 (0.96, 1.46)	1.18 (0.96, 1.44)
Dominant			0.93 (0.68, 1.27)	0.94 (0.70, 1.27)			1.17 (0.88, 1.55)	1.15 (0.88, 1.51)
Recessive			0.66 (0.39, 1.14)	0.73 (0.46, 1.15)			1.48 (0.95, 2.30)	1.40 (0.93, 2.09)
KARS (rs9266)								
C:C	177 (55.1)	672 (61.1)	1.00	1.00	249 (56.3)	736 (58.2)	1.00	1.00
C:T	85 (26.5)	335 (30.5)	0.81 (0.58, 1.14)	0.84 (0.61, 1.15)	96 (21.7)	365 (28.9)	0.73 (0.53, 1.00)	0.76 (0.56, 1.02)
T:T	11 (3.4)	39 (3.5)	1.15 (0.53, 2.48)	1.08 (0.59, 1.99)	29 (6.6)	76 (6.0)	0.86 (0.49, 1.52)	0.93 (0.57, 1.50)
Log-Additive			0.91 (0.69, 1.20)	0.92 (0.71, 1.20)			0.83 (0.66, 1.05)	0.85 (0.68, 1.07)
Dominant			0.85 (0.61, 1.17)	0.87 (0.64, 1.18)			0.75 (0.56, 1.01)	0.78 (0.59, 1.03)
Recessive			1.23 (0.58, 2.63)	1.12 (0.61, 2.06)			0.94 (0.54, 1.65)	0.99 (0.61, 1.60)

Notes: aOR: adjusted odds ratios; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Ca: Cases; Co: Controls; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28 kg/m^2), and total energy intake (continuous, kcal/day).

Table 5.13. Associations between selected SNPs related to the Stem cell pathway and stomach cancer by dietary intake of total flavonoids

	Low Flavonoids				High Flavonoids			
dbSNP no.	Ca, n(%)	Co, n(%)	aOR*	sbOR*	Ca, n(%)	Co, n(%)	aOR*	sbOR*
HEY1 (rs1046472)								
C:C	167 (52.0)	663 (60.3)	1.00	1.00	228 (51.6)	740 (58.5)	1.00	1.00
A:C	90 (28.0)	342 (31.1)	1.10 (0.79, 1.53)	1.09 (0.80, 1.50)	122 (27.6)	375 (29.7)	1.08 (0.80, 1.46)	1.06 (0.80, 1.41)
A:A	19 (5.9)	46 (4.2)	1.42 (0.72, 2.80)	1.25 (0.71, 2.21)	31 (7.0)	62 (4.9)	1.47 (0.85, 2.54)	1.34 (0.83, 2.17)
Log-Additive			1.14 (0.88, 1.48)	1.14 (0.89, 1.46)			1.15 (0.92, 1.44)	1.14 (0.92, 1.42)
Dominant			1.14 (0.83, 1.56)	1.14 (0.84, 1.53)			1.14 (0.86, 1.51)	1.12 (0.86, 1.47)
Recessive			1.37 (0.70, 2.68)	1.23 (0.70, 2.15)			1.43 (0.84, 2.45)	1.32 (0.82, 2.12)
Oct4 (rs13409)								
C:C	94 (29.3)	376 (34.2)	1.00	1.00	138 (31.2)	430 (34.0)	1.00	1.00
C:T	129 (40.2)	467 (42.5)	0.98 (0.69, 1.39)	1.01 (0.73, 1.39)	151 (34.2)	535 (42.3)	0.79 (0.58, 1.08)	0.82 (0.61, 1.09)
T:T	49 (15.3)	198 (18.0)	0.85 (0.55, 1.32)	0.87 (0.59, 1.29)	81 (18.3)	216 (17.1)	1.02 (0.70, 1.50)	1.02 (0.72, 1.45)
Log-Additive			0.93 (0.75, 1.15)	0.93 (0.76, 1.15)			0.97 (0.80, 1.18)	0.97 (0.81, 1.17)
Dominant			0.94 (0.68, 1.30)	0.96 (0.70, 1.30)			0.86 (0.65, 1.14)	0.87 (0.66, 1.14)
Recessive			0.86 (0.58, 1.27)	0.87 (0.60, 1.24)			1.15 (0.81, 1.63)	1.12 (0.81, 1.55)
AXIN1 (rs1981492)								
G:G	160 (49.8)	549 (49.9)	1.00	1.00	192 (43.4)	579 (45.8)	1.00	1.00
A:G	84 (26.2)	400 (36.4)	**0.64 (0.46, 0.91)**	**0.68 (0.50, 0.93)**	140 (31.7)	457 (36.2)	0.89 (0.66, 1.20)	0.91 (0.69, 1.21)
A:A	34 (10.6)	84 (7.6)	1.12 (0.67, 1.90)	1.14 (0.72, 1.80)	50 (11.3)	131 (10.4)	0.87 (0.56, 1.37)	0.90 (0.60, 1.34)
Log-Additive			0.88 (0.69, 1.12)	0.90 (0.71, 1.13)			0.92 (0.75, 1.13)	0.93 (0.76, 1.13)
Dominant			**0.73 (0.53, 0.99)**	0.76 (0.57, 1.02)			0.89 (0.67, 1.17)	0.90 (0.69, 1.18)
Recessive			1.33 (0.80, 2.22)	1.28 (0.82, 2.02)			0.92 (0.60, 1.41)	0.93 (0.63, 1.37)
DVL2 (rs222851)								
A:A	101 (31.5)	400 (36.4)	1.00	1.00	152 (34.4)	472 (37.3)	1.00	1.00
A:G	124 (38.6)	475 (43.2)	1.19 (0.84, 1.68)	1.18 (0.86, 1.62)	165 (37.3)	511 (40.4)	1.08 (0.80, 1.46)	1.07 (0.81, 1.43)
G:G	33 (10.3)	144 (13.1)	0.96 (0.58, 1.61)	0.98 (0.63, 1.53)	57 (12.9)	180 (14.2)	1.04 (0.68, 1.60)	1.04 (0.71, 1.53)
Log-Additive			1.03 (0.82, 1.30)	1.04 (0.83, 1.30)			1.03 (0.85, 1.26)	1.04 (0.85, 1.26)
Dominant			1.14 (0.82, 1.58)	1.14 (0.83, 1.55)			1.07 (0.81, 1.42)	1.07 (0.82, 1.40)
Recessive			0.87 (0.54, 1.40)	0.91 (0.60, 1.39)			1.00 (0.68, 1.49)	1.01 (0.70, 1.45)
FZD3 (rs2241802)								
G:G	97 (30.2)	329 (29.9)	1.00	1.00	128 (29.0)	375 (29.7)	1.00	1.00
A:G	108 (33.6)	482 (43.8)	0.89 (0.62, 1.28)	0.87 (0.63, 1.22)	164 (37.1)	497 (39.3)	1.03 (0.74, 1.42)	1.03 (0.76, 1.40)
A:A	56 (17.4)	180 (16.4)	1.32 (0.84, 2.05)	1.26 (0.84, 1.87)	62 (14.0)	251 (19.9)	0.83 (0.55, 1.24)	0.86 (0.60, 1.25)
Log-Additive			1.11 (0.89, 1.40)	1.10 (0.89, 1.37)			0.92 (0.76, 1.13)	0.93 (0.77, 1.13)
Dominant			1.00 (0.71, 1.40)	0.99 (0.72, 1.36)			0.96 (0.71, 1.30)	0.97 (0.73, 1.29)
Recessive			1.41 (0.95, 2.09)	1.34 (0.93, 1.94)			0.82 (0.57, 1.17)	0.85 (0.61, 1.19)

Dec1 (rs2269700)								
T:T	200 (62.3)	705 (64.1)	1.00	1.00	272 (61.5)	794 (62.8)	1.00	1.00
C:T	73 (22.7)	297 (27.0)	0.91 (0.64, 1.28)	0.93 (0.67, 1.28)	105 (23.8)	345 (27.3)	0.88 (0.65, 1.20)	0.89 (0.66, 1.19)
C:C	5 (1.6)	45 (4.1)	0.40 (0.14, 1.15)	0.62 (0.32, 1.21)	6 (1.4)	45 (3.6)	0.85 (0.34, 2.14)	0.88 (0.45, 1.70)
Log-Additive			0.81 (0.60, 1.08)	0.82 (0.62, 1.07)			0.89 (0.68, 1.17)	0.89 (0.69, 1.15)
Dominant			0.84 (0.60, 1.17)	0.85 (0.62, 1.17)			0.88 (0.65, 1.19)	0.88 (0.66, 1.17)
Recessive			0.41 (0.14, 1.18)	0.63 (0.32, 1.22)			0.88 (0.35, 2.20)	0.89 (0.46, 1.73)
Oct4 (rs3130932)								
T:T	144 (44.9)	490 (44.5)	1.00	1.00	196 (44.3)	544 (43.0)	1.00	1.00
G:T	104 (32.4)	437 (39.7)	0.97 (0.70, 1.35)	0.94 (0.69, 1.27)	132 (29.9)	504 (39.9)	0.79 (0.58, 1.06)	0.81 (0.61, 1.08)
G:G	29 (9.0)	115 (10.5)	1.14 (0.68, 1.90)	1.06 (0.68, 1.67)	48 (10.9)	137 (10.8)	1.01 (0.65, 1.57)	1.01 (0.68, 1.51)
Log-Additive			1.03 (0.82, 1.30)	1.00 (0.80, 1.25)			0.93 (0.76, 1.14)	0.94 (0.77, 1.14)
Dominant			1.00 (0.74, 1.36)	0.97 (0.72, 1.29)			0.83 (0.63, 1.10)	0.85 (0.65, 1.11)
Recessive			1.16 (0.71, 1.89)	1.09 (0.70, 1.69)			1.12 (0.74, 1.71)	1.09 (0.74, 1.61)
WNT2 (rs3729629)								
G:G	131 (40.8)	445 (40.5)	1.00	1.00	197 (44.6)	561 (44.4)	1.00	1.00
C:G	117 (36.4)	474 (43.1)	0.82 (0.59, 1.13)	0.87 (0.64, 1.17)	146 (33.0)	502 (39.7)	0.86 (0.64, 1.15)	0.88 (0.67, 1.16)
C:C	28 (8.7)	126 (11.5)	0.71 (0.42, 1.22)	0.77 (0.49, 1.23)	31 (7.0)	118 (9.3)	0.79 (0.48, 1.30)	0.82 (0.53, 1.28)
Log-Additive			0.83 (0.66, 1.05)	0.85 (0.68, 1.07)			0.87 (0.71, 1.08)	0.88 (0.71, 1.08)
Dominant			0.80 (0.59, 1.08)	0.83 (0.62, 1.11)			0.84 (0.64, 1.11)	0.86 (0.66, 1.12)
Recessive			0.78 (0.47, 1.31)	0.82 (0.52, 1.28)			0.85 (0.52, 1.38)	0.86 (0.56, 1.33)
HEY2 (rs3734637)								
A:A	171 (53.3)	608 (55.3)	1.00	1.00	225 (50.9)	716 (56.6)	1.00	1.00
A:C	94 (29.3)	360 (32.7)	0.99 (0.71, 1.37)	1.02 (0.74, 1.38)	117 (26.5)	383 (30.3)	0.93 (0.68, 1.26)	0.95 (0.71, 1.28)
C:C	7 (2.2)	71 (6.5)	**0.32 (0.13, 0.77)**	**0.50 (0.27, 0.91)**	23 (5.2)	83 (6.6)	0.82 (0.46, 1.46)	0.87 (0.53, 1.42)
Log-Additive			0.79 (0.60, 1.02)	0.79 (0.62, 1.02)			0.92 (0.73, 1.15)	0.93 (0.75, 1.16)
Dominant			0.86 (0.63, 1.19)	0.87 (0.64, 1.18)			0.91 (0.68, 1.21)	0.93 (0.71, 1.23)
Recessive			**0.32 (0.13, 0.77)**	**0.50 (0.27, 0.90)**			0.84 (0.47, 1.48)	0.88 (0.54, 1.43)
Ctbp2 (rs3740535)								
G:G	158 (49.2)	588 (53.5)	1.00	1.00	193 (43.7)	626 (49.5)	1.00	1.00
A:G	85 (26.5)	383 (34.8)	0.74 (0.53, 1.04)	0.76 (0.55, 1.05)	133 (30.1)	452 (35.8)	1.02 (0.76, 1.38)	1.03 (0.78, 1.36)
A:A	27 (8.4)	72 (6.5)	1.25 (0.72, 2.17)	1.18 (0.73, 1.92)	44 (10.0)	102 (8.1)	1.17 (0.73, 1.89)	1.14 (0.75, 1.75)
Log-Additive			0.95 (0.74, 1.21)	0.95 (0.75, 1.20)			1.06 (0.86, 1.31)	1.07 (0.87, 1.30)
Dominant			0.82 (0.60, 1.13)	0.84 (0.62, 1.13)			1.05 (0.80, 1.39)	1.06 (0.81, 1.39)
Recessive			1.40 (0.81, 2.40)	1.28 (0.80, 2.06)			1.16 (0.74, 1.84)	1.13 (0.75, 1.71)
WNT2 (rs4730775)								
C:C	150 (46.7)	594 (54.0)	1.00	1.00	234 (52.9)	671 (53.1)	1.00	1.00
C:T	101 (31.5)	367 (33.4)	0.89 (0.64, 1.24)	0.96 (0.70, 1.30)	115 (26.0)	418 (33.1)	0.75 (0.55, 1.01)	0.78 (0.59, 1.04)
T:T	12 (3.7)	74 (6.7)	0.72 (0.36, 1.46)	0.81 (0.46, 1.42)	20 (4.5)	75 (5.9)	0.98 (0.55, 1.77)	0.99 (0.60, 1.64)

Log-Additive			0.87 (0.67, 1.13)	0.90 (0.70, 1.16)			0.86 (0.68, 1.09)	0.88 (0.70, 1.10)
Dominant			0.86 (0.63, 1.19)	0.92 (0.68, 1.24)			0.78 (0.59, 1.04)	0.81 (0.62, 1.06)
Recessive			0.75 (0.38, 1.51)	0.82 (0.47, 1.43)			1.09 (0.61, 1.94)	1.06 (0.64, 1.74)
WNT8A (rs4835761)								
A:A	102 (31.8)	333 (30.3)	1.00	1.00	150 (33.9)	402 (31.8)	1.00	1.00
A:G	103 (32.1)	486 (44.2)	0.75 (0.52, 1.06)	0.75 (0.54, 1.04)	155 (35.1)	532 (42.1)	0.73 (0.54, 1.00)	0.76 (0.57, 1.01)
G:G	59 (18.4)	189 (17.2)	0.98 (0.64, 1.50)	1.00 (0.68, 1.47)	71 (16.1)	212 (16.8)	0.98 (0.67, 1.45)	0.99 (0.69, 1.41)
Log-Additive			0.95 (0.77, 1.18)	0.95 (0.77, 1.18)			0.95 (0.78, 1.15)	0.94 (0.78, 1.14)
Dominant			0.81 (0.59, 1.13)	0.82 (0.60, 1.11)			0.80 (0.60, 1.07)	0.82 (0.62, 1.07)
Recessive			1.15 (0.78, 1.69)	1.14 (0.80, 1.63)			1.16 (0.81, 1.64)	1.13 (0.81, 1.57)
Notch4 (rs520692)								
A:A	205 (63.9)	808 (73.5)	1.00	1.00	262 (59.3)	898 (71.0)	1.00	1.00
A:G	60 (18.7)	230 (20.9)	0.94 (0.65, 1.36)	0.93 (0.66, 1.32)	87 (19.7)	265 (21.0)	0.97 (0.70, 1.34)	0.99 (0.73, 1.35)
G:G	3 (0.9)	11 (1.0)	1.27 (0.33, 4.84)	1.08 (0.48, 2.39)	3 (0.7)	28 (2.2)	0.43 (0.12, 1.49)	0.70 (0.34, 1.44)
Log-Additive			0.97 (0.69, 1.36)	0.96 (0.70, 1.32)			0.88 (0.66, 1.18)	0.90 (0.69, 1.19)
Dominant			0.95 (0.66, 1.37)	0.95 (0.68, 1.33)			0.92 (0.67, 1.27)	0.94 (0.70, 1.27)
Recessive			1.29 (0.34, 4.90)	1.08 (0.49, 2.41)			0.43 (0.13, 1.49)	0.70 (0.34, 1.44)
Rex1 (rs6815391)								
T:T	120 (37.4)	436 (39.6)	1.00	1.00	172 (38.9)	524 (41.5)	1.00	1.00
C:T	99 (30.8)	453 (41.2)	0.85 (0.60, 1.20)	0.86 (0.62, 1.18)	145 (32.8)	458 (36.2)	0.99 (0.73, 1.35)	0.99 (0.74, 1.32)
C:C	45 (14.0)	128 (11.6)	1.52 (0.97, 2.40)	1.42 (0.94, 2.14)	50 (11.3)	164 (13.0)	0.85 (0.55, 1.30)	0.85 (0.58, 1.26)
Log-Additive			1.14 (0.91, 1.42)	1.13 (0.91, 1.41)			0.94 (0.77, 1.14)	0.93 (0.77, 1.13)
Dominant			0.99 (0.72, 1.37)	1.00 (0.74, 1.35)			0.95 (0.71, 1.26)	0.94 (0.72, 1.23)
Recessive			**1.65 (1.08, 2.52)**	**1.51 (1.02, 2.24)**			0.85 (0.57, 1.28)	0.86 (0.59, 1.24)
HES2 (rs8708)								
A:A	185 (57.6)	689 (62.6)	1.00	1.00	261 (59.0)	802 (63.4)	1.00	1.00
A:G	63 (19.6)	307 (27.9)	0.98 (0.68, 1.40)	0.96 (0.69, 1.34)	99 (22.4)	315 (24.9)	0.98 (0.71, 1.34)	0.99 (0.74, 1.34)
G:G	11 (3.4)	43 (3.9)	1.14 (0.54, 2.44)	1.06 (0.58, 1.94)	7 (1.6)	46 (3.6)	0.63 (0.25, 1.57)	0.78 (0.41, 1.48)
Log-Additive			1.02 (0.77, 1.35)	1.00 (0.76, 1.30)			0.91 (0.70, 1.19)	0.92 (0.72, 1.19)
Dominant			1.00 (0.71, 1.41)	0.98 (0.71, 1.34)			0.94 (0.69, 1.28)	0.95 (0.71, 1.27)
Recessive			1.15 (0.54, 2.44)	1.07 (0.59, 1.95)			0.64 (0.26, 1.58)	0.78 (0.41, 1.48)
Notch4 (rs915894)								
C:C	94 (29.3)	299 (27.2)	1.00	1.00	122 (27.6)	351 (27.8)	1.00	1.00
A:C	115 (35.8)	488 (44.4)	**0.70 (0.49, 1.00)**	0.75 (0.54, 1.05)	161 (36.4)	558 (44.1)	0.91 (0.65, 1.26)	0.93 (0.68, 1.25)
A:A	64 (19.9)	240 (21.8)	0.85 (0.56, 1.29)	0.90 (0.62, 1.32)	91 (20.6)	255 (20.2)	1.04 (0.71, 1.53)	1.09 (0.77, 1.54)
Log-Additive			0.90 (0.73, 1.12)	0.92 (0.75, 1.13)			1.01 (0.84, 1.23)	1.04 (0.86, 1.25)
Dominant			0.74 (0.54, 1.04)	0.79 (0.58, 1.08)			0.95 (0.70, 1.29)	0.98 (0.74, 1.31)
Recessive			1.05 (0.73, 1.51)	1.05 (0.75, 1.47)			1.11 (0.80, 1.54)	1.13 (0.83, 1.54)
NF-κB pathway								

miR-300 (rs12894467)								
T:T	145 (45.2)	616 (56.0)	1.00	1.00	203 (45.9)	727 (57.5)	1.00	1.00
C:T	92 (28.7)	343 (31.2)	1.28 (0.91, 1.80)	1.25 (0.91, 1.72)	122 (27.6)	359 (28.4)	**1.41 (1.03, 1.92)**	**1.35 (1.01, 1.81)**
C:C	19 (5.9)	58 (5.3)	0.98 (0.48, 1.97)	1.03 (0.59, 1.79)	39 (8.8)	67 (5.3)	**2.07 (1.24, 3.47)**	**1.80 (1.14, 2.84)**
Log-Additive			1.13 (0.87, 1.46)	1.14 (0.89, 1.45)			**1.43 (1.15, 1.78)**	**1.42 (1.15, 1.76)**
Dominant			1.23 (0.89, 1.71)	1.22 (0.90, 1.66)			**1.52 (1.14, 2.03)**	**1.49 (1.13, 1.96)**
Recessive			0.89 (0.45, 1.78)	0.97 (0.56, 1.68)			**1.83 (1.11, 3.01)**	**1.65 (1.06, 2.58)**
IKBKAP (rs1538660)								
C:C	135 (42.1)	443 (40.3)	1.00	1.00	177 (40.0)	579 (45.8)	1.00	1.00
C:T	109 (34.0)	463 (42.1)	**0.63 (0.45, 0.88)**	**0.68 (0.50, 0.93)**	149 (33.7)	457 (36.2)	1.04 (0.77, 1.41)	1.02 (0.77, 1.36)
T:T	33 (10.3)	125 (11.4)	0.72 (0.43, 1.22)	0.89 (0.57, 1.38)	49 (11.1)	130 (10.3)	1.42 (0.92, 2.20)	1.31 (0.88, 1.95)
Log-Additive			**0.76 (0.60, 0.97)**	0.83 (0.66, 1.04)			1.15 (0.94, 1.40)	1.13 (0.93, 1.37)
Dominant			**0.65 (0.48, 0.89)**	**0.71 (0.53, 0.96)**			1.13 (0.85, 1.49)	1.10 (0.85, 1.44)
Recessive			0.90 (0.55, 1.48)	1.03 (0.67, 1.58)			1.40 (0.92, 2.12)	1.30 (0.88, 1.90)
IKBKAP (rs2230793)								
A:A	128 (39.9)	486 (44.2)	1.00	1.00	197 (44.6)	580 (45.9)	1.00	1.00
A:C	106 (33.0)	453 (41.2)	0.86 (0.62, 1.20)	0.87 (0.64, 1.19)	135 (30.5)	468 (37.0)	0.88 (0.66, 1.19)	0.88 (0.67, 1.17)
C:C	36 (11.2)	97 (8.8)	**1.78 (1.08, 2.93)**	**1.66 (1.06, 2.59)**	52 (11.8)	128 (10.1)	1.41 (0.92, 2.17)	1.27 (0.86, 1.89)
Log-Additive			1.15 (0.91, 1.46)	1.18 (0.94, 1.47)			1.09 (0.89, 1.33)	1.06 (0.87, 1.29)
Dominant			1.00 (0.74, 1.37)	1.03 (0.77, 1.38)			0.99 (0.75, 1.30)	0.97 (0.75, 1.26)
Recessive			**1.90 (1.18, 3.07)**	**1.74 (1.13, 2.68)**			1.49 (0.98, 2.25)	1.33 (0.91, 1.95)
IKBKAP (rs3204145)								
T:T	134 (41.7)	461 (41.9)	1.00	1.00	182 (41.2)	579 (45.8)	1.00	1.00
A:T	113 (35.2)	473 (43.0)	**0.66 (0.48, 0.92)**	**0.71 (0.52, 0.97)**	157 (35.5)	475 (37.6)	0.98 (0.73, 1.31)	0.96 (0.72, 1.26)
A:A	28 (8.7)	123 (11.2)	0.63 (0.36, 1.09)	0.81 (0.52, 1.28)	43 (9.7)	123 (9.7)	1.29 (0.82, 2.01)	1.19 (0.80, 1.79)
Log-Additive			**0.74 (0.58, 0.94)**	0.80 (0.64, 1.01)			1.08 (0.88, 1.32)	1.06 (0.87, 1.29)
Dominant			**0.65 (0.48, 0.89)**	**0.72 (0.53, 0.96)**			1.04 (0.79, 1.36)	1.01 (0.78, 1.31)
Recessive			0.77 (0.45, 1.30)	0.93 (0.59, 1.44)			1.30 (0.84, 2.00)	1.21 (0.82, 1.80)

Notes: aOR: adjusted odds ratios; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Ca: Cases; Co: Controls; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28 kg/m^2), and total energy intake (continuous, kcal/day).

Table 5.14. Associations between selected SNPs related to the GWAS and stomach cancer by dietary intake of total flavonoids

	Low Flavonoids				High Flavonoids			
dbSNP no.	Ca, n(%)	Co, n(%)	aOR*	sbOR*	Ca, n(%)	Co, n(%)	aOR*	sbOR*
RUNX1 (rs2014300)								
G:G	205 (63.9)	809 (73.5)	1.00	1.00	290 (65.6)	909 (71.9)	1.00	1.00
A:G	61 (19.0)	220 (20.0)	1.21 (0.84, 1.75)	1.18 (0.84, 1.65)	67 (15.2)	252 (19.9)	0.84 (0.58, 1.21)	0.87 (0.62, 1.22)
A:A	8 (2.5)	20 (1.8)	1.68 (0.61, 4.63)	1.25 (0.61, 2.56)	14 (3.2)	30 (2.4)	1.14 (0.51, 2.54)	1.09 (0.58, 2.02)
Log-Additive			1.24 (0.91, 1.69)	1.21 (0.90, 1.62)			0.93 (0.70, 1.24)	0.95 (0.72, 1.24)
Dominant			1.25 (0.88, 1.78)	1.21 (0.87, 1.69)			0.88 (0.62, 1.23)	0.90 (0.66, 1.24)
Recessive			1.60 (0.58, 4.41)	1.23 (0.60, 2.51)			1.18 (0.53, 2.62)	1.10 (0.59, 2.06)
PLCE1 (rs2274223)								
A:A	147 (45.8)	665 (60.5)	1.00	1.00	185 (41.9)	715 (56.6)	1.00	1.00
A:G	82 (25.5)	311 (28.3)	1.00 (0.69, 1.43)	1.03 (0.74, 1.44)	132 (29.9)	389 (30.8)	**1.44 (1.05, 1.97)**	1.34 (1.00, 1.81)
G:G	12 (3.7)	42 (3.8)	1.24 (0.59, 2.63)	1.13 (0.62, 2.06)	16 (3.6)	52 (4.1)	1.57 (0.81, 3.03)	1.35 (0.77, 2.34)
Log-Additive			1.05 (0.79, 1.39)	1.07 (0.81, 1.40)			**1.34 (1.05, 1.72)**	**1.30 (1.03, 1.65)**
Dominant			1.03 (0.73, 1.45)	1.06 (0.77, 1.46)			**1.45 (1.07, 1.97)**	**1.38 (1.03, 1.84)**
Recessive			1.25 (0.59, 2.61)	1.12 (0.62, 2.04)			1.37 (0.72, 2.61)	1.25 (0.72, 2.15)
GPC5 (rs2352028)								
C:C	190 (59.2)	654 (59.5)	1.00	1.00	243 (55.0)	756 (59.8)	1.00	1.00
C:T	85 (26.5)	340 (30.9)	0.86 (0.61, 1.19)	0.87 (0.64, 1.19)	125 (28.3)	367 (29.0)	1.02 (0.76, 1.37)	1.04 (0.79, 1.38)
T:T	15 (4.7)	60 (5.5)	0.85 (0.43, 1.67)	0.86 (0.50, 1.50)	20 (4.5)	64 (5.1)	0.68 (0.34, 1.36)	0.76 (0.44, 1.32)
Log-Additive			0.89 (0.68, 1.15)	0.88 (0.69, 1.13)			0.93 (0.74, 1.18)	0.94 (0.75, 1.18)
Dominant			0.85 (0.62, 1.17)	0.86 (0.64, 1.15)			0.97 (0.73, 1.29)	0.98 (0.75, 1.29)
Recessive			0.89 (0.45, 1.75)	0.89 (0.51, 1.54)			0.68 (0.34, 1.34)	0.76 (0.44, 1.31)
TERT (rs2736100)								
T:T	121 (37.7)	323 (29.4)	1.00	1.00	136 (30.8)	378 (29.9)	1.00	1.00
G:T	101 (31.5)	479 (43.5)	**0.50 (0.35, 0.71)**	**0.55 (0.40, 0.77)**	176 (39.8)	527 (41.7)	0.94 (0.68, 1.28)	0.96 (0.72, 1.29)
G:G	50 (15.6)	191 (17.4)	**0.63 (0.41, 0.99)**	0.70 (0.47, 1.03)	52 (11.8)	209 (16.5)	**0.53 (0.34, 0.83)**	**0.60 (0.41, 0.90)**
Log-Additive			**0.73 (0.59, 0.92)**	**0.74 (0.60, 0.92)**			**0.77 (0.63, 0.95)**	**0.78 (0.64, 0.96)**
Dominant			**0.53 (0.39, 0.74)**	**0.57 (0.42, 0.77)**			0.81 (0.60, 1.10)	0.83 (0.62, 1.10)
Recessive			0.93 (0.62, 1.39)	0.92 (0.64, 1.34)			**0.55 (0.37, 0.83)**	**0.62 (0.43, 0.89)**
CRPP1 -CRP (rs2808630)								
T:T	195 (60.7)	780 (70.9)	1.00	1.00	290 (65.6)	870 (68.8)	1.00	1.00
C:T	61 (19.0)	226 (20.5)	1.18 (0.81, 1.70)	1.17 (0.83, 1.65)	65 (14.7)	273 (21.6)	0.76 (0.53, 1.10)	0.79 (0.56, 1.10)
C:C	13 (4.0)	35 (3.2)	1.59 (0.75, 3.41)	1.37 (0.75, 2.50)	16 (3.6)	30 (2.4)	1.59 (0.76, 3.29)	1.36 (0.75, 2.46)
Log-Additive			1.22 (0.92, 1.61)	1.23 (0.94, 1.60)			0.96 (0.73, 1.26)	0.97 (0.74, 1.26)
Dominant			1.23 (0.87, 1.74)	1.24 (0.90, 1.71)			0.86 (0.61, 1.19)	0.87 (0.64, 1.20)
Recessive			1.54 (0.72, 3.27)	1.34 (0.74, 2.45)			1.67 (0.81, 3.46)	1.40 (0.77, 2.53)

PLCE1 (rs3781264)								
T:T	203 (63.2)	733 (66.6)	1.00	1.00	263 (59.5)	787 (62.3)	1.00	1.00
C:T	58 (18.1)	236 (21.5)	0.84 (0.57, 1.23)	0.87 (0.61, 1.23)	99 (22.4)	297 (23.5)	1.08 (0.78, 1.48)	1.04 (0.77, 1.40)
C:C	7 (2.2)	19 (1.7)	1.33 (0.50, 3.58)	1.14 (0.56, 2.31)	15 (3.4)	31 (2.5)	1.60 (0.79, 3.23)	1.36 (0.76, 2.43)
Log-Additive			0.93 (0.68, 1.29)	0.94 (0.70, 1.28)			1.16 (0.90, 1.49)	1.13 (0.88, 1.44)
Dominant			0.88 (0.61, 1.27)	0.90 (0.64, 1.26)			1.13 (0.84, 1.54)	1.10 (0.82, 1.47)
Recessive			1.39 (0.52, 3.71)	1.16 (0.57, 2.35)			1.57 (0.78, 3.15)	1.35 (0.76, 2.41)
CLPTM1L (rs401681)								
C:C	130 (40.5)	464 (42.2)	1.00	1.00	182 (41.2)	537 (42.5)	1.00	1.00
C:T	101 (31.5)	442 (40.2)	0.76 (0.54, 1.06)	0.78 (0.57, 1.07)	145 (32.8)	479 (37.9)	0.88 (0.66, 1.19)	0.88 (0.66, 1.17)
T:T	34 (10.6)	115 (10.5)	1.09 (0.65, 1.82)	1.09 (0.69, 1.71)	47 (10.6)	128 (10.1)	1.14 (0.73, 1.78)	1.13 (0.75, 1.68)
Log-Additive			0.93 (0.73, 1.18)	0.94 (0.75, 1.19)			1.01 (0.82, 1.24)	1.01 (0.82, 1.23)
Dominant			0.82 (0.60, 1.12)	0.84 (0.62, 1.13)			0.94 (0.71, 1.24)	0.93 (0.72, 1.22)
Recessive			1.24 (0.75, 2.03)	1.19 (0.77, 1.85)			1.21 (0.79, 1.85)	1.18 (0.80, 1.75)
GKN2 -GKN1 (rs4254535)								
T:T	150 (46.7)	589 (53.5)	1.00	1.00	219 (49.5)	659 (52.1)	1.00	1.00
C:T	86 (26.8)	368 (33.5)	0.92 (0.65, 1.30)	0.94 (0.69, 1.29)	120 (27.1)	417 (33.0)	0.85 (0.62, 1.15)	0.86 (0.65, 1.15)
C:C	32 (10.0)	80 (7.3)	**1.78 (1.07, 2.98)**	**1.63 (1.04, 2.58)**	32 (7.2)	99 (7.8)	1.02 (0.62, 1.69)	0.97 (0.62, 1.52)
Log-Additive			1.18 (0.93, 1.49)	1.20 (0.96, 1.50)			0.94 (0.76, 1.17)	0.93 (0.75, 1.15)
Dominant			1.07 (0.78, 1.46)	1.10 (0.82, 1.48)			0.88 (0.66, 1.17)	0.88 (0.67, 1.15)
Recessive			**1.84 (1.12, 3.02)**	**1.66 (1.07, 2.60)**			1.08 (0.66, 1.78)	1.02 (0.65, 1.58)
CCR4 -GLB1 (rs4678680)								
T:T	257 (80.1)	948 (86.2)	1.00	1.00	347 (78.5)	1,067 (84.4)	1.00	1.00
G:T	27 (8.4)	111 (10.1)	1.00 (0.61, 1.64)	1.00 (0.65, 1.55)	45 (10.2)	137 (10.8)	0.99 (0.64, 1.54)	0.99 (0.66, 1.46)
G:G	3 (0.9)	4 (0.4)	1.68 (0.17, 16.50)	1.30 (0.53, 3.20)	5 (1.1)	7 (0.6)	2.25 (0.65, 7.79)	1.36 (0.62, 2.97)
Log-Additive			1.04 (0.65, 1.65)	1.11 (0.74, 1.67)			1.13 (0.78, 1.62)	1.11 (0.79, 1.56)
Dominant			1.02 (0.62, 1.66)	1.06 (0.69, 1.63)			1.07 (0.71, 1.62)	1.06 (0.72, 1.54)
Recessive			1.68 (0.17, 16.49)	1.30 (0.53, 3.20)			2.25 (0.65, 7.79)	1.36 (0.62, 2.98)
TERT -CLPTM1L (rs4975616)								
A:A	207 (64.5)	726 (66.0)	1.00	1.00	273 (61.8)	862 (68.2)	1.00	1.00
A:G	59 (18.4)	273 (24.8)	0.75 (0.52, 1.09)	0.77 (0.55, 1.08)	83 (18.8)	287 (22.7)	1.14 (0.82, 1.58)	1.10 (0.81, 1.50)
G:G	10 (3.1)	33 (3.0)	1.47 (0.66, 3.26)	1.25 (0.66, 2.36)	21 (4.8)	34 (2.7)	1.72 (0.85, 3.45)	1.43 (0.80, 2.54)
Log-Additive			0.91 (0.68, 1.23)	0.91 (0.69, 1.21)			1.21 (0.94, 1.56)	1.19 (0.93, 1.52)
Dominant			0.82 (0.58, 1.16)	0.83 (0.60, 1.15)			1.21 (0.89, 1.64)	1.18 (0.88, 1.58)
Recessive			1.57 (0.71, 3.49)	1.30 (0.69, 2.45)			1.66 (0.83, 3.32)	1.40 (0.79, 2.49)
CHEK2 (rs738722)								
C:C	126 (39.3)	561 (51.0)	1.00	1.00	197 (44.6)	641 (50.7)	1.00	1.00

C:T	102 (31.8)	380 (34.5)	1.17 (0.83, 1.64)	1.09 (0.79, 1.49)	140 (31.7)	416 (32.9)	1.21 (0.90, 1.64)	1.18 (0.89, 1.57)
T:T	34 (10.6)	79 (7.2)	**2.20 (1.30, 3.70)**	**1.82 (1.14, 2.89)**	37 (8.4)	98 (7.8)	1.13 (0.70, 1.83)	1.11 (0.72, 1.70)
Log-Additive			**1.37 (1.08, 1.73)**	**1.32 (1.05, 1.67)**			1.11 (0.90, 1.37)	1.11 (0.91, 1.36)
Dominant			1.32 (0.97, 1.82)	1.26 (0.94, 1.70)			1.20 (0.90, 1.58)	1.18 (0.90, 1.54)
Recessive			**2.06 (1.25, 3.39)**	**1.76 (1.12, 2.77)**			1.05 (0.66, 1.66)	1.05 (0.69, 1.59)
TGM5 (rs748404)								
T:T	244 (76.0)	948 (86.2)	1.00	1.00	342 (77.4)	1,051 (83.1)	1.00	1.00
C:T	25 (7.8)	93 (8.5)	1.01 (0.59, 1.73)	1.00 (0.62, 1.60)	30 (6.8)	119 (9.4)	0.90 (0.56, 1.44)	0.90 (0.59, 1.37)
C:C	0	3 (0.3)	NA	0.80 (0.32, 2.01)	6 (1.4)	9 (0.7)	1.11 (0.25, 4.92)	1.04 (0.46, 2.35)
Log-Additive			0.89 (0.53, 1.49)	0.90 (0.57, 1.41)			0.94 (0.63, 1.41)	0.93 (0.64, 1.35)
Dominant			0.95 (0.56, 1.62)	0.94 (0.59, 1.51)			0.92 (0.58, 1.44)	0.91 (0.61, 1.37)
Recessive			NA	0.80 (0.32, 2.01)			1.12 (0.25, 4.96)	1.04 (0.46, 2.36)
IL1RAP (rs7626795)								
A:A	190 (59.2)	679 (61.7)	1.00	1.00	257 (58.1)	784 (62.0)	1.00	1.00
A:G	78 (24.3)	313 (28.5)	0.80 (0.57, 1.14)	0.84 (0.61, 1.16)	102 (23.1)	342 (27.1)	1.00 (0.73, 1.36)	0.99 (0.73, 1.32)
G:G	13 (4.0)	46 (4.2)	0.66 (0.31, 1.44)	0.76 (0.42, 1.38)	19 (4.3)	54 (4.3)	1.05 (0.55, 1.98)	1.09 (0.64, 1.85)
Log-Additive			0.81 (0.61, 1.06)	0.82 (0.63, 1.07)			1.01 (0.80, 1.28)	1.02 (0.81, 1.29)
Dominant			0.78 (0.56, 1.09)	0.81 (0.59, 1.11)			1.01 (0.75, 1.35)	1.01 (0.76, 1.33)
Recessive			0.71 (0.33, 1.53)	0.79 (0.44, 1.43)			1.05 (0.56, 1.97)	1.09 (0.65, 1.85)
CHRNA3 (rs8042374)								
G:G	144 (44.9)	512 (46.5)	1.00	1.00	185 (41.9)	574 (45.4)	1.00	1.00
A:G	100 (31.2)	414 (37.6)	0.81 (0.58, 1.14)	0.85 (0.62, 1.16)	134 (30.3)	470 (37.2)	0.81 (0.60, 1.10)	0.81 (0.61, 1.08)
A:A	20 (6.2)	84 (7.6)	0.81 (0.44, 1.50)	0.85 (0.51, 1.43)	47 (10.6)	104 (8.2)	**1.77 (1.12, 2.80)**	1.51 (1.00, 2.29)
Log-Additive			0.86 (0.67, 1.11)	0.87 (0.68, 1.11)			1.13 (0.91, 1.40)	1.09 (0.89, 1.34)
Dominant			0.81 (0.59, 1.12)	0.84 (0.62, 1.13)			0.96 (0.72, 1.27)	0.95 (0.72, 1.24)
Recessive			0.89 (0.49, 1.62)	0.89 (0.54, 1.49)			**1.93 (1.24, 3.00)**	**1.63 (1.09, 2.44)**
FTO (rs8050136)								
C:C	206 (64.2)	831 (75.5)	1.00	1.00	294 (66.5)	935 (74.0)	1.00	1.00
A:C	62 (19.3)	203 (18.5)	1.28 (0.88, 1.87)	1.30 (0.92, 1.84)	83 (18.8)	219 (17.3)	1.24 (0.87, 1.76)	1.17 (0.85, 1.63)
A:A	3 (0.9)	18 (1.6)	0.42 (0.09, 2.04)	0.76 (0.35, 1.67)	2 (0.5)	31 (2.5)	**0.11 (0.01, 0.84)**	0.50 (0.24, 1.06)
Log-Additive			1.09 (0.78, 1.52)	1.12 (0.82, 1.53)			0.93 (0.69, 1.25)	0.91 (0.68, 1.21)
Dominant			1.20 (0.83, 1.73)	1.22 (0.86, 1.71)			1.07 (0.76, 1.50)	1.02 (0.74, 1.40)
Recessive			0.40 (0.08, 1.94)	0.75 (0.34, 1.64)			**0.11 (0.01, 0.81)**	0.50 (0.24, 1.04)
ZBTB12-C2 (rs9267673)								
C:C	201 (62.6)	740 (67.3)	1.00	1.00	256 (57.9)	845 (66.9)	1.00	1.00
C:T	60 (18.7)	278 (25.3)	0.74 (0.51, 1.08)	0.76 (0.54, 1.06)	98 (22.2)	285 (22.5)	1.05 (0.76, 1.46)	1.01 (0.74, 1.37)
T:T	16 (5.0)	23 (2.1)	**2.68 (1.23, 5.81)**	**1.97 (1.06, 3.65)**	19 (4.3)	45 (3.6)	1.26 (0.64, 2.50)	1.15 (0.65, 2.01)
Log-Additive			1.04 (0.77, 1.39)	1.06 (0.80, 1.40)			1.09 (0.84, 1.39)	1.05 (0.83, 1.34)

Dominant			0.88 (0.62, 1.24)	0.90 (0.65, 1.25)			1.08 (0.80, 1.47)	1.04 (0.78, 1.39)
Recessive			**2.88 (1.33, 6.21)**	**2.05 (1.10, 3.80)**			1.24 (0.63, 2.45)	1.14 (0.65, 2.00)
HLA-DQB1- HLA-DQA2 (rs9275572)								
G:G	143 (44.5)	537 (48.8)	1.00	1.00	194 (43.9)	628 (49.7)	1.00	1.00
A:G	94 (29.3)	409 (37.2)	0.84 (0.59, 1.18)	0.88 (0.64, 1.21)	137 (31.0)	436 (34.5)	0.88 (0.65, 1.20)	0.90 (0.67, 1.19)
A:A	25 (7.8)	92 (8.4)	1.34 (0.79, 2.27)	1.26 (0.79, 2.02)	40 (9.0)	114 (9.0)	1.04 (0.65, 1.67)	1.03 (0.68, 1.58)
Log-Additive			1.03 (0.81, 1.31)	1.04 (0.83, 1.32)			0.97 (0.79, 1.20)	0.97 (0.79, 1.19)
Dominant			0.92 (0.67, 1.27)	0.96 (0.71, 1.29)			0.92 (0.69, 1.21)	0.92 (0.71, 1.21)
Recessive			1.44 (0.86, 2.41)	1.32 (0.83, 2.09)			1.09 (0.69, 1.73)	1.07 (0.71, 1.62)
SEMA5B (rs9868873)								
G:G	186 (57.9)	687 (62.5)	1.00	1.00	259 (58.6)	801 (63.4)	1.00	1.00
A:G	75 (23.4)	329 (29.9)	0.77 (0.55, 1.09)	0.81 (0.59, 1.11)	92 (20.8)	326 (25.8)	0.89 (0.65, 1.24)	0.93 (0.68, 1.26)
A:A	18 (5.6)	32 (2.9)	1.87 (0.91, 3.83)	1.52 (0.85, 2.72)	29 (6.6)	57 (4.5)	1.59 (0.91, 2.77)	1.44 (0.88, 2.34)
Log-Additive			0.99 (0.76, 1.30)	1.01 (0.78, 1.31)			1.09 (0.86, 1.37)	1.10 (0.88, 1.38)
Dominant			0.87 (0.63, 1.20)	0.90 (0.67, 1.22)			1.00 (0.74, 1.35)	1.03 (0.78, 1.37)
Recessive			2.02 (0.99, 4.11)	1.59 (0.89, 2.84)			1.64 (0.95, 2.84)	1.46 (0.90, 2.37)

Notes: aOR: adjusted odds ratios; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Ca: Cases; Co: Controls; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28 kg/m^2), and total energy intake (continuous, kcal/day).

Table 5.15. Associations between selected SNPs related to the HIF and Beta-carotene metabolism pathway and stomach cancer by dietary intake of total flavonoids

	Low Flavonoids				High Flavonoids			
dbSNP no.	Ca, n(%)	Co, n(%)	aOR*	sbOR*	Ca, n(%)	Co, n(%)	aOR*	sbOR*
HIF pathway								
HIF1A (rs2057482)								
C:C	173 (53.9)	644 (58.5)	1.00	1.00	266 (60.2)	790 (62.5)	1.00	1.00
T:C	100 (31.2)	341 (31.0)	1.07 (0.77, 1.49)	1.12 (0.82, 1.52)	116 (26.2)	324 (25.6)	1.01 (0.75, 1.37)	1.01 (0.76, 1.35)
T:T	12 (3.7)	48 (4.4)	1.11 (0.53, 2.34)	1.07 (0.59, 1.95)	18 (4.1)	52 (4.1)	0.87 (0.44, 1.73)	0.96 (0.55, 1.66)
Log-Additive			1.06 (0.82, 1.39)	1.09 (0.85, 1.41)			0.98 (0.77, 1.24)	0.99 (0.79, 1.25)
Dominant			1.08 (0.78, 1.48)	1.12 (0.83, 1.51)			0.99 (0.75, 1.32)	1.00 (0.76, 1.32)
Recessive			1.08 (0.52, 2.26)	1.04 (0.58, 1.89)			0.87 (0.44, 1.72)	0.95 (0.55, 1.65)
HIF1AN (rs2295778)								
C:C	154 (48.0)	576 (52.4)	1.00	1.00	217 (49.1)	614 (48.6)	1.00	1.00
C:G	110 (34.3)	337 (30.6)	1.17 (0.84, 1.63)	1.15 (0.84, 1.57)	145 (32.8)	383 (30.3)	1.12 (0.83, 1.53)	1.11 (0.83, 1.48)
G:G	15 (4.7)	56 (5.1)	1.19 (0.59, 2.38)	1.10 (0.62, 1.94)	20 (4.5)	71 (5.6)	0.85 (0.46, 1.57)	0.89 (0.53, 1.49)
Log-Additive			1.13 (0.87, 1.47)	1.12 (0.87, 1.43)			1.02 (0.80, 1.28)	1.01 (0.81, 1.27)
Dominant			1.17 (0.85, 1.61)	1.15 (0.85, 1.56)			1.08 (0.80, 1.45)	1.07 (0.81, 1.41)
Recessive			1.11 (0.56, 2.20)	1.06 (0.60, 1.85)			0.81 (0.44, 1.48)	0.86 (0.52, 1.43)
Beta-carotene metabolism related								
R267S (rs12934922)								
A:A	204 (63.6)	778 (70.7)	1.00	1.00	296 (67.0)	872 (69.0)	1.00	1.00
A:T	67 (20.9)	242 (22.0)	1.20 (0.84, 1.70)	1.14 (0.82, 1.59)	73 (16.5)	274 (21.7)	0.71 (0.50, 1.01)	0.75 (0.54, 1.05)
T:T	8 (2.5)	18 (1.6)	1.72 (0.62, 4.74)	1.27 (0.62, 2.62)	13 (2.9)	32 (2.5)	1.81 (0.88, 3.73)	1.48 (0.82, 2.68)
Log-Additive			1.23 (0.91, 1.67)	1.19 (0.89, 1.59)			0.94 (0.71, 1.23)	0.96 (0.74, 1.25)
Dominant			1.23 (0.87, 1.73)	1.18 (0.85, 1.63)			0.81 (0.59, 1.13)	0.85 (0.63, 1.16)
Recessive			1.64 (0.60, 4.51)	1.25 (0.61, 2.57)			1.95 (0.95, 4.00)	1.53 (0.85, 2.78)
A379V (rs7501331)								
C:C	215 (67.0)	774 (70.4)	1.00	1.00	309 (69.9)	916 (72.5)	1.00	1.00
C:T	53 (16.5)	247 (22.5)	0.84 (0.57, 1.23)	0.84 (0.59, 1.20)	64 (14.5)	249 (19.7)	0.78 (0.54, 1.12)	0.81 (0.58, 1.13)
T:T	13 (4.0)	28 (2.5)	2.08 (0.96, 4.50)	1.49 (0.81, 2.77)	12 (2.7)	35 (2.8)	1.14 (0.54, 2.40)	1.10 (0.61, 2.00)
Log-Additive			1.08 (0.80, 1.44)	1.04 (0.79, 1.38)			0.90 (0.68, 1.19)	0.91 (0.70, 1.19)
Dominant			0.96 (0.68, 1.37)	0.95 (0.68, 1.32)			0.83 (0.59, 1.16)	0.85 (0.62, 1.17)
Recessive			2.16 (1.00, 4.66)	1.53 (0.82, 2.83)			1.20 (0.57, 2.51)	1.13 (0.63, 2.05)

Notes: aOR: adjusted odds ratios; sbOR: adjusted odds ratios with semi-Bayes shrinkage method; Ca: Cases; Co: Controls; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28 kg/m^2), and total energy intake (continuous, kcal/day).

Table 5.16. Odds ratios for joint associations of dietary fatty acids (High vs. Low) and susceptibility variants with stomach cancer

	Traditional method			Semi-shrinkage method		
dbsnp no.	Low fatty acids OR (95%)*	High fatty acids OR (95%)*	Interaction	Low fatty acids OR (95%)*	High fatty acids OR (95%)*	Interaction
HEY1 (rs1046472)						
C:C	1.00	1.19 (0.89, 1.59)	RERI:0.05(-0.44,0.54)	1.00	1.25 (0.95, 1.63)	RERI:0.03(-0.46,0.51)
A:C+A:A	1.12 (0.82, 1.53)	1.36 (0.99, 1.86)	ROR:1.02(0.67,1.56)	1.14 (0.84, 1.55)	**1.41 (1.05, 1.89)**	ROR:0.99(0.67,1.48)
IL15 (rs10519613)						
C:A +A:A	1.00	**1.39 (1.04, 1.87)**	RERI: -0.22(-0.8,0.36)	1.00	**1.42 (1.08, 1.85)**	RERI: -0.19(-0.74,0.35)
C:C	1.29 (0.95, 1.77)	**1.47 (1.05, 2.04)**	ROR:0.81(0.53,1.25)	1.27 (0.93, 1.73)	**1.47 (1.08, 2.00)**	ROR:0.83(0.55,1.25)
miR-196a2 (rs11614913)						
T:T	1.00	**1.73 (1.17, 2.56)**	RERI: -0.65(-1.34,0.05)	1.00	**1.76 (1.21, 2.55)**	RERI: -0.55(-1.19,0.09)
C:T+C:C	1.17 (0.83, 1.64)	1.25 (0.87, 1.79)	**ROR:0.62(0.39,0.97)**	1.18 (0.85, 1.66)	1.33 (0.95, 1.86)	ROR:0.66(0.43,1.02)
WWOX (rs12828)						
G:G	1.00	1.24 (0.87, 1.77)	RERI: -0.02(-0.54,0.49)	1.00	1.25 (0.89, 1.76)	RERI:0.01(-0.48,0.5)
A:G+A:A	1.19 (0.87, 1.64)	1.41 (1.02, 1.96)	ROR:0.95(0.62,1.46)	1.20 (0.88, 1.64)	**1.46 (1.08, 1.99)**	ROR:0.98(0.65,1.47)
miR-300 (rs12894467)						
T:T	1.00	1.02 (0.75, 1.39)	RERI:0.47(-0.05,0.99)	1.00	1.10 (0.83, 1.47)	RERI:0.42(-0.11,0.94)
C:T+C:C	1.17 (0.85, 1.60)	**1.66 (1.19, 2.33)**	ROR:1.39(0.91,2.14)	1.23 (0.91, 1.68)	**1.78 (1.31, 2.42)**	ROR:1.28(0.85,1.92)
R267S (rs12934922)						
A:A	1.00	1.23 (0.94, 1.61)	RERI: -0.14(-0.66,0.38)	1.00	**1.29 (1.02, 1.65)**	RERI: -0.16(-0.66,0.35)
A:T+T:T	1.04 (0.73, 1.48)	1.13 (0.80, 1.59)	ROR:0.88(0.55,1.42)	1.06 (0.75, 1.50)	1.18 (0.86, 1.63)	ROR:0.87(0.56,1.36)
Oct4 (rs13409)						
C:T+T:T	1.00	1.11 (0.83, 1.48)	RERI:0.17(-0.3,0.64)	1.00	1.16 (0.89, 1.51)	RERI:0.2(-0.26,0.66)
C:C	1.03 (0.75, 1.41)	1.31 (0.95, 1.81)	ROR:1.15(0.75,1.76)	1.01 (0.74, 1.38)	**1.39 (1.03, 1.86)**	ROR:1.17(0.78,1.75)
Ran (rs14035)						
C:C	1.00	1.32 (0.99, 1.76)	RERI: -0.29(-0.84,0.26)	1.00	**1.35 (1.04, 1.75)**	RERI: -0.26(-0.77,0.26)
C:T+T:T	1.16 (0.84, 1.61)	1.19 (0.84, 1.69)	ROR:0.78(0.5,1.22)	1.14 (0.83, 1.57)	1.21 (0.87, 1.68)	ROR:0.80(0.52,1.22)
IKBKAP (rs1538660)						
C:T+T:T	1.00	1.20 (0.88, 1.65)	RERI: -0.11(-0.61,0.39)	1.00	1.24 (0.93, 1.66)	RERI: -0.05(-0.52,0.42)
C:C	1.20 (0.89, 1.63)	1.30 (0.95, 1.78)	ROR:0.9(0.59,1.35)	1.15 (0.86, 1.55)	1.33 (1.00, 1.78)	ROR:0.94(0.64,1.39)
CXCL12 (rs1804429)						
T:T	1.00	1.21 (0.94, 1.56)	RERI: -0.39(-1.03,0.24)	1.00	1.24 (0.99, 1.55)	RERI: -0.28(-0.83,0.28)
T:C+C:C	1.00 (0.64, 1.58)	0.82 (0.49, 1.35)	ROR:0.67(0.35,1.30)	0.94 (0.60, 1.48)	0.85 (0.53, 1.37)	ROR:0.77(0.43,1.39)
Gemin3 (rs197412)						
T:T	1.00	1.32 (0.95, 1.83)	RERI: -0.25(-0.74,0.24)	1.00	**1.41 (1.04, 1.91)**	RERI: -0.24(-0.72,0.23)
T:C+C:C	1.00 (0.74, 1.36)	1.07 (0.78, 1.48)	ROR:0.81(0.53,1.23)	1.01 (0.75, 1.36)	1.15 (0.85, 1.55)	ROR:0.82(0.56,1.22)
AXIN1 (rs1981492)						
A:G+A:A	1.00	1.20 (0.87, 1.67)	RERI:0.14(-0.35,0.63)	1.00	1.22 (0.90, 1.65)	RERI:0.17(-0.3,0.64)
G:G	1.18 (0.87, 1.60)	**1.52 (1.11, 2.08)**	ROR:1.07(0.71,1.62)	1.14 (0.85, 1.54)	**1.54 (1.15, 2.06)**	ROR:1.10(0.74,1.62)
RUNX1 (rs2014300)						
A:G+A:A	1.00	1.30 (0.83, 2.04)	RERI: -0.14(-0.73,0.44)	1.00	1.38 (0.90, 2.13)	RERI: -0.15(-0.72,0.41)
G:G	1.03 (0.72, 1.47)	1.18 (0.81, 1.72)	ROR:0.89(0.54,1.45)	1.02 (0.71, 1.46)	1.23 (0.86, 1.76)	ROR:0.89(0.56,1.40)

HIF1A (rs2057482)						
T:C+T:T	1.00	1.42 (0.99, 2.03)	RERI: -0.19(-0.72,0.34)	1.00	**1.41 (1.00, 1.98)**	RERI: -0.12(-0.60,0.37)
C:C	1.06 (0.77, 1.45)	1.28 (0.92, 1.78)	ROR:0.85(0.56,1.31)	0.99 (0.73, 1.35)	1.27 (0.94, 1.72)	ROR:0.92(0.62,1.37)
E2F2 (rs2075993)						
G:A+A:A	1.00	1.14 (0.84, 1.54)	RERI:0.17(-0.34,0.68)	1.00	1.19 (0.90, 1.57)	RERI:0.17(-0.33,0.67)
G:G	1.20 (0.89, 1.64)	**1.51 (1.09, 2.10)**	ROR:1.10(0.73,1.68)	1.21 (0.89, 1.64)	**1.58 (1.17, 2.14)**	ROR:1.09(0.73,1.62)
DVL2 (rs222851)						
A:A	1.00	1.13 (0.79, 1.61)	RERI:0.09(-0.37,0.55)	1.00	1.18 (0.84, 1.65)	RERI:0.08(-0.37,0.53)
A:G+G:G	1.06 (0.77, 1.45)	1.28 (0.92, 1.78)	ROR:1.07(0.70,1.64)	1.07 (0.78, 1.46)	1.34 (0.98, 1.82)	ROR:1.05(0.70,1.58)
IKBKAP (rs2230793)						
A:A	1.00	1.27 (0.92, 1.75)	RERI: -0.10(-0.57,0.38)	1.00	**1.34 (1.00, 1.80)**	RERI: -0.12(-0.58,0.34)
A:C+C:C	1.04 (0.77, 1.40)	1.21 (0.88, 1.67)	ROR:0.92(0.61,1.39)	1.05 (0.78, 1.42)	1.27 (0.94, 1.70)	ROR:0.90(0.61,1.33)
FZD3 (rs2241802)						
A:G+A:A	1.00	1.28 (0.95, 1.72)	RERI: -0.22(-0.76,0.32)	1.00	1.28 (0.98, 1.68)	RERI: -0.20(-0.71,0.30)
G:G	1.14 (0.82, 1.59)	1.19 (0.85, 1.67)	ROR:0.82(0.52,1.29)	1.14 (0.83, 1.59)	1.20 (0.87, 1.65)	ROR:0.83(0.54,1.28)
Dec1 (rs2269700)						
T:T	1.00	1.28 (0.97, 1.68)	RERI: -0.35(-0.84,0.15)	1.00	**1.37 (1.07, 1.76)**	RERI: -0.32(-0.79,0.16)
C:T+C:C	1.03 (0.74, 1.42)	0.96 (0.68, 1.35)	ROR:0.73(0.47,1.14)	1.01 (0.73, 1.40)	1.04 (0.76, 1.42)	ROR:0.77(0.50,1.17)
PLCE1 (rs2274223)						
A:A	1.00	0.99 (0.72, 1.36)	RERI:0.30(-0.20,0.80)	1.00	1.03 (0.77, 1.38)	RERI:0.26(-0.23,0.74)
A:G+G:G	1.11 (0.80, 1.54)	1.40 (0.99, 1.96)	ROR:1.28(0.81,2.00)	1.13 (0.82, 1.57)	**1.44 (1.06, 1.98)**	ROR:1.21(0.79,1.85)
THBS1 (rs2292305)						
C:T+C:C	1.00	1.27 (0.93, 1.75)	RERI: -0.18(-0.69,0.33)	1.00	**1.37 (1.02, 1.84)**	RERI: -0.18(-0.70,0.33)
T:T	1.16 (0.85, 1.58)	1.25 (0.91, 1.72)	ROR:0.85(0.56,1.29)	1.22 (0.90, 1.66)	**1.38 (1.03, 1.86)**	ROR:0.84(0.56,1.26)
HIF1AN (rs2295778)						
C:C	1.00	1.21 (0.88, 1.67)	RERI:0.03(-0.47,0.53)	1.00	1.25 (0.93, 1.67)	RERI:0.06(-0.42,0.54)
C:G+G:G	1.11 (0.81, 1.52)	1.35 (0.97, 1.88)	ROR:1.01(0.65,1.55)	1.09 (0.80, 1.49)	**1.40 (1.03, 1.91)**	ROR:1.03(0.68,1.55)
GPC5 (rs2352028)						
C:T+T:T	1.00	1.22 (0.85, 1.76)	RERI:0.04(-0.44,0.51)	1.00	1.24 (0.88, 1.74)	RERI:0.05(-0.41,0.50)
C:C	1.07 (0.78, 1.47)	1.34 (0.96, 1.86)	ROR:1.02(0.67,1.55)	1.06 (0.78, 1.44)	1.34 (0.99, 1.83)	ROR:1.03(0.69,1.53)
TERT (rs2736100)						
G:T+G:G	1.00	**1.44 (1.06, 1.94)**	RERI: -0.68(-1.44,0.08)	1.00	**1.48 (1.12, 1.94)**	RERI: -0.59(-1.3,0.12)
T:T	**1.92 (1.39, 2.65)**	**1.68 (1.20, 2.34)**	**ROR:0.61(0.39,0.94)**	**1.92 (1.39, 2.64)**	**1.73 (1.27, 2.35)**	**ROR:0.64(0.42,0.97)**
CRPP1 -CRP (rs2808630)						
C:T+C:C	1.00	1.34 (0.87, 2.06)	RERI: -0.14(-0.72,0.44)	1.00	1.30 (0.86, 1.96)	RERI: -0.08(-0.60,0.44)
T:T	1.04 (0.73, 1.47)	1.24 (0.85, 1.79)	ROR:0.89(0.55,1.43)	0.99 (0.70, 1.40)	1.20 (0.85, 1.69)	ROR:0.94(0.60,1.47)
pre-miR-146a (rs2910164)						
C:C	1.00	1.23 (0.84, 1.79)	RERI: -0.02(-0.52,0.49)	1.00	1.25 (0.88, 1.78)	RERI:0.02(-0.45,0.50)
G:C+G:G	1.10 (0.80, 1.51)	1.32 (0.94, 1.84)	ROR:0.97(0.63,1.50)	1.09 (0.80, 1.49)	**1.37 (1.00, 1.86)**	ROR:1.00(0.66,1.51)
CTNNB1 (rs2953)						
G:T+G:G	1.00	1.09 (0.77, 1.54)	RERI:0.26(-0.19,0.71)	1.00	1.09 (0.79, 1.50)	RERI:0.23(-0.19,0.66)
T:T	1.05 (0.77, 1.43)	**1.40 (1.01, 1.94)**	ROR:1.22(0.80,1.86)	1.03 (0.76, 1.40)	**1.37 (1.01, 1.86)**	ROR:1.20(0.81,1.79)
Oct4 (rs3130932)						
T:T	1.00	1.28 (0.93, 1.75)	RERI: -0.26(-0.73,0.21)	1.00	**1.40 (1.05, 1.87)**	RERI: -0.30(-0.76,0.17)

G:T+G:G	1.01 (0.75, 1.36)	1.03 (0.75, 1.41)	ROR:0.80(0.53,1.20)	1.02 (0.76, 1.37)	1.10 (0.82, 1.47)	ROR:0.79(0.53,1.16)
IKBKAP (rs3204145)						
A:T+A:A	1.00	1.22 (0.90, 1.67)	RERI:0.06(-0.43,0.55)	1.00	1.23 (0.92, 1.65)	RERI:0.09(-0.37,0.55)
T:T	1.16 (0.86, 1.57)	**1.44 (1.06, 1.97)**	ROR:1.01(0.67,1.52)	1.13 (0.84, 1.52)	**1.46 (1.10, 1.94)**	ROR:1.04(0.71,1.54)
WNT2 (rs3729629)						
C:G+C:C	1.00	1.32 (0.97, 1.81)	RERI: -0.15(-0.68,0.39)	1.00	**1.34 (1.01, 1.79)**	RERI: -0.11(-0.62,0.40)
G:G	1.30 (0.96, 1.76)	**1.47 (1.07, 2.03)**	ROR:0.86(0.57,1.29)	1.27 (0.94, 1.71)	**1.49 (1.11, 2.00)**	ROR:0.88(0.60,1.30)
HEY2 (rs3734637)						
A:C+C:C	1.00	1.17 (0.82, 1.68)	RERI: -0.07(-0.57,0.42)	1.00	1.22 (0.87, 1.71)	RERI: -0.07(-0.55,0.41)
A:A	1.17 (0.86, 1.60)	1.28 (0.92, 1.78)	ROR:0.93(0.60,1.42)	1.17 (0.86, 1.59)	1.31 (0.97, 1.78)	ROR:0.93(0.62,1.39)
Ctbp2 (rs3740535)						
G:G	1.00	1.32 (0.97, 1.79)	RERI: -0.23(-0.73,0.26)	1.00	**1.35 (1.02, 1.80)**	RERI: -0.23(-0.70,0.24)
A:G+A:A	1.06 (0.79, 1.44)	1.15 (0.83, 1.58)	ROR:0.82(0.54,1.24)	1.08 (0.80, 1.45)	1.18 (0.88, 1.59)	ROR:0.82(0.56,1.22)
PLCE1 (rs3781264)						
C:T+C:C	1.00	1.41 (0.93, 2.14)	RERI: -0.21(-0.80,0.38)	1.00	1.40 (0.94, 2.08)	RERI: -0.16(-0.70,0.38)
T:T	1.06 (0.75, 1.51)	1.26 (0.87, 1.82)	ROR:0.84(0.53,1.34)	1.05 (0.75, 1.48)	1.28 (0.91, 1.80)	ROR:0.88(0.57,1.36)
DOCK4 (rs3801790)						
A:A	1.00	**1.46 (1.03, 2.09)**	RERI: -0.39(-0.94,0.16)	1.00	**1.50 (1.08, 2.10)**	RERI: -0.36(-0.89,0.17)
A:G+G:G	1.06 (0.77, 1.45)	1.13 (0.81, 1.58)	ROR:0.73(0.48,1.12)	1.08 (0.79, 1.47)	1.18 (0.87, 1.62)	ROR:0.75(0.50,1.12)
Rbl2 (rs3929)						
C:G+C:C	1.00	**1.53 (1.06, 2.20)**	RERI: -0.45(-1.04,0.13)	1.00	**1.56 (1.11, 2.21)**	RERI: -0.40(-0.96,0.15)
G:G	1.10 (0.81, 1.52)	1.18 (0.85, 1.64)	ROR:0.70(0.46,1.07)	1.11 (0.81, 1.52)	1.23 (0.90, 1.69)	ROR:0.73(0.49,1.09)
CLPTM1L (rs401681)						
C:C	1.00	1.29 (0.93, 1.79)	RERI: -0.28(-0.77,0.21)	1.00	**1.38 (1.02, 1.87)**	RERI: -0.28(-0.75,0.20)
C:T+T:T	1.02 (0.75, 1.38)	1.03 (0.74, 1.42)	ROR:0.78(0.52,1.19)	1.02 (0.75, 1.37)	1.10 (0.81, 1.49)	ROR:0.80(0.54,1.19)
IL6R (rs4072391)						
C:T+T:T	1.00	1.69 (1.00, 2.86)	RERI: -0.5(-1.36,0.36)	1.00	**1.78 (1.07, 2.96)**	RERI: -0.46(-1.24,0.33)
C:C	1.21 (0.79, 1.85)	1.40 (0.90, 2.17)	ROR:0.68(0.39,1.20)	1.24 (0.81, 1.89)	1.47 (0.97, 2.25)	ROR:0.71(0.42,1.18)
CDK6 (rs42031)						
A:A	1.00	**1.28 (1.00, 1.65)**	RERI:0.37(-0.54,1.28)	1.00	**1.31 (1.05, 1.63)**	RERI:0.32(-0.49,1.14)
A:T+T:T	1.05 (0.63, 1.75)	**1.70 (1.06, 2.73)**	ROR:1.26(0.64,2.49)	1.03 (0.62, 1.72)	**1.72 (1.10, 2.70)**	ROR:1.22(0.67,2.23)
GKN2 -GKN1 (rs4254535)						
T:T	1.00	**1.60 (1.18, 2.17)**	**RERI: -0.67(-1.27, -0.07)**	1.00	**1.65 (1.25, 2.18)**	**RERI:-0.65(-1.22, -0.08)**
C:T+C:C	1.27 (0.94, 1.73)	1.20 (0.87, 1.67)	**ROR:0.59(0.39,0.90)**	1.30 (0.96, 1.76)	1.24 (0.91, 1.67)	**ROR:0.60(0.40,0.90)**
CCR4 -GLB1 (rs4678680)						
T:T	1.00	**1.28 (1.00, 1.63)**	RERI: -0.10(-0.85,0.66)	1.00	**1.33 (1.07, 1.65)**	RERI: -0.04(-0.75,0.67)
G:T+G:G	1.12 (0.70, 1.80)	1.30 (0.84, 2.03)	ROR:0.91(0.48,1.71)	1.13 (0.71, 1.79)	1.40 (0.92, 2.14)	ROR:0.95(0.54,1.67)
WNT2 (rs4730775)						
C:T+T:T	1.00	1.20 (0.84, 1.71)	RERI:0.09(-0.41,0.59)	1.00	1.19 (0.85, 1.65)	RERI:0.14(-0.31,0.60)
C:C	1.18 (0.86, 1.61)	**1.46 (1.05, 2.03)**	ROR:1.04(0.68,1.59)	1.10 (0.81, 1.50)	**1.44 (1.06, 1.95)**	ROR:1.09(0.73,1.64)
WNT8A (rs4835761)						
A:G+G:G	1.00	1.26 (0.94, 1.69)	RERI: -0.18(-0.74,0.39)	1.00	**1.33 (1.01, 1.74)**	RERI: -0.18(-0.74,0.38)
A:A	1.36 (0.99, 1.87)	**1.45 (1.04, 2.01)**	ROR:0.84(0.55,1.29)	**1.40 (1.03, 1.91)**	**1.53 (1.13, 2.06)**	ROR:0.83(0.56,1.25)

Ago2 (rs4961280)						
C:A +A:A	1.00	1.30 (0.81, 2.09)	RERI: -0.09(-0.72,0.54)	1.00	1.37 (0.87, 2.16)	RERI: -0.07(-0.66,0.53)
C:C	1.30 (0.88, 1.91)	**1.51 (1.01, 2.26)**	ROR:0.90(0.54,1.50)	1.31 (0.89, 1.91)	**1.59 (1.09, 2.33)**	ROR:0.90(0.56,1.45)
TERT -CLPTM1L (rs4975616)						
A:G+G:G	1.00	1.45 (0.97, 2.19)	RERI: -0.31(-0.92,0.30)	1.00	**1.51 (1.02, 2.23)**	RERI: -0.31(-0.89,0.27)
A:A	1.13 (0.80, 1.59)	1.27 (0.88, 1.82)	ROR:0.77(0.49,1.22)	1.15 (0.82, 1.62)	1.32 (0.94, 1.85)	ROR:0.78(0.50,1.20)
Notch4 (rs520692)						
A:G+G:G	1.00	1.19 (0.77, 1.83)	RERI:0.08(-0.43,0.60)	1.00	1.17 (0.77, 1.77)	RERI:0.12(-0.36,0.60)
A:A	1.04 (0.73, 1.47)	1.31 (0.90, 1.89)	ROR:1.06(0.66,1.71)	1.01 (0.72, 1.43)	1.32 (0.93, 1.86)	ROR:1.10(0.70,1.72)
Rex1 (rs6815391)						
T:T	1.00	**1.45 (1.03, 2.05)**	RERI: -0.48(-1.05,0.10)	1.00	**1.55 (1.13, 2.13)**	RERI: -0.50(-1.06,0.05)
C:T+C:C	1.21 (0.88, 1.64)	1.18 (0.85, 1.65)	ROR:0.67(0.44,1.03)	1.22 (0.90, 1.66)	1.22 (0.90, 1.66)	ROR:0.67(0.45,1.00)
miR-26a1 (rs7372209)						
C:T+T:T	1.00	1.17 (0.85, 1.62)	RERI:0.15(-0.30,0.60)	1.00	1.24 (0.92, 1.68)	RERI:0.16(-0.30,0.62)
C:C	1.03 (0.76, 1.40)	1.36 (0.98, 1.87)	ROR:1.12(0.74,1.69)	1.08 (0.80, 1.46)	**1.50 (1.12, 2.01)**	ROR:1.10(0.74,1.63)
CHEK2 (rs738722)						
C:C	1.00	1.30 (0.95, 1.79)	RERI: -0.06(-0.61,0.49)	1.00	1.32 (0.98, 1.77)	RERI: -0.01(-0.52,0.51)
C:T+T:T	1.32 (0.97, 1.80)	**1.56 (1.13, 2.17)**	ROR:0.91(0.60,1.38)	1.27 (0.94, 1.72)	**1.57 (1.16, 2.13)**	ROR:0.95(0.64,1.40)
TGM5 (rs748404)						
T:T	1.00	1.25 (0.97, 1.60)	RERI: -0.19(-0.94,0.57)	1.00	**1.26 (1.01, 1.58)**	RERI: -0.10(-0.76,0.56)
C:T+C:C	1.05 (0.63, 1.75)	1.11 (0.68, 1.81)	ROR:0.85(0.43,1.70)	0.99 (0.59, 1.65)	1.13 (0.71, 1.81)	ROR:0.93(0.50,1.72)
A379V (rs7501331)						
C:T+T:T	1.00	1.33 (0.85, 2.08)	RERI: -0.09(-0.69,0.50)	1.00	1.41 (0.92, 2.17)	RERI: -0.09(-0.67,0.48)
C:C	1.16 (0.81, 1.67)	1.40 (0.97, 2.04)	ROR:0.91(0.56,1.47)	1.18 (0.83, 1.69)	**1.49 (1.05, 2.12)**	ROR:0.90(0.57,1.42)
IL1RAP (rs7626795)						
A:G+G:G	1.00	1.38 (0.94, 2.03)	RERI: -0.21(-0.78,0.36)	1.00	1.31 (0.91, 1.88)	RERI: -0.07(-0.57,0.43)
A:A	1.23 (0.89, 1.70)	1.40 (1.00, 1.97)	ROR:0.82(0.53,1.28)	1.16 (0.84, 1.59)	**1.39 (1.02, 1.90)**	ROR:0.92(0.61,1.39)
Gemin4 (rs7813)						
C:T+C:C	1.00	1.26 (0.91, 1.74)	RERI: -0.23(-0.72,0.26)	1.00	1.28 (0.95, 1.73)	RERI: -0.19(-0.65,0.27)
T:T	1.05 (0.77, 1.43)	1.08 (0.78, 1.50)	ROR:0.82(0.54,1.24)	1.03 (0.76, 1.40)	1.11 (0.82, 1.49)	ROR:0.85(0.57,1.26)
CHRNA3 (rs8042374)						
A:G+A:A	1.00	1.11 (0.80, 1.54)	RERI:0.10(-0.35,0.56)	1.00	1.19 (0.87, 1.61)	RERI:0.11(-0.34,0.56)
G:G	1.06 (0.78, 1.45)	1.27 (0.92, 1.77)	ROR:1.08(0.71,1.64)	1.07 (0.79, 1.46)	**1.38 (1.02, 1.86)**	ROR:1.08(0.72,1.60)
FTO (rs8050136)						
C:C	1.00	1.17 (0.90, 1.52)	RERI:0.14(-0.46,0.74)	1.00	1.23 (0.97, 1.55)	RERI:0.10(-0.47,0.68)
A:C+A:A	1.08 (0.75, 1.55)	1.39 (0.95, 2.02)	ROR:1.10(0.67,1.82)	1.09 (0.76, 1.56)	**1.43 (1.00, 2.04)**	ROR:1.06(0.66,1.69)
HES2 (rs8708)						
A:G+G:G	1.00	1.14 (0.76, 1.71)	RERI:0.03(-0.45,0.51)	1.00	1.21 (0.83, 1.77)	RERI:0.02(-0.46,0.49)
A:A	1.02 (0.73, 1.42)	1.19 (0.83, 1.69)	ROR:1.02(0.65,1.61)	1.03 (0.74, 1.44)	1.26 (0.90, 1.76)	ROR:1.01(0.66,1.55)
Notch4 (rs915894)						
A:C+A:A	1.00	1.29 (0.97, 1.71)	RERI: -0.30(-0.89,0.28)	1.00	**1.35 (1.05, 1.74)**	RERI: -0.26(-0.81,0.29)
C:C	1.33 (0.97, 1.84)	1.32 (0.94, 1.87)	ROR:0.77(0.49,1.20)	1.29 (0.94, 1.77)	1.35 (0.98, 1.86)	ROR:0.79(0.52,1.21)
KRAS (rs9266)						
C:T+T:T	1.00	1.30 (0.89, 1.90)	RERI: -0.04(-0.60,0.51)	1.00	1.33 (0.93, 1.91)	RERI:0.00(-0.52,0.51)

C:C	1.31 (0.95, 1.82)	**1.57 (1.11, 2.22)**	ROR:0.92(0.59,1.42)	1.28 (0.93, 1.76)	**1.60 (1.16, 2.20)**	ROR:0.94(0.63,1.43)
ZBTB12-C2 (rs9267673)						
C:T+T:T	1.00	1.34 (0.89, 2.01)	RERI: -0.19(-0.76,0.37)	1.00	1.40 (0.95, 2.06)	RERI: -0.18(-0.72,0.36)
C:C	1.12 (0.80, 1.56)	1.26 (0.89, 1.79)	ROR:0.84(0.54,1.33)	1.14 (0.82, 1.58)	1.34 (0.96, 1.85)	ROR:0.85(0.56,1.31)
HLA-DQB1- HLA-DQA2 (rs9275572)						
G:G	1.00	1.32 (0.96, 1.80)	RERI: -0.23(-0.72,0.26)	1.00	**1.38 (1.03, 1.84)**	RERI: -0.22(-0.70,0.25)
A:G+A:A	1.04 (0.76, 1.41)	1.13 (0.81, 1.56)	ROR:0.82(0.54,1.25)	1.06 (0.78, 1.43)	1.19 (0.88, 1.61)	ROR:0.83(0.56,1.24)
SEMA5B (rs9868873)						
A:G+A:A	1.00	1.43 (0.98, 2.08)	RERI: -0.26(-0.84,0.32)	1.00	1.41 (0.98, 2.02)	RERI: -0.19(-0.71,0.33)
G:G	1.20 (0.86, 1.66)	1.37 (0.97, 1.93)	ROR:0.80(0.52,1.24)	1.14 (0.83, 1.57)	1.34 (0.97, 1.85)	ROR:0.85(0.56,1.28)

Note: Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28 kg/m^2), and total energy intake (continuous, kcal/day).

Table 5.17. Odds ratios for joint associations of dietary cholesterol (High vs. Low) and susceptibility variants with stomach cancer

	Traditional method			Semi-shrinkage method		
dbsnp no.	Low Cholesterol OR (95%)*	High Cholesterol OR (95%)*	Interaction	Low Cholesterol OR (95%)*	High Cholesterol OR (95%)*	Interaction
HEY1 (rs1046472)						
C:C	1.00	1.09 (0.82, 1.44)	RERI:0.11(-0.37,0.58)	1.00	1.16 (0.88, 1.51)	RERI:0.10(-0.37,0.57)
A:C+A:A	1.10 (0.82, 1.47)	1.29 (0.94, 1.76)	ROR:1.08(0.71,1.65)	1.10 (0.83, 1.48)	**1.37 (1.01, 1.85)**	ROR:1.07(0.71,1.59)
IL15 (rs10519613)						
C:A +A:A	1.00	1.16 (0.87, 1.53)	RERI:0.09(-0.41,0.60)	1.00	1.22 (0.93, 1.60)	RERI:0.09(-0.40,0.58)
C:C	1.12 (0.84, 1.51)	1.37 (1.00, 1.88)	ROR:1.06(0.69,1.62)	1.11 (0.83, 1.49)	**1.42 (1.05, 1.94)**	ROR:1.05(0.70,1.57)
miR-196a2 (rs11614913)						
T:T	1.00	1.45 (0.99, 2.12)	RERI: -0.38(-0.97,0.20)	1.00	**1.53 (1.06, 2.23)**	RERI: -0.35(-0.92,0.22)
C:T+C:C	1.04 (0.76, 1.42)	1.11 (0.79, 1.55)	ROR:0.73(0.47,1.15)	1.06 (0.78, 1.45)	1.21 (0.87, 1.68)	ROR:0.76(0.50,1.16)
WWOX (rs12828)						
G:G	1.00	1.14 (0.81, 1.62)	RERI:0.06(-0.43,0.55)	1.00	1.18 (0.84, 1.67)	RERI:0.09(-0.39,0.56)
A:G+A:A	1.16 (0.86, 1.55)	1.36 (0.99, 1.86)	ROR:1.03(0.67,1.58)	1.17 (0.87, 1.56)	**1.44 (1.06, 1.96)**	ROR:1.04(0.69,1.56)
miR-300 (rs12894467)						
T:T	1.00	0.95 (0.70, 1.28)	RERI:0.47(-0.04,0.98)	1.00	1.03 (0.77, 1.37)	RERI:0.47(-0.05,0.99)
C:T+C:C	1.17 (0.87, 1.58)	**1.59 (1.15, 2.20)**	ROR:1.43(0.93,2.20)	1.21 (0.90, 1.63)	**1.74 (1.28, 2.37)**	ROR:1.36(0.91,2.04)
R267S (rs12934922)						
A:A	1.00	**1.44 (1.12, 1.86)**	**RERI: -0.86(-1.47, -0.25)**	1.00	**1.53 (1.20, 1.96)**	**RERI: -0.81(-1.39, -0.22)**
A:T+T:T	1.37 (1.00, 1.86)	0.94 (0.65, 1.37)	**ROR:0.48(0.30,0.77)**	**1.39 (1.02, 1.89)**	1.01 (0.70, 1.45)	**ROR:0.51(0.33,0.80)**
Oct4 (rs13409)						
C:C	1.00	**1.48 (1.04, 2.10)**	RERI: -0.49(-1.06,0.09)	1.00	**1.61 (1.14, 2.27)**	RERI: -0.50(-1.07,0.07)
C:T+T:T	1.09 (0.81, 1.46)	1.08 (0.78, 1.48)	ROR:0.67(0.44,1.03)	1.11 (0.82, 1.49)	1.17 (0.86, 1.59)	ROR:0.68(0.45,1.02)
Ran (rs14035)						
C:C	1.00	1.21 (0.92, 1.59)	RERI: -0.12(-0.63,0.39)	1.00	1.27 (0.97, 1.64)	RERI: -0.10(-0.59,0.40)
C:T+T:T	1.07 (0.79, 1.45)	1.16 (0.83, 1.63)	ROR:0.90(0.57,1.40)	1.05 (0.78, 1.42)	1.21 (0.87, 1.68)	ROR:0.92(0.60,1.40)
IKBKAP (rs1538660)						
C:T+T:T	1.00	1.30 (0.96, 1.75)	RERI: -0.36(-0.89,0.18)	1.00	**1.37 (1.02, 1.84)**	RERI: -0.30(-0.82,0.21)
C:C	1.31 (0.99, 1.75)	1.25 (0.92, 1.71)	ROR:0.74(0.49,1.11)	1.28 (0.96, 1.70)	1.31 (0.98, 1.77)	ROR:0.77(0.52,1.14)
CXCL12 (rs1804429)						
T:C+C:C	1.00	1.47 (0.78, 2.76)	RERI: -0.34(-1.27,0.59)	1.00	1.64 (0.88, 3.06)	RERI: -0.33(-1.19,0.53)
T:T	1.41 (0.88, 2.27)	1.54 (0.95, 2.51)	ROR:0.74(0.38,1.44)	1.49 (0.93, 2.40)	**1.71 (1.06, 2.76)**	ROR:0.74(0.41,1.34)
Gemin3 (rs197412)						
T:C+C:C	1.00	1.15 (0.86, 1.55)	RERI:0.00(-0.48,0.48)	1.00	1.25 (0.94, 1.66)	RERI:0.01(-0.47,0.48)
T:T	1.12 (0.84, 1.49)	1.28 (0.93, 1.74)	ROR:0.99(0.65,1.49)	1.12 (0.84, 1.49)	**1.37 (1.02, 1.86)**	ROR:0.98(0.66,1.45)
AXIN1 (rs1981492)						
A:G+A:A	1.00	1.17 (0.86, 1.61)	RERI:0.08(-0.41,0.57)	1.00	1.24 (0.92, 1.69)	RERI:0.09(-0.39,0.57)
G:G	1.21 (0.91, 1.61)	**1.47 (1.08, 1.99)**	ROR:1.03(0.68,1.55)	1.19 (0.90, 1.58)	**1.53 (1.14, 2.05)**	ROR:1.03(0.70,1.52)
RUNX1 (rs2014300)						
A:G+A:A	1.00	1.46 (0.94, 2.27)	RERI: -0.40(-1.08,0.27)	1.00	1.54 (1.00, 2.37)	RERI: -0.34(-0.97,0.28)
G:G	1.14 (0.80, 1.61)	1.19 (0.83, 1.72)	ROR:0.72(0.44,1.17)	1.11 (0.78, 1.56)	1.25 (0.88, 1.79)	ROR:0.76(0.48,1.20)

HIF1A (rs2057482)						
T:C+T:T	1.00	1.38 (0.97, 1.96)	RERI: -0.18(-0.70,0.34)	1.00	**1.44 (1.02, 2.02)**	RERI: -0.15(-0.65,0.35)
C:C	1.04 (0.78, 1.40)	1.24 (0.91, 1.70)	ROR:0.86(0.57,1.32)	1.00 (0.75, 1.35)	1.28 (0.95, 1.73)	ROR:0.90(0.60,1.34)
E2F2 (rs2075993)						
G:G	1.00	**1.56 (1.12, 2.18)**	**RERI: -0.63(-1.21, -0.05)**	1.00	**1.65 (1.19, 2.28)**	**RERI: -0.60(-1.16, -0.05)**
G:A+A:A	1.01 (0.75, 1.35)	0.94 (0.68, 1.28)	**ROR:0.59(0.39,0.91)**	1.00 (0.75, 1.34)	0.99 (0.73, 1.35)	**ROR:0.63(0.42,0.93)**
DVL2 (rs222851)						
A:A	1.00	1.24 (0.88, 1.75)	RERI: -0.21(-0.73,0.31)	1.00	1.32 (0.94, 1.85)	RERI: -0.20(-0.71,0.31)
A:G+G:G	1.21 (0.89, 1.63)	1.23 (0.90, 1.70)	ROR:0.83(0.54,1.27)	1.22 (0.90, 1.64)	1.32 (0.97, 1.81)	ROR:0.83(0.56,1.25)
IKBKAP (rs2230793)						
A:C+C:C	1.00	1.34 (0.99, 1.81)	RERI: -0.24(-0.75,0.26)	1.00	**1.40 (1.04, 1.87)**	RERI: -0.19(-0.67,0.3)
A:A	1.12 (0.84, 1.48)	1.21 (0.89, 1.63)	ROR:0.81(0.54,1.22)	1.09 (0.82, 1.45)	1.28 (0.96, 1.72)	ROR:0.85(0.58,1.26)
FZD3 (rs2241802)						
A:G+A:A	1.00	1.23 (0.92, 1.63)	RERI: -0.20(-0.72,0.32)	1.00	1.29 (0.99, 1.69)	RERI: -0.24(-0.75,0.27)
G:G	1.12 (0.82, 1.52)	1.15 (0.82, 1.61)	ROR:0.83(0.53,1.31)	1.15 (0.85, 1.56)	1.18 (0.85, 1.64)	ROR:0.81(0.53,1.23)
Dec1 (rs2269700)						
C:T+C:C	1.00	1.03 (0.70, 1.52)	RERI:0.25(-0.2,0.69)	1.00	1.10 (0.76, 1.60)	RERI:0.27(-0.17,0.71)
T:T	1.04 (0.76, 1.42)	1.32 (0.96, 1.83)	ROR:1.23(0.79,1.91)	1.03 (0.76, 1.41)	**1.43 (1.04, 1.96)**	ROR:1.22(0.8,1.86)
PLCE1 (rs2274223)						
A:A	1.00	1.05 (0.77, 1.43)	RERI:0.10(-0.43,0.62)	1.00	1.11 (0.83, 1.50)	RERI:0.07(-0.45,0.59)
A:G+G:G	1.22 (0.89, 1.67)	1.37 (0.98, 1.91)	ROR:1.07(0.68,1.67)	1.25 (0.91, 1.70)	**1.44 (1.04, 1.98)**	ROR:1.03(0.68,1.57)
THBS1 (rs2292305)						
C:T+C:C	1.00	**1.44 (1.06, 1.95)**	RERI: -0.56(-1.14,0.03)	1.00	**1.52 (1.13, 2.05)**	RERI: -0.48(-1.05,0.09)
T:T	1.32 (0.99, 1.77)	1.21 (0.87, 1.66)	**ROR:0.63(0.42,0.97)**	**1.36 (1.02, 1.82)**	1.35 (0.99, 1.84)	ROR:0.68(0.45,1.01)
HIF1AN (rs2295778)						
C:C	1.00	**1.48 (1.09, 1.99)**	RERI: -0.49(-1.09,0.12)	1.00	**1.53 (1.15, 2.05)**	RERI: -0.43(-1.01,0.14)
C:G+G:G	1.34 (1.00, 1.79)	1.33 (0.95, 1.84)	ROR:0.67(0.44,1.03)	1.33 (1.00, 1.78)	**1.38 (1.00, 1.90)**	ROR:0.70(0.47,1.05)
GPC5 (rs2352028)						
C:T+T:T	1.00	**1.56 (1.10, 2.21)**	RERI: -0.39(-0.99,0.21)	1.00	**1.60 (1.14, 2.26)**	RERI: -0.34(-0.91,0.23)
C:C	1.27 (0.94, 1.71)	**1.44 (1.05, 1.98)**	ROR:0.73(0.48,1.11)	1.25 (0.92, 1.68)	**1.48 (1.08, 2.01)**	ROR:0.76(0.51,1.13)
TERT (rs2736100)						
G:T+G:G	1.00	1.21 (0.91, 1.61)	RERI: -0.26(-0.90,0.39)	1.00	1.29 (0.98, 1.70)	RERI: -0.24(-0.87,0.39)
T:T	**1.63 (1.21, 2.20)**	**1.58 (1.14, 2.19)**	ROR:0.80(0.52,1.24)	**1.65 (1.23, 2.22)**	**1.67 (1.22, 2.30)**	ROR:0.80(0.53,1.21)
CRPP1 -CRP (rs2808630)						
T:T	1.00	**1.31 (1.01, 1.69)**	RERI: -0.45(-1.03,0.13)	1.00	**1.37 (1.07, 1.75)**	RERI: -0.44(-1.00,0.12)
C:T+C:C	1.23 (0.90, 1.70)	1.09 (0.75, 1.57)	ROR:0.67(0.42,1.09)	1.27 (0.92, 1.74)	1.14 (0.80, 1.64)	ROR:0.69(0.44,1.08)
pre-miR-146a (rs2910164)						
C:C	1.00	1.37 (0.96, 1.97)	RERI: -0.29(-0.87,0.28)	1.00	1.42 (1.00, 2.02)	RERI: -0.22(-0.76,0.32)
G:C+G:G	1.23 (0.91, 1.67)	1.31 (0.95, 1.82)	ROR:0.78(0.50,1.20)	1.22 (0.90, 1.65)	**1.39 (1.02, 1.91)**	ROR:0.82(0.54,1.24)
CTNNB1 (rs2953)						
G:T+G:G	1.00	1.06 (0.76, 1.47)	RERI:0.31(-0.13,0.75)	1.00	1.09 (0.79, 1.51)	RERI:0.29(-0.14,0.72)
T:T	1.03 (0.77, 1.38)	**1.40 (1.03, 1.90)**	ROR:1.28(0.84,1.95)	1.01 (0.76, 1.35)	**1.41 (1.05, 1.90)**	ROR:1.25(0.84,1.86)
Oct4 (rs3130932)						
G:T+G:G	1.00	1.12 (0.82, 1.51)	RERI:0.13(-0.32,0.58)	1.00	1.19 (0.89, 1.61)	RERI:0.17(-0.28,0.62)

T:T	1.07 (0.80, 1.42)	1.31 (0.96, 1.78)	ROR:1.10(0.73,1.66)	1.06 (0.80, 1.41)	**1.44 (1.07, 1.93)**	ROR:1.12(0.76,1.65)
IKBKAP (rs3204145)						
A:T+A:A	1.00	**1.38 (1.02, 1.87)**	RERI: -0.29(-0.85,0.26)	1.00	**1.45 (1.08, 1.94)**	RERI: -0.25(-0.78,0.28)
T:T	1.33 (1.00, 1.77)	**1.42 (1.05, 1.91)**	ROR:0.77(0.51,1.16)	1.30 (0.98, 1.73)	**1.47 (1.10, 1.97)**	ROR:0.80(0.54,1.17)
WNT2 (rs3729629)						
C:G+C:C	1.00	1.15 (0.85, 1.56)	RERI:0.02(-0.47,0.51)	1.00	1.22 (0.91, 1.63)	RERI:0.03(-0.44,0.51)
G:G	1.20 (0.90, 1.59)	**1.37 (1.01, 1.87)**	ROR:0.99(0.66,1.5)	1.18 (0.89, 1.57)	**1.43 (1.07, 1.93)**	ROR:1.00(0.67,1.47)
HEY2 (rs3734637)						
A:C+C:C	1.00	1.09 (0.77, 1.54)	RERI:0.09(-0.37,0.55)	1.00	1.16 (0.82, 1.62)	RERI:0.08(-0.38,0.53)
A:A	1.09 (0.81, 1.46)	1.27 (0.93, 1.74)	ROR:1.07(0.7,1.64)	1.09 (0.81, 1.46)	1.33 (0.98, 1.79)	ROR:1.05(0.7,1.57)
Ctbp2 (rs3740535)						
G:G	1.00	1.23 (0.92, 1.65)	RERI: -0.11(-0.58,0.35)	1.00	1.29 (0.97, 1.71)	RERI: -0.10(-0.55,0.35)
A:G+A:A	1.00 (0.75, 1.33)	1.11 (0.82, 1.52)	ROR:0.91(0.60,1.37)	1.00 (0.75, 1.33)	1.18 (0.88, 1.59)	ROR:0.93(0.62,1.37)
PLCE1 (rs3781264)						
C:T+C:C	1.00	1.27 (0.85, 1.90)	RERI: -0.11(-0.65,0.43)	1.00	1.30 (0.87, 1.92)	RERI: -0.07(-0.58,0.44)
T:T	1.01 (0.73, 1.40)	1.17 (0.83, 1.64)	ROR:0.91(0.57,1.45)	1.00 (0.73, 1.38)	1.22 (0.88, 1.70)	ROR:0.95(0.61,1.46)
DOCK4 (rs3801790)						
A:G+G:G	1.00	1.24 (0.94, 1.65)	RERI: -0.06(-0.58,0.45)	1.00	1.30 (1.00, 1.71)	RERI: -0.06(-0.55,0.44)
A:A	1.16 (0.87, 1.56)	1.34 (0.98, 1.85)	ROR:0.93(0.61,1.41)	1.14 (0.86, 1.53)	**1.39 (1.02, 1.88)**	ROR:0.93(0.63,1.39)
Rbl2 (rs3929)						
C:G+C:C	1.00	**1.47 (1.03, 2.10)**	RERI: -0.37(-0.93,0.19)	1.00	**1.56 (1.11, 2.21)**	RERI: -0.37(-0.92,0.18)
G:G	1.05 (0.78, 1.42)	1.16 (0.84, 1.59)	ROR:0.74(0.49,1.14)	1.08 (0.80, 1.46)	1.23 (0.90, 1.68)	ROR:0.75(0.50,1.12)
CLPTM1L (rs401681)						
C:T+T:T	1.00	1.03 (0.76, 1.40)	RERI:0.23(-0.20,0.67)	1.00	1.10 (0.82, 1.48)	RERI:0.24(-0.19,0.67)
C:C	1.02 (0.77, 1.36)	1.28 (0.94, 1.74)	ROR:1.22(0.81,1.84)	1.02 (0.76, 1.35)	**1.38 (1.02, 1.85)**	ROR:1.21(0.81,1.79)
IL6R (rs4072391)						
C:T+T:T	1.00	**1.68 (1.01, 2.82)**	RERI: -0.58(-1.45,0.30)	1.00	**1.80 (1.09, 2.98)**	RERI: -0.52(-1.32,0.28)
C:C	1.21 (0.82, 1.80)	1.32 (0.87, 1.98)	ROR:0.65(0.37,1.12)	1.23 (0.83, 1.81)	1.41 (0.95, 2.11)	ROR:0.68(0.41,1.13)
CDK6 (rs42031)						
A:T+T:T	1.00	1.65 (0.86, 3.17)	RERI: -0.49(-1.53,0.55)	1.00	1.87 (0.98, 3.55)	RERI: -0.51(-1.46,0.45)
A:A	1.01 (0.62, 1.64)	1.16 (0.71, 1.92)	ROR:0.70(0.36,1.38)	1.05 (0.64, 1.71)	1.28 (0.78, 2.09)	ROR:0.71(0.39,1.29)
GKN2 -GKN1 (rs4254535)						
T:T	1.00	1.32 (0.99, 1.76)	RERI: -0.36(-0.86,0.14)	1.00	**1.40 (1.06, 1.85)**	RERI: -0.35(-0.84,0.14)
C:T+C:C	1.12 (0.84, 1.49)	1.08 (0.79, 1.47)	ROR:0.73(0.48,1.11)	1.13 (0.85, 1.50)	1.14 (0.84, 1.55)	ROR:0.75(0.50,1.11)
CCR4 -GLB1 (rs4678680)						
G:T+G:G	1.00	1.59 (0.87, 2.91)	RERI: -0.32(-1.22,0.59)	1.00	1.74 (0.96, 3.13)	RERI: -0.32(-1.16,0.51)
T:T	1.06 (0.68, 1.66)	1.33 (0.84, 2.11)	ROR:0.79(0.42,1.49)	1.05 (0.67, 1.63)	1.40 (0.89, 2.19)	ROR:0.80(0.45,1.41)
WNT2 (rs4730775)						
C:T+T:T	1.00	1.04 (0.74, 1.47)	RERI:0.23(-0.22,0.68)	1.00	1.10 (0.79, 1.53)	RERI:0.23(-0.21,0.66)
C:C	1.10 (0.82, 1.47)	**1.37 (1.00, 1.87)**	ROR:1.20(0.79,1.84)	1.06 (0.79, 1.42)	**1.40 (1.04, 1.89)**	ROR:1.19(0.79,1.77)
WNT8A (rs4835761)						
A:G+G:G	1.00	1.27 (0.96, 1.68)	RERI: -0.26(-0.83,0.31)	1.00	**1.34 (1.02, 1.75)**	RERI: -0.22(-0.78,0.34)
A:A	**1.39 (1.03, 1.86)**	**1.39 (1.01, 1.92)**	ROR:0.79(0.52,1.22)	**1.41 (1.05, 1.89)**	**1.50 (1.10, 2.04)**	ROR:0.81(0.54,1.21)
Ago2 (rs4961280)						

C:A +A:A	1.00	0.98 (0.62, 1.57)	RERI:0.19(-0.31,0.69)	1.00	1.05 (0.67, 1.66)	RERI:0.20(-0.29,0.68)
C:C	1.13 (0.80, 1.60)	1.30 (0.91, 1.86)	ROR:1.17(0.70,1.95)	1.12 (0.80, 1.59)	1.39 (0.98, 1.98)	ROR:1.15(0.72,1.85)
TERT -CLPTM1L (rs4975616)						
A:G+G:G	1.00	**1.58 (1.06, 2.36)**	RERI: -0.50(-1.18,0.17)	1.00	**1.66 (1.12, 2.47)**	RERI: -0.46(-1.10,0.18)
A:A	1.21 (0.87, 1.69)	1.29 (0.90, 1.84)	ROR:0.67(0.42,1.07)	1.23 (0.88, 1.72)	1.37 (0.97, 1.94)	ROR:0.70(0.45,1.08)
Notch4 (rs520692)						
A:G+G:G	1.00	1.19 (0.78, 1.82)	RERI:0.07(-0.45,0.60)	1.00	1.23 (0.81, 1.86)	RERI:0.09(-0.41,0.60)
A:A	1.04 (0.75, 1.46)	1.31 (0.92, 1.85)	ROR:1.05(0.65,1.69)	1.04 (0.75, 1.44)	1.36 (0.97, 1.91)	ROR:1.07(0.68,1.67)
Rex1 (rs6815391)						
T:T	1.00	1.18 (0.85, 1.64)	RERI: -0.07(-0.53,0.39)	1.00	1.25 (0.91, 1.72)	RERI: -0.08(-0.53,0.38)
C:T+C:C	1.00 (0.75, 1.34)	1.11 (0.81, 1.52)	ROR:0.94(0.62,1.43)	1.00 (0.75, 1.33)	1.17 (0.86, 1.58)	ROR:0.94(0.63,1.40)
miR-26a1 (rs7372209)						
C:T+T:T	1.00	1.20 (0.88, 1.64)	RERI: -0.01(-0.48,0.47)	1.00	1.26 (0.93, 1.70)	RERI:0.08(-0.39,0.55)
C:C	1.11 (0.83, 1.47)	1.30 (0.96, 1.77)	ROR:0.98(0.65,1.47)	1.12 (0.84, 1.49)	**1.47 (1.09, 1.97)**	ROR:1.04(0.70,1.53)
CHEK2 (rs738722)						
C:C	1.00	1.33 (0.98, 1.80)	RERI: -0.26(-0.82,0.31)	1.00	**1.37 (1.02, 1.84)**	RERI: -0.16(-0.69,0.38)
C:T+T:T	**1.40 (1.05, 1.87)**	**1.47 (1.08, 2.02)**	ROR:0.79(0.52,1.20)	1.33 (1.00, 1.78)	**1.52 (1.12, 2.06)**	ROR:0.85(0.57,1.26)
TGM5 (rs748404)						
T:T	1.00	1.23 (0.97, 1.55)	RERI: -0.51(-1.28,0.25)	1.00	**1.28 (1.02, 1.61)**	RERI: -0.37(-1.05,0.30)
C:T+C:C	1.22 (0.75, 1.98)	0.93 (0.57, 1.53)	ROR:0.62(0.31,1.24)	1.16 (0.71, 1.88)	0.98 (0.60, 1.59)	ROR:0.71(0.39,1.32)
A379V (rs7501331)						
C:T+T:T	1.00	1.15 (0.74, 1.78)	RERI:0.05(-0.48,0.58)	1.00	1.21 (0.79, 1.86)	RERI:0.08(-0.43,0.59)
C:C	1.08 (0.78, 1.51)	1.29 (0.91, 1.82)	ROR:1.03(0.64,1.68)	1.08 (0.78, 1.50)	1.38 (0.99, 1.93)	ROR:1.05(0.66,1.65)
IL1RAP (rs7626795)						
A:G+G:G	1.00	1.38 (0.95, 2.01)	RERI: -0.29(-0.88,0.29)	1.00	1.40 (0.97, 2.02)	RERI: -0.20(-0.74,0.34)
A:A	1.26 (0.93, 1.72)	1.35 (0.97, 1.87)	ROR:0.77(0.50,1.20)	1.22 (0.90, 1.65)	**1.40 (1.02, 1.91)**	ROR:0.83(0.55,1.26)
Gemin4 (rs7813)						
C:T+C:C	1.00	1.35 (0.98, 1.85)	RERI: -0.47(-1.00,0.06)	1.00	**1.38 (1.02, 1.88)**	RERI: -0.39(-0.88,0.11)
T:T	1.14 (0.86, 1.53)	1.03 (0.75, 1.40)	ROR:0.66(0.44,1.01)	1.12 (0.84, 1.49)	1.07 (0.79, 1.45)	ROR:0.72(0.48,1.07)
CHRNA3 (rs8042374)						
A:G+A:A	1.00	1.27 (0.92, 1.75)	RERI: -0.26(-0.78,0.27)	1.00	1.36 (1.00, 1.85)	RERI: -0.22(-0.73,0.30)
G:G	1.24 (0.92, 1.66)	1.25 (0.91, 1.72)	ROR:0.80(0.52,1.21)	1.24 (0.93, 1.66)	1.36 (1.00, 1.85)	ROR:0.82(0.55,1.22)
FTO (rs8050136)						
C:C	1.00	1.20 (0.93, 1.54)	RERI: -0.35(-0.96,0.27)	1.00	**1.28 (1.01, 1.63)**	RERI: -0.34(-0.93,0.25)
A:C+A:A	1.30 (0.93, 1.82)	1.15 (0.78, 1.69)	ROR:0.74(0.45,1.22)	1.31 (0.94, 1.83)	1.21 (0.83, 1.75)	ROR:0.75(0.47,1.19)
HES2 (rs8708)						
A:A	1.00	1.13 (0.87, 1.48)	RERI: -0.12(-0.60,0.36)	1.00	1.22 (0.94, 1.57)	RERI: -0.13(-0.60,0.34)
A:G+G:G	1.03 (0.75, 1.40)	1.04 (0.74, 1.47)	ROR:0.90(0.57,1.41)	1.03 (0.76, 1.40)	1.10 (0.79, 1.54)	ROR:0.89(0.58,1.37)
Notch4 (rs915894)						
A:C+A:A	1.00	**1.40 (1.07, 1.83)**	**RERI: -0.67(-1.30, -0.04)**	1.00	**1.49 (1.15, 1.92)**	**RERI: -0.61(-1.20, -0.02)**
C:C	**1.49 (1.10, 2.02)**	1.22 (0.87, 1.71)	**ROR:0.58(0.38,0.91)**	**1.46 (1.08, 1.97)**	1.27 (0.91, 1.75)	**ROR:0.61(0.40,0.93)**
KRAS (rs9266)						
C:T+T:T	1.00	1.20 (0.83, 1.73)	RERI: -0.06(-0.59,0.47)	1.00	1.32 (0.93, 1.89)	RERI: -0.10(-0.63,0.43)
C:C	1.30 (0.96, 1.77)	**1.44 (1.04, 1.99)**	ROR:0.92(0.60,1.43)	1.31 (0.97, 1.78)	**1.52 (1.11, 2.09)**	ROR:0.89(0.59,1.34)

ZBTB12-C2 (rs9267673)						
C:T+T:T	1.00	1.13 (0.77, 1.68)	RERI:0.04(-0.44,0.53)	1.00	1.18 (0.80, 1.73)	RERI:0.07(-0.39,0.54)
C:C	1.01 (0.73, 1.38)	1.18 (0.85, 1.64)	ROR:1.04(0.66,1.63)	1.00 (0.73, 1.37)	1.26 (0.92, 1.74)	ROR:1.06(0.69,1.63)
HLA-DQB1- HLA-DQA2 (rs9275572)						
G:G	1.00	1.31 (0.98, 1.76)	RERI: -0.31(-0.80,0.19)	1.00	**1.38 (1.03, 1.84)**	RERI: -0.27(-0.75,0.21)
A:G+A:A	1.06 (0.80, 1.42)	1.07 (0.78, 1.46)	ROR:0.76(0.50,1.16)	1.06 (0.80, 1.42)	1.15 (0.85, 1.56)	ROR:0.80(0.54,1.19)
SEMA5B (rs9868873)						
A:G+A:A	1.00	1.37 (0.95, 1.99)	RERI: -0.20(-0.76,0.36)	1.00	**1.44 (1.00, 2.06)**	RERI: -0.19(-0.72,0.34)
G:G	1.15 (0.85, 1.56)	1.32 (0.96, 1.82)	ROR:0.84(0.54,1.3)	1.11 (0.82, 1.51)	1.34 (0.98, 1.83)	ROR:0.85(0.56,1.28)

Note: Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28 kg/m^2), and total energy intake (continuous, kcal/day).

Table 5.18. Odds ratios for joint associations of dietary flavonoids (High vs. Low) and susceptibility variants with stomach cancer

	Traditional method			Semi-shrinkage method		
dbsnp no.	High Flavonoids OR (95%)*	Low Flavonoids OR (95%)*	Interaction	High Flavonoids OR (95%)*	Low Flavonoids OR (95%)*	Interaction
HEY1 (rs1046472)						
C:C	1.00	1.01 (0.76, 1.33)	RERI:0.03(-0.43,0.49)	1.00	0.96 (0.74, 1.25)	RERI:0.04(-0.38,0.47)
A:C+A:A	1.12 (0.85, 1.49)	1.17 (0.85, 1.60)	ROR:1.03(0.67,1.57)	1.12 (0.85, 1.48)	1.13 (0.83, 1.53)	ROR:1.04(0.7,1.56)
IL15 (rs10519613)						
C:A +A:A	1.00	0.97 (0.73, 1.28)	RERI:0.13(-0.33,0.59)	1.00	0.92 (0.71, 1.21)	RERI:0.13(-0.29,0.55)
C:C	1.09 (0.82, 1.46)	1.19 (0.87, 1.63)	ROR:1.12(0.73,1.72)	1.07 (0.80, 1.42)	1.13 (0.84, 1.53)	ROR:1.13(0.76,1.70)
miR-196a2 (rs11614913)						
C:T+C:C	1.00	1.12 (0.86, 1.47)	RERI: -0.41(-0.95,0.12)	1.00	1.07 (0.82, 1.38)	RERI: -0.34(-0.82,0.14)
T:T	1.31 (0.98, 1.76)	1.02 (0.72, 1.45)	ROR:0.69(0.44,1.09)	1.27 (0.95, 1.69)	0.95 (0.68, 1.33)	ROR:0.73(0.48,1.12)
WWOX (rs12828)						
G:G	1.00	0.94 (0.66, 1.33)	RERI:0.17(-0.25,0.60)	1.00	0.92 (0.65, 1.29)	RERI:0.12(-0.29,0.53)
A:G+A:A	1.09 (0.82, 1.45)	1.20 (0.88, 1.64)	ROR:1.18(0.77,1.81)	1.12 (0.85, 1.50)	1.17 (0.87, 1.58)	ROR:1.12(0.75,1.68)
miR-300 (rs12894467)						
T:T	1.00	1.09 (0.81, 1.46)	RERI: -0.21(-0.77,0.35)	1.00	1.04 (0.78, 1.39)	RERI: -0.22(-0.75,0.31)
C:T+C:C	**1.49 (1.12, 1.99)**	1.37 (1.00, 1.88)	ROR:0.84(0.55,1.30)	**1.53 (1.15, 2.04)**	1.33 (0.98, 1.82)	ROR:0.85(0.57,1.28)
R267S (rs12934922)						
A:T+T:T	1.00	1.39 (0.92, 2.10)	RERI: -0.46(-1.10,0.18)	1.00	1.28 (0.85, 1.92)	RERI: -0.34(-0.89,0.21)
A:A	1.22 (0.88, 1.68)	1.15 (0.82, 1.63)	ROR:0.68(0.43,1.09)	1.18 (0.86, 1.63)	1.08 (0.77, 1.50)	ROR:0.74(0.47,1.14)
Oct4 (rs13409)						
C:T+T:T	1.00	1.11 (0.84, 1.46)	RERI: -0.09(-0.58,0.40)	1.00	1.06 (0.81, 1.37)	RERI: -0.09(-0.55,0.36)
C:C	1.16 (0.87, 1.54)	1.18 (0.85, 1.64)	ROR:0.92(0.60,1.41)	1.15 (0.87, 1.53)	1.11 (0.81, 1.52)	ROR:0.92(0.61,1.38)
Ran (rs14035)						
C:T+T:T	1.00	1.36 (0.93, 1.98)	RERI: -0.46(-1.05,0.13)	1.00	1.29 (0.89, 1.86)	RERI: -0.39(-0.92,0.14)
C:C	1.18 (0.87, 1.60)	1.07 (0.77, 1.49)	ROR:0.67(0.43,1.05)	1.19 (0.88, 1.61)	1.05 (0.76, 1.44)	ROR:0.71(0.46,1.08)
IKBKAP (rs1538660)						
C:C	1.00	**1.37 (1.01, 1.87)**	**RERI: -0.60(-1.12, -0.07)**	1.00	1.27 (0.94, 1.70)	RERI: -0.44(-0.90,0.02)
C:T+T:T	1.12 (0.85, 1.47)	0.89 (0.66, 1.21)	**ROR:0.58(0.38,0.88)**	1.10 (0.83, 1.44)	0.88 (0.66, 1.18)	**ROR:0.66(0.44,0.98)**
CXCL12 (rs1804429)						
T:C+C:C	1.00	1.01 (0.54, 1.88)	RERI:0.04(-0.63,0.70)	1.00	1.05 (0.56, 1.93)	RERI: -0.04(-0.67,0.59)
T:T	1.20 (0.77, 1.88)	1.25 (0.79, 1.98)	ROR:1.03(0.53,1.98)	1.27 (0.82, 1.99)	1.27 (0.81, 2.00)	ROR:0.96(0.53,1.74)
Gemin3 (rs197412)						
T:C+C:C	1.00	1.23 (0.91, 1.65)	RERI: -0.48(-1.01,0.05)	1.00	1.19 (0.89, 1.58)	RERI: -0.46(-0.95,0.03)
T:T	**1.34 (1.01, 1.76)**	1.08 (0.79, 1.48)	ROR:0.66(0.43,1.00)	**1.35 (1.02, 1.78)**	1.03 (0.76, 1.39)	**ROR:0.67(0.45,0.99)**
AXIN1 (rs1981492)						
A:G+A:A	1.00	0.92 (0.67, 1.26)	RERI:0.23(-0.20,0.65)	1.00	0.89 (0.66, 1.21)	RERI:0.18(-0.22,0.58)
G:G	1.12 (0.85, 1.47)	1.26 (0.94, 1.70)	ROR:1.23(0.81,1.86)	1.11 (0.85, 1.46)	1.20 (0.90, 1.59)	ROR:1.19(0.80,1.76)
RUNX1 (rs2014300)						
A:G+A:A	1.00	1.37 (0.88, 2.12)	RERI: -0.37(-1.02,0.27)	1.00	1.25 (0.82, 1.92)	RERI: -0.26(-0.81,0.29)
G:G	1.12 (0.80, 1.57)	1.11 (0.78, 1.60)	ROR:0.73(0.45,1.19)	1.07 (0.77, 1.50)	1.03 (0.73, 1.46)	ROR:0.79(0.50,1.25)

HIF1A (rs2057482)						
T:C+T:T	1.00	1.04 (0.73, 1.47)	RERI: -0.09(-0.52,0.35)	1.00	1.00 (0.72, 1.40)	RERI: -0.10(-0.50,0.31)
C:C	1.01 (0.76, 1.34)	0.96 (0.70, 1.31)	ROR:0.92(0.60,1.40)	1.00 (0.75, 1.32)	0.89 (0.66, 1.21)	ROR:0.90(0.60,1.35)
E2F2 (rs2075993)						
G:A+A:A	1.00	1.08 (0.81, 1.44)	RERI: -0.16(-0.68,0.36)	1.00	1.05 (0.79, 1.38)	RERI: -0.16(-0.65,0.32)
G:G	**1.34 (1.01, 1.78)**	1.27 (0.93, 1.74)	ROR:0.87(0.57,1.33)	1.35 (1.02, 1.78)	1.22 (0.90, 1.65)	ROR:0.87(0.59, 1.30)
DVL2 (rs222851)						
A:A	1.00	0.94 (0.66, 1.33)	RERI:0.08(-0.35,0.50)	1.00	0.90 (0.64, 1.26)	RERI:0.07(-0.33,0.46)
A:G+G:G	1.06 (0.80, 1.41)	1.08 (0.79, 1.47)	ROR:1.08(0.70,1.66)	1.07 (0.81, 1.41)	1.04 (0.77, 1.40)	ROR:1.07(0.71,1.62)
IKBKAP (rs2230793)						
A:C+C:C	1.00	1.03 (0.76, 1.39)	RERI: -0.03(-0.45,0.40)	1.00	1.01 (0.76, 1.35)	RERI: -0.07(-0.47,0.33)
A:A	1.02 (0.78, 1.34)	1.03 (0.75, 1.40)	ROR:0.98(0.65,1.47)	1.04 (0.80, 1.37)	0.98 (0.73, 1.32)	ROR:0.93(0.63,1.38)
FZD3 (rs2241802)						
A:G+A:A	1.00	1.10 (0.83, 1.45)	RERI: -0.05(-0.54,0.44)	1.00	1.06 (0.81, 1.39)	RERI: -0.02(-0.47,0.43)
G:G	1.05 (0.78, 1.43)	1.10 (0.78, 1.54)	ROR:0.95(0.61,1.49)	1.04 (0.77, 1.41)	1.08 (0.78, 1.50)	ROR:0.98(0.64,1.50)
Dec1 (rs2269700)						
C:T+C:C	1.00	1.04 (0.71, 1.53)	RERI:0.01(-0.47,0.49)	1.00	0.98 (0.67, 1.43)	RERI:0.01(-0.42,0.45)
T:T	1.15 (0.86, 1.55)	1.20 (0.87, 1.66)	ROR:1.00(0.64,1.57)	1.14 (0.85, 1.53)	1.14 (0.83, 1.55)	ROR:1.01(0.67,1.55)
PLCE1 (rs2274223)						
A:A	1.00	1.28 (0.94, 1.73)	RERI: -0.40(-1.02,0.23)	1.00	1.21 (0.91, 1.63)	RERI: -0.29(-0.85,0.28)
A:G+G:G	**1.46 (1.08, 1.97)**	1.34 (0.95, 1.90)	ROR:0.72(0.46,1.13)	**1.43 (1.07, 1.93)**	1.33 (0.95, 1.86)	ROR:0.78(0.51,1.20)
THBS1 (rs2292305)						
C:T+C:C	1.00	1.03 (0.76, 1.40)	RERI: -0.02(-0.46,0.43)	1.00	0.99 (0.73, 1.33)	RERI: -0.04(-0.47,0.38)
T:T	1.07 (0.81, 1.42)	1.09 (0.80, 1.50)	ROR:0.98(0.64,1.50)	1.13 (0.86, 1.50)	1.08 (0.79, 1.46)	ROR:0.96(0.64,1.44)
HIF1AN (rs2295778)						
C:C	1.00	1.00 (0.74, 1.34)	RERI:0.12(-0.33,0.57)	1.00	0.95 (0.71, 1.27)	RERI:0.11(-0.31,0.53)
C:G+G:G	1.06 (0.79, 1.41)	1.17 (0.85, 1.61)	ROR:1.11(0.72,1.71)	1.05 (0.79, 1.40)	1.12 (0.83, 1.52)	ROR:1.11(0.74,1.67)
GPC5 (rs2352028)						
C:T+T:T	1.00	0.95 (0.67, 1.35)	RERI:0.13(-0.28,0.54)	1.00	0.90 (0.64, 1.27)	RERI:0.14(-0.23,0.52)
C:C	1.02 (0.77, 1.35)	1.11 (0.81, 1.51)	ROR:1.14(0.74,1.73)	0.99 (0.75, 1.32)	1.05 (0.78, 1.41)	ROR:1.16(0.78,1.73)
TERT (rs2736100)						
G:T+G:G	1.00	0.89 (0.67, 1.18)	RERI:0.53(-0.01,1.08)	1.00	0.87 (0.66, 1.14)	RERI:0.46(-0.05,0.97)
T:T	1.22 (0.91, 1.64)	**1.64 (1.19, 2.26)**	ROR:1.51(0.98,2.35)	1.23 (0.91, 1.65)	**1.60 (1.17, 2.18)**	ROR:1.45(0.96,2.19)
CRPP1 -CRP (rs2808630)						
C:T+C:C	1.00	1.37 (0.90, 2.08)	RERI: -0.44(-1.08,0.20)	1.00	1.36 (0.90, 2.05)	RERI: -0.42(-1.00,0.17)
T:T	1.17 (0.84, 1.62)	1.09 (0.77, 1.55)	ROR:0.68(0.43,1.10)	1.16 (0.84, 1.62)	1.05 (0.75, 1.48)	ROR:0.69(0.44,1.08)
pre-miR-146a (rs2910164)						
C:C	1.00	1.17 (0.82, 1.68)	RERI: -0.23(-0.75,0.28)	1.00	1.13 (0.80, 1.61)	RERI: -0.23(-0.71,0.25)
G:C+G:G	1.20 (0.89, 1.61)	1.13 (0.82, 1.56)	ROR:0.81(0.52,1.25)	1.22 (0.91, 1.63)	1.10 (0.81, 1.50)	ROR:0.81(0.54,1.23)
CTNNB1 (rs2953)						
G:T+G:G	1.00	0.99 (0.71, 1.37)	RERI:0.12(-0.32,0.56)	1.00	0.94 (0.69, 1.30)	RERI:0.13(-0.27,0.54)
T:T	1.11 (0.84, 1.47)	1.22 (0.89, 1.66)	ROR:1.11(0.73,1.69)	1.07 (0.81, 1.41)	1.16 (0.86, 1.56)	ROR:1.14(0.76,1.69)
Oct4 (rs3130932)						
G:T+G:G	1.00	1.16 (0.86, 1.58)	RERI: -0.21(-0.7,0.28)	1.00	1.09 (0.81, 1.46)	RERI: -0.15(-0.59,0.29)

T:T	1.21 (0.92, 1.60)	1.16 (0.86, 1.58)	ROR:0.83(0.55,1.25)	1.20 (0.91, 1.58)	1.12 (0.84, 1.50)	ROR:0.87(0.59,1.29)
IKBKAP (rs3204145)						
T:T	1.00	1.25 (0.92, 1.69)	RERI: -0.45(-0.93,0.02)	1.00	1.14 (0.85, 1.53)	RERI: -0.31(-0.72,0.11)
A:T+A:A	1.03 (0.79, 1.35)	0.82 (0.61, 1.11)	**ROR:0.64(0.43,0.97)**	1.00 (0.77, 1.31)	0.81 (0.61, 1.08)	ROR:0.72(0.49,1.07)
WNT2 (rs3729629)						
C:G+C:C	1.00	1.01 (0.75, 1.37)	RERI:0.09(-0.36,0.55)	1.00	0.99 (0.74, 1.31)	RERI:0.07(-0.36,0.49)
G:G	1.16 (0.88, 1.52)	1.26 (0.93, 1.72)	ROR:1.08(0.71,1.62)	1.15 (0.87, 1.51)	1.20 (0.89, 1.62)	ROR:1.06(0.72,1.56)
HEY2 (rs3734637)						
A:C+C:C	1.00	1.04 (0.74, 1.48)	RERI:0.07(-0.38,0.53)	1.00	0.99 (0.71, 1.38)	RERI:0.09(-0.33,0.51)
A:A	1.10 (0.82, 1.46)	1.21 (0.89, 1.66)	ROR:1.06(0.69,1.63)	1.08 (0.81, 1.44)	1.17 (0.86, 1.58)	ROR:1.08(0.72,1.62)
Ctbp2 (rs3740535)						
G:G	1.00	1.16 (0.87, 1.56)	RERI: -0.29(-0.75,0.18)	1.00	1.14 (0.86, 1.50)	RERI: -0.27(-0.70,0.17)
A:G+A:A	1.08 (0.82, 1.42)	0.95 (0.69, 1.31)	ROR:0.76(0.5,1.16)	1.09 (0.83, 1.43)	0.93 (0.69, 1.27)	ROR:0.77(0.52,1.15)
PLCE1 (rs3781264)						
T:T	1.00	1.09 (0.84, 1.42)	RERI: -0.28(-0.80,0.23)	1.00	1.05 (0.82, 1.34)	RERI: -0.22(-0.69,0.25)
C:T+C:C	1.16 (0.86, 1.57)	0.97 (0.67, 1.41)	ROR:0.77(0.48,1.23)	1.14 (0.84, 1.53)	0.94 (0.65, 1.34)	ROR:0.81(0.52,1.26)
DOCK4 (rs3801790)						
A:G+G:G	1.00	1.08 (0.82, 1.44)	RERI: -0.30(-0.79,0.20)	1.00	1.05 (0.80, 1.37)	RERI: -0.25(-0.70,0.20)
A:A	1.26 (0.95, 1.66)	1.04 (0.76, 1.44)	ROR:0.77(0.50,1.17)	1.23 (0.93, 1.62)	1.00 (0.73, 1.36)	ROR:0.79(0.53,1.19)
Rbl2 (rs3929)						
G:G	1.00	1.14 (0.87, 1.48)	RERI: -0.36(-0.86,0.15)	1.00	1.09 (0.84, 1.40)	RERI: -0.31(-0.77,0.15)
C:G+C:C	1.26 (0.95, 1.67)	1.04 (0.75, 1.44)	ROR:0.73(0.47,1.11)	1.24 (0.94, 1.64)	0.98 (0.71, 1.35)	ROR:0.75(0.50,1.13)
CLPTM1L (rs401681)						
C:T+T:T	1.00	0.94 (0.70, 1.27)	RERI:0.16(-0.26,0.58)	1.00	0.90 (0.67, 1.20)	RERI:0.12(-0.27,0.51)
C:C	1.05 (0.79, 1.38)	1.15 (0.84, 1.56)	ROR:1.17(0.77,1.77)	1.06 (0.80, 1.39)	1.09 (0.81, 1.46)	ROR:1.13(0.76,1.68)
IL6R (rs4072391)						
C:C	1.00	1.11 (0.87, 1.42)	RERI: -0.29(-0.89,0.31)	1.00	1.07 (0.85, 1.34)	RERI: -0.24(-0.78,0.30)
C:T+T:T	1.15 (0.80, 1.67)	0.98 (0.64, 1.49)	ROR:0.76(0.44,1.32)	1.15 (0.80, 1.65)	0.93 (0.62, 1.41)	ROR:0.79(0.48,1.32)
CDK6 (rs42031)						
A:A	1.00	1.07 (0.85, 1.35)	RERI: -0.36(-1.18,0.45)	1.00	1.03 (0.82, 1.28)	RERI: -0.26(-0.97,0.45)
A:T+T:T	1.36 (0.87, 2.10)	1.06 (0.63, 1.81)	ROR:0.73(0.37,1.45)	1.33 (0.86, 2.06)	1.04 (0.62, 1.75)	ROR:0.80(0.44,1.47)
GKN2 -GKN1 (rs4254535)						
C:T+C:C	1.00	1.15 (0.83, 1.59)	RERI: -0.20(-0.68,0.28)	1.00	1.13 (0.82, 1.55)	RERI: -0.22(-0.67,0.23)
T:T	1.13 (0.85, 1.50)	1.08 (0.79, 1.48)	ROR:0.83(0.55,1.27)	1.14 (0.86, 1.51)	1.03 (0.76, 1.39)	ROR:0.81(0.55,1.21)
CCR4 -GLB1 (rs4678680)						
T:T	1.00	1.02 (0.81, 1.28)	RERI: -0.02(-0.70,0.65)	1.00	0.98 (0.79, 1.21)	RERI:0.00(-0.60,0.61)
G:T+G:G	1.07 (0.71, 1.61)	1.06 (0.65, 1.73)	ROR:0.98(0.52,1.85)	1.08 (0.72, 1.63)	1.06 (0.66, 1.70)	ROR:1.00(0.57,1.77)
WNT2 (rs4730775)						
C:T+T:T	1.00	1.06 (0.75, 1.49)	RERI: -0.12(-0.61,0.37)	1.00	1.04 (0.75, 1.44)	RERI: -0.14(-0.59,0.31)
C:C	1.26 (0.95, 1.67)	1.20 (0.88, 1.64)	ROR:0.90(0.59,1.38)	1.23 (0.93, 1.63)	1.11 (0.82, 1.51)	ROR:0.88(0.59,1.33)
WNT8A (rs4835761)						
A:G+G:G	1.00	0.99 (0.75, 1.31)	RERI: -0.04(-0.53,0.46)	1.00	0.95 (0.73, 1.24)	RERI: -0.03(-0.50,0.43)
A:A	1.26 (0.95, 1.67)	1.21 (0.88, 1.67)	ROR:0.97(0.63,1.49)	1.28 (0.96, 1.69)	1.19 (0.87, 1.62)	ROR:0.98(0.65,1.47)
Ago2 (rs4961280)						

C:A +A:A	1.00	0.92 (0.58, 1.48)	RERI:0.15(-0.35,0.64)	1.00	0.91 (0.58, 1.43)	RERI:0.09(-0.37,0.56)
C:C	1.15 (0.82, 1.60)	1.22 (0.85, 1.74)	ROR:1.15(0.69,1.92)	1.16 (0.83, 1.62)	1.18 (0.83, 1.66)	ROR:1.1(0.68,1.77)
TERT-CLPTM1L (rs4975616)						
A:A	1.00	1.20 (0.92, 1.55)	RERI: -0.44(-0.98,0.09)	1.00	1.14 (0.89, 1.46)	RERI: -0.39(-0.87,0.10)
A:G+G:G	1.22 (0.90, 1.66)	0.98 (0.68, 1.39)	ROR:0.67(0.42,1.06)	1.20 (0.89, 1.63)	0.91 (0.65, 1.29)	ROR:0.69(0.45,1.07)
Notch4 (rs520692)						
A:G+G:G	1.00	1.07 (0.70, 1.64)	RERI: -0.01(-0.52,0.50)	1.00	1.00 (0.66, 1.52)	RERI:0.01(-0.44,0.47)
A:A	1.07 (0.78, 1.47)	1.13 (0.81, 1.58)	ROR:0.99(0.61,1.59)	1.06 (0.77, 1.45)	1.07 (0.78, 1.49)	ROR:1.01(0.65,1.59)
Rex1 (rs6815391)						
C:T+C:C	1.00	1.06 (0.79, 1.43)	RERI: -0.03(-0.47,0.42)	1.00	1.04 (0.78, 1.38)	RERI: -0.06(-0.48,0.36)
T:T	1.04 (0.78, 1.38)	1.08 (0.78, 1.48)	ROR:0.97(0.64,1.49)	1.06 (0.80, 1.40)	1.04 (0.76, 1.41)	ROR:0.95(0.63,1.42)
miR-26a1 (rs7372209)						
C:T+T:T	1.00	1.11 (0.82, 1.51)	RERI: -0.14(-0.61,0.33)	1.00	1.06 (0.78, 1.43)	RERI: -0.14(-0.58,0.30)
C:C	1.16 (0.88, 1.53)	1.13 (0.83, 1.54)	ROR:0.88(0.58,1.33)	1.22 (0.92, 1.60)	1.12 (0.83, 1.51)	ROR:0.88(0.60,1.30)
CHEK2 (rs738722)						
C:C	1.00	0.96 (0.71, 1.31)	RERI:0.10(-0.35,0.56)	1.00	0.94 (0.70, 1.26)	RERI:0.07(-0.36,0.49)
C:T+T:T	1.20 (0.91, 1.58)	1.26 (0.93, 1.71)	ROR:1.10(0.72,1.67)	1.18 (0.89, 1.55)	1.19 (0.89, 1.60)	ROR:1.07(0.72,1.59)
TGM5 (rs748404)						
C:T+C:C	1.00	1.12 (0.57, 2.18)	RERI: -0.11(-0.89,0.67)	1.00	1.08 (0.56, 2.10)	RERI: -0.08(-0.75,0.58)
T:T	1.09 (0.69, 1.71)	1.10 (0.69, 1.76)	ROR:0.90(0.45,1.81)	1.11 (0.71, 1.74)	1.08 (0.68, 1.72)	ROR:0.92(0.49,1.72)
A379V (rs7501331)						
C:T+T:T	1.00	1.19 (0.77, 1.84)	RERI: -0.17(-0.75,0.40)	1.00	1.10 (0.72, 1.68)	RERI: -0.12(-0.62,0.39)
C:C	1.19 (0.85, 1.66)	1.21 (0.85, 1.72)	ROR:0.85(0.53,1.38)	1.18 (0.85, 1.64)	1.15 (0.82, 1.62)	ROR:0.90(0.57,1.41)
IL1RAP (rs7626795)						
A:A	1.00	1.17 (0.90, 1.52)	RERI: -0.28(-0.74,0.18)	1.00	1.11 (0.87, 1.43)	RERI: -0.22(-0.64,0.20)
A:G+G:G	1.01 (0.75, 1.35)	0.90 (0.65, 1.25)	ROR:0.76(0.49,1.18)	1.00 (0.75, 1.34)	0.87 (0.63, 1.20)	ROR:0.80(0.53,1.21)
Gemin4 (rs7813)						
T:T	1.00	1.13 (0.83, 1.55)	RERI: -0.22(-0.70,0.26)	1.00	1.09 (0.81, 1.47)	RERI: -0.18(-0.63,0.26)
C:T+C:C	1.16 (0.88, 1.54)	1.07 (0.78, 1.46)	ROR:0.81(0.53,1.24)	1.16 (0.87, 1.53)	1.05 (0.78, 1.41)	ROR:0.84(0.57,1.26)
CHRNA3 (rs8042374)						
A:G+A:A	1.00	0.98 (0.71, 1.35)	RERI:0.20(-0.23,0.63)	1.00	0.93 (0.68, 1.27)	RERI:0.15(-0.25,0.55)
G:G	1.02 (0.77, 1.35)	1.20 (0.88, 1.62)	ROR:1.20(0.79,1.83)	1.04 (0.79, 1.38)	1.14 (0.85, 1.53)	ROR:1.16(0.78,1.73)
FTO (rs8050136)						
C:C	1.00	1.00 (0.78, 1.28)	RERI:0.14(-0.41,0.70)	1.00	0.93 (0.73, 1.17)	RERI:0.19(-0.30,0.69)
A:C+A:A	1.06 (0.76, 1.49)	1.21 (0.83, 1.75)	ROR:1.13(0.69,1.87)	1.02 (0.73, 1.43)	1.17 (0.81, 1.67)	ROR:1.21(0.76,1.92)
HES2 (rs8708)						
A:G+G:G	1.00	1.10 (0.74, 1.63)	RERI: -0.09(-0.58,0.40)	1.00	1.00 (0.68, 1.46)	RERI: -0.02(-0.45,0.42)
A:A	1.07 (0.79, 1.45)	1.08 (0.77, 1.50)	ROR:0.92(0.58,1.45)	1.04 (0.77, 1.41)	1.02 (0.74, 1.41)	ROR:0.98(0.64,1.51)
Notch4 (rs915894)						
A:C+A:A	1.00	0.99 (0.76, 1.29)	RERI:0.28(-0.21,0.77)	1.00	0.94 (0.73, 1.22)	RERI:0.22(-0.22,0.66)
C:C	1.04 (0.77, 1.40)	1.31 (0.94, 1.81)	ROR:1.27(0.82,1.98)	1.02 (0.76, 1.37)	1.20 (0.88, 1.65)	ROR:1.22(0.80,1.86)
KRAS (rs9266)						
C:T+T:T	1.00	1.14 (0.79, 1.63)	RERI: -0.14(-0.66,0.39)	1.00	1.08 (0.76, 1.54)	RERI: -0.14(-0.61,0.34)
C:C	1.32 (0.99, 1.77)	1.32 (0.96, 1.82)	ROR:0.88(0.57,1.36)	1.30 (0.97, 1.74)	1.23 (0.91, 1.68)	ROR:0.89(0.59,1.34)

ZBTB12-C2 (rs9267673)						
C:C	1.00	1.12 (0.86, 1.45)	RERI: -0.23(-0.71,0.26)	1.00	1.06 (0.83, 1.35)	RERI: -0.14(-0.57,0.29)
C:T+T:T	1.07 (0.79, 1.45)	0.96 (0.68, 1.36)	ROR:0.80(0.51,1.27)	1.03 (0.76, 1.39)	0.93 (0.66, 1.30)	ROR:0.87(0.56,1.34)
HLA-DQB1- HLA-DQA2 (rs9275572)						
G:G	1.00	1.03 (0.75, 1.42)	RERI: -0.05(-0.49,0.40)	1.00	1.00 (0.74, 1.37)	RERI: -0.07(-0.49,0.34)
A:G+A:A	1.09 (0.83, 1.44)	1.08 (0.79, 1.47)	ROR:0.96(0.63,1.45)	1.09 (0.83, 1.44)	1.02 (0.75, 1.37)	ROR:0.93(0.63,1.39)
SEMA5B (rs9868873)						
A:G+A:A	1.00	1.09 (0.83, 1.42)	RERI: -0.13(-0.58,0.32)	1.00	1.04 (0.81, 1.34)	RERI: -0.08(-0.50,0.33)
G:G	1.00 (0.75, 1.34)	0.96 (0.70, 1.33)	ROR:0.88(0.57,1.37)	1.02 (0.76, 1.36)	0.97 (0.71, 1.32)	ROR:0.92(0.61,1.39)

Note: Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28 kg/m^2), and total energy intake (continuous, kcal/day).

Table 5.19. Associations between genetic risk scores and stomach cancer in the JFC study

	Ca/Co	cOR	aOR*
PRS			
Q1 (0-1.0522)	93/463	1.00	1.00
Q2 (>1.0522-1.2910)	118/463	1.27 (0.94, 1.71)	**1.67 (1.14, 2.43)**
Q3 (>1.2910-1.5239)	132/463	**1.42 (1.06, 1.91)**	**1.86 (1.29, 2.68)**
Q4 (>1.5239)	180/462	**1.94 (1.46, 2.57)**	**2.52 (1.77, 3.59)**
P value for trend		**<0.001**	**<0.001**
MGI Weighted			
Q1 (0-0.6366)	80/463	1.00	1.00
Q2 (>0.6366-0.8884)	120/463	**1.50 (1.10, 2.05)**	**1.50 (1.02, 2.21)**
Q3 (>0.8884-1.1329)	148/464	**1.85 (1.37, 2.50)**	**2.16 (1.50, 3.12)**
Q4 (>1.1329)	175/461	**2.20 (1.64, 2.95)**	**2.54 (1.77, 3.65)**
P value for trend		**<0.001**	**<0.001**

Note: Ca/Co, case/control; cOR, crude odds ratios; aOR, adjusted odds ratio; PRS, polygenic risk score; MGI, multigenetic index; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), and body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28 kg/m^2).

Table 5.20. Odds ratios for joint associations of dietary fatty acids, cholesterol, flavonoids and genetic risk scores (High vs. Low) with stomach cancer

		Ca/Co	aOR(95%CI)*	rOR(95%CI)*	RERI	ROR
Total fatty acids						
Low	Low PRS (≤1.29)	102/477	1.00	1.00	RERI: -0.08 (-0.23, 0.07)	ROR: 0.93 (0.82, 1.05)
Low	High PRS (>1.29)	148/430	**1.29 (1.15, 1.46)**	**1.27 (1.12, 1.44)**	rRERI: -0.10 (-0.25, 0.05)	rROR: 0.91 (0.80, 1.03)
High	Low PRS (≤1.29)	101/437	1.03 (0.89, 1.19)	1.07 (0.94, 1.21)		
High	High PRS (>1.29)	151/482	**1.24 (1.01, 1.53)**	1.23 (0.99, 1.53)		
Low	Low weighted MGI (≤0.89)	94/449	1.00	1.00	RERI: -0.04 (-0.20, 0.13)	ROR: 0.96 (0.85, 1.09)
Low	High weighted MGI (>0.89)	156/458	**1.36 (1.20, 1.54)**	**1.34 (1.18, 1.52)**	rRERI: -0.08 (-0.25, 0.08)	rROR: 0.92 (0.82, 1.05)
High	Low weighted MGI (≤0.89)	102/467	1.05 (0.91, 1.21)	1.08 (0.95, 1.23)		
High	High weighted MGI (>0.89)	150/452	**1.37 (1.11, 1.69)**	**1.34 (1.08, 1.66)**		
Total cholesterol						
Low	Low PRS (≤1.29)	106/554	1.00	1.00	RERI:0.06 (-0.10, 0.23)	ROR:1.05 (0.93, 1.19)
Low	High PRS (>1.29)	135/533	**1.30 (1.15, 1.47)**	**1.30 (1.15, 1.48)**	rRERI: 0.03 (-0.13, 0.19)	rROR: 1.04 (0.92, 1.17)
High	Low PRS (≤1.29)	97/360	0.99 (0.86, 1.13)	0.95 (0.83, 1.10)		
High	High PRS (>1.29)	164/379	**1.35 (1.10, 1.66)**	**1.29 (1.03, 1.61)**		
Low	Low weighted MGI (≤0.89)	96/556	1.00	1.00	RERI:0.05 (-0.12, 0.22)	ROR:1.04 (0.92, 1.17)
Low	High weighted MGI (>0.89)	145/531	**1.36 (1.20, 1.54)**	**1.36 (1.20, 1.54)**	rRERI: -0.01 (-0.17, 0.15)	rROR: 1.00 (0.88, 1.13)
High	Low weighted MGI (≤0.89)	100/360	1.00 (0.87, 1.14)	0.96 (0.84, 1.11)		
High	High weighted MGI (>0.89)	161/379	**1.41 (1.14, 1.74)**	**1.31 (1.05, 1.63)**		
Total flavonoids						
High	Low PRS (≤1.29)	123/464	1.00	1.00	RERI:0.10 (-0.08, 0.27)	ROR:1.07 (0.94, 1.20)
High	High PRS (>1.29)	161/494	**1.30 (1.15, 1.47)**	**1.29 (1.15, 1.46)**	rRERI: 0.03 (-0.13, 0.19)	rROR: 1.02 (0.90, 1.15)
Low	Low PRS (≤1.29)	80/450	1.03 (0.91, 1.18)	1.03 (0.91, 1.17)		
Low	High PRS (>1.29)	138/418	**1.43 (1.16, 1.77)**	**1.36 (1.11, 1.66)**		
Low	Low weighted MGI (≤0.89)	121/470	1.00	1.00	RERI:0.12 (-0.07, 0.30)	ROR:1.08 (0.95, 1.22)
Low	High weighted MGI (>0.89)	163/488	**1.36 (1.21, 1.54)**	**1.36 (1.20, 1.53)**	rRERI: 0.00 (-0.17, 0.17)	rROR: 0.99 (0.88, 1.12)
High	Low weighted MGI (≤0.89)	75/446	1.03 (0.90, 1.17)	1.04 (0.91, 1.18)		
High	High weighted MGI (>0.89)	143/422	**1.51 (1.23, 1.86)**	**1.39 (1.14, 1.71)**		

Note: Ca/Co, case/control; aOR, adjusted odds ratio; rOR, adjusted odds ratio with residual method; PRS, polygenic risk score; MGI, multigenetic index; RERI, relative excess risk due to interaction; ROR, ratio of odds ratios; Numbers in bold face indicate statistically significant.

*: Adjusted for study area, age (continuous), gender (male/female), education level (illiterate, primary school, middle school, high school or above), income ten years ago (<1000, 1000-<1500, 1500-<2500, ≥2500), tobacco smoking (continuous, pack-years), alcohol drinking (continuous, g ethanol/day), family history of stomach cancer (yes/no), *H. pylori* infection (positive/negative), body mass index (BMI, <18.5, 18.5-24, 24-28, ≥28 kg/m^2), and total energy intake (continuous, kcal/day).

FIGURES

Figure 2.1. The study flowchart showing sample size for specific aim 1

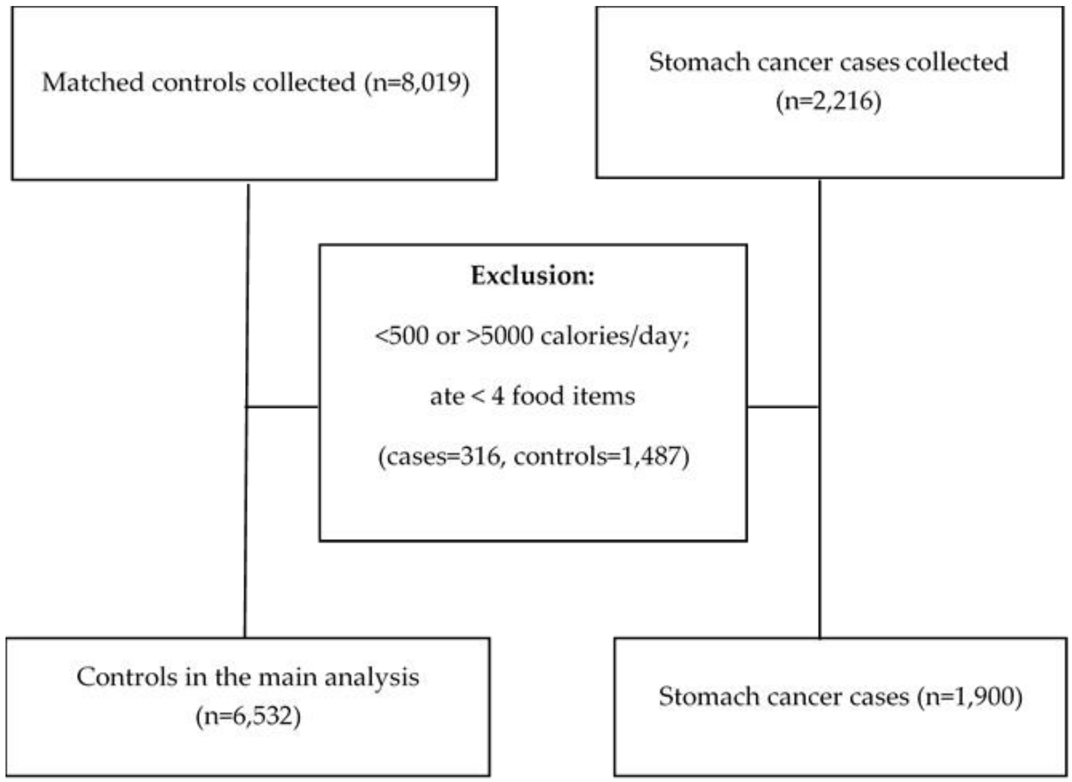

Figure 2.2. (a) Natural indirect effect and (b) natural direct effect of SFAs on stomach cancer (SC), with mediator *H. pylori* infection.

REFERENCES

1. Zhu Y-H, Jeong S, Wu M, et al. Dietary intake of fatty acids, total cholesterol, and stomach cancer in a Chinese population. *Nutrients*. 2019;11(8):1730. doi:10.3390/nu11081730

2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global Cancer Statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68:394-424. doi:10.3322/caac.21492

3. Chen W, Zheng R, Baade PD, et al. Cancer statistics in China , 2015. *CA CANCER J CLIN*. 2016;66(April):115-132. doi:10.3322/caac.21338.

4. Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37513025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet (London, England)*. 2018;391(10125):1023-1075. doi:10.1016/S0140-6736(17)33326-3

5. Rawla P, Barsouk A. Epidemiology of gastric cancer: Global trends, risk factors and prevention. *Prz Gastroenterol*. 2019;14(1):26-38. doi:10.5114/pg.2018.80001

6. Jemal A, Center MM, Desantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. *Cancer Epidemiol Biomarkers Prev*. 2010;19(8):1893-1907. doi:10.1158/1055-9965.EPI-10-0437

7. Botterweck AA, Schouten LJ, Volovics A, Dorant E, van den Brandt PA. Trends in incidence of adenocarcinoma of the oesophagus and gastric cardia in ten European countries. *Int J Epidemiol*. 2000;29:645-654.

8. Mccoll KEL, Going JJ. Aetiology and classification of adenocarcinoma of the gastro-oesophageal junction/cardia. *Gut*. 2010;59:282-284.

9. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. *Gastric Cancer*. 2011;14(2):101-112. doi:10.1007/s10120-011-0041-5

10. Lauren P. The two histological main types of gastric carcinoma: Diffuse and so-called intestinal-type carcinoma. An attempt at a histo-clinical classification. *Acta Pathol Microbiol Scand*. 1965;64:31-49.

11. Correa P, Haenszel W, Cuello C, Tannenbaum S, Archer M. A model for gastric cancer epidemiology. *Lancet (London, England)*. 1975;2(7924):58-60.

12. Correa P. A human model of gastric carcinogenesis. *CANCER Res Perspect Cancer Res*. 1988;48:3554-3560.

13. Møller H, Heseltine E, Vainio H. Working group report on schistosomes, liver flukes andHelicobacter pylori. Meeting held at IARC, LYON, 7–14 june 1994. *Int J Cancer*. 1995;60(5):587-589. doi:10.1002/ijc.2910600502

14. Rickinson A. Co-infections, inflammation and oncogenesis: Future directions for EBV research. *Semin Cancer Biol*. 2014;26:99-115. doi:10.1016/j.semcancer.2014.04.004

15. Plummer M, Franceschi S, Vignat J, Forman D, De Martel C. Global burden of gastric cancer attributable to Helicobacter pylori. *Int J Cancer*. 2015;136(2):487-490. doi:10.1002/ijc.28999

16. Lee Y-C, Chiang T-H, Chou C-K, et al. Association between Helicobacter pylori eradication and gastric cancer incidence: a systematic review and meta-analysis. *Gastroenterology*. 2016;150:1113-1124. doi:10.1053/j.gastro.2016.01.028

17. Ford AC, Forman D, Hunt R, Yuan Y, Moayyedi P. Helicobacter pylori eradication for the prevention of gastric neoplasia. Moayyedi P, ed. *Cochrane Database Syst Rev*. 2015;(7):CD005583.

18. Helicobacter and Cancer Collaborative Group. Gastric cancer and Helicobacter pylori: a combined analysis of 12 case control studies nested within prospective cohorts. *Gut*. 2001;49:347-353.

19. D 'elia L, Rossi G, Ippolito R, Cappuccio FP, Strazzullo P. Habitual salt intake and risk of gastric cancer: A meta-analysis of prospective studies. 2012;31:489-498. doi:10.1016/j.clnu.2012.01.003

20. Ren J-S, Kamangar F, Forman D, Islami F. Pickled food and risk of gastric cancer—a systematic review and meta-analysis of English and Chinese Literature. *Cancer Epidemiol Biomarkers Prev*. 2012;21(6):905-915. doi:10.1158/1055-9965.EPI-12-0202

21. Gaddy JA, Radin JN, Loh JT, et al. High dietary salt intake exacerbates Helicobacter pylori-induced gastric carcinogenesis. *Infect Immun*. 2013;81(6):2258-2267. doi:10.1128/IAI.01271-12

22. Jakszyn P, Bingham S, Pera G, et al. Endogenous versus exogenous exposure to N-nitroso compounds and gastric cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC-EURGAST) study. *Carcinogenesis*. 2006;27(7):1497-1501. doi:10.1093/carcin/bgl019

23. Cook MB, Kamangar F, Weinstein SJ, et al. Iron in relation to gastric cancer in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Cancer Epidemiol Prev Biomarkers*. 2012;21(11):2033-2042.

24. Steevens J, Van Den Brandt PA, Goldbohm RA, Schouten LJ. Selenium status and the risk of esophageal and gastric cancer subtypes: The Netherlands Cohort Study. *Gastroenterology*. 2010;138:1704-1713. doi:10.1053/j.gastro.2009.12.004

25. Campos FI, Koriyama C, Akiba S, et al. Toenail zinc level and gastric cancer risk in Cali, Colombia. *J Cancer Res Clin Oncol*. 2008;134:169-178. doi:10.1007/s00432-007-0266-1

26. Jenab M, Riboli E, Ferrari P, et al. Plasma and dietary vitamin C levels and risk of gastric cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC-EURGAST). *Carcinogenesis*. 2006;27(11):2250-2257. doi:10.1093/carcin/bgl096

27. Pelucchi C, Tramacere I, Bertuccio P, Tavani A, Negri E, La Vecchia C. Dietary intake of selected micronutrients and gastric cancer risk: an Italian case-control study. *Ann Oncol*. 2008;20(1):160-165. doi:10.1093/annonc/mdn536

28. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Tobacco Smoke and Involuntary Smoking. *IARC Monogr Eval Carcinog Risks Hum*. 2004;83:1–1438.

29. Praud D, Rota M, Pelucchi C, et al. Cigarette smoking and gastric cancer in the Stomach Cancer Pooling (StoP) Project. *Eur J cancer Prev*. 2018;27(2):124-133. doi:10.1097/CEJ.0000000000000290

30. Ladeiras-Lopes R, Pereira AK, Nogueira A, et al. Smoking and gastric cancer: systematic review and meta-analysis of cohort studies. 2008;19:689-701. doi:10.1007/s10552-008-9132-y

31. Shimazu T, Tsuji I, Inoue M, et al. Alcohol drinking and gastric cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. *Jpn J Clin Oncol*. 2008;38(1):8-25. doi:10.1093/jjco/hym152

32. Rota M, Pelucchi C, Bertuccio P, et al. Alcohol consumption and gastric cancer risk — A pooled analysis within the StoP project consortium. *Int J Cancer*. 2017;141(10):1950-1962. doi:10.1002/ijc.30891

33. Moy KA, Fan Y, Wang R, Gao Y-T, Yu MC, Yuan J-M. Alcohol and tobacco use in relation to gastric cancer: A prospective study of men in Shanghai, China. *Cancer Epidemiol Biomarkers Prev*. 2010;19(9):2287-2297. doi:10.1158/1055-9965.EPI-10-0362

34. Yang P, Zhou Y, Chen B, et al. Overweight, obesity and gastric cancer risk: Results from a meta-analysis of cohort studies. *Eur J Cancer*. 2009;45:2867-2873.

35. Singh S, Varayil JE, Devanna S, Murad MH, Iyer PG. Physical activity is associated with reduced risk of gastric cancer: A systematic review and meta-analysis. *Cancer Prev Res*. 2014;7(1):12-22.

36. Behrens G, Jochem C, Keimling M, et al. The association between physical activity and gastroesophageal cancer: systematic review and meta-analysis. *Eur Epidemiol*. 2014;29:151-170.

37. Shephard RJ. Cancers of the esophagus and stomach: potential mechanisms behind the beneficial influence of physical activity. *Clin J Sport Med*. 2016;0(0):1-7. doi:10.1097/JSM.0000000000000353

38. Uthman OA, Jadidi E, Moradi T. Socioeconomic position and incidence of gastric cancer:

a systematic review and meta-analysis. *J Epidemiol Community Heal*. 2013;0:1-7.

39. Geyer S, Hemström Ö, Peter R, Vågerö D. Education, income, and occupational class cannot be used interchangeably in social epidemiology. Empirical evidence against a common practice. *J Epidemiol Community Health*. 2006;60(9):804-810. doi:10.1136/jech.2005.041319

40. Graham DY, Malaty HM, Evans DGDJ, Evans DGDJ, Klein PD, Adam E. Epidemiology of Helicobacter pylori in an asymptomatic population in the United States effect of age, race, and socioeconomic status. *Gastroenterology*. 1991;100:1495-1501.

41. Boylan S, Lallukka T, Lahelma E, et al. Socio-economic circumstances and food habits in Eastern, Central and Western European populations. *Public Health Nutr*. 2009;14(4):678-687. doi:10.1017/S1368980010002570

42. Øvrum A. Socioeconomic status and lifestyle choices: evidence from latent class analysis. *Health Econ*. 2011;20(8):971-984. doi:10.1002/hec.1662

43. Epplein M, Signorello LB, Zheng W, et al. Race, African ancestry, and Helicobacter pylori infection in a low-income United States population. *Cancer Epidemiol Biomarkers Prev*. 2011;20(5):826-834. doi:10.1158/1055-9965.EPI-10-1258

44. Carneiro F. Hereditary gastric cancer. *Pathologe*. 2012;33(S2):231-234. doi:10.1007/s00292-012-1677-6

45. McLean MH, El-Omar EM. Genetics of gastric cancer. *Nat Rev Gastroenterol Hepatol*. 2014;11(11):664-674. doi:10.1038/nrgastro.2014.143

46. Choi YJ, Kim N, Jang W, et al. Familial Clustering of Gastric Cancer. *Med (United States)*. 2016;95(20). doi:10.1097/MD.0000000000003606

47. Ma J, Wu D, Hu X, Li J, Cao M, Dong W. Associations between cytokine gene polymorphisms and susceptibility to Helicobacter pylori infection and Helicobacter pylori related gastric cancer, peptic ulcer disease: A meta-analysis. Yamaoka Y, ed. *PLoS One*. 2017;12(4):e0176463. doi:10.1371/journal.pone.0176463

48. Cheng C, Lingyan W, Yi H, et al. Association between TLR2, MTR, MTRR, XPC, TP73, TP53 genetic polymorphisms and gastric cancer: A meta-analysis. *Clin Res Hepatol Gastroenterol*. 2014;38(3):346-359. doi:10.1016/j.clinre.2013.12.009

49. Mocellin S, Verdi D, Pooley KA, Nitti D. Genetic variation and gastric cancer risk: a field synopsis and meta-analysis. *Gut*. 2015;64:1209-1219. doi:10.1136/gutjnl-2015-309168

50. González CA, Sala N, Rokkas T. Gastric cancer: epidemiologic aspects. *Helicobacter*. 2013;18(S1):34-38. doi:10.1111/hel.12082

51. Isomoto H, Matsushima K, Inoue N, et al. Interweaving MicroRNAs and proinflammatory

cytokines in gastric mucosa with reference to H. pylori infection. *J Clin Immunol*. 2012;32(2):290-299. doi:10.1007/s10875-011-9626-3

52. Bandhavkar S. Cancer stem cells: a metastasizing menace. *Cancer Med*. 2016;5(4):649-655. doi:10.1002/cam4.629

53. Fu Y, Li H, Hao X. The self-renewal signaling pathways utilized by gastric cancer stem cells. *Tumor Biol*. 2017;39(4):1-7. doi:10.1177/1010428317697577

54. Takaishi S, Okumura T, Tu S, et al. Identification of gastric cancer stem cells using the cell surface marker CD44. *Stem Cells*. 2009;27(5):1006-1020. doi:10.1002/stem.30

55. Neumann M, Naumann M. Beyond IkappaBs: alternative regulation of NF-kappaB activity. *FASEB J*. 2007;21(11):2642-2254. doi:10.1096/fj.06-7615rev

56. Naumann M, Sokolova O. NF-κB signaling in gastric cancer. *Toxins (Basel)*. 2017;9(4):119. doi:10.3390/toxins9040119

57. Sasaki N, Morisaki T, Hashizume K, et al. Nuclear factor-κB p65 (RelA) transcription factor is constitutively activated in human gastric carcinoma tissue. *Clin Cancer Res*. 2001;7(12):4136-4142.

58. Wang W, Luo H-S, Yu B-P. Expression of NF-kappaB and human telomerase reverse transcriptase in gastric cancer and precancerous lesions. *World J Gastroenterol*. 2004;10(2):177-181.

59. Lamb A, Yang X-D, Tsang Y-HN, et al. Helicobacter pylori CagA activates NF-kappaB by targeting TAK1 for TRAF6-mediated Lys 63 ubiquitination. *EMBO Rep*. 2009;10(11):1242-1249. doi:10.1038/embor.2009.210

60. Endo F, Nishizuka SS, Kume K, et al. A compensatory role of NF-κB to p53 in response to 5-FU-based chemotherapy for gastric cancer cell lines. Hofmann TG, ed. *PLoS One*. 2014;9(2):e90155. doi:10.1371/journal.pone.0090155

61. Sakamoto H, Yoshimura K, Saeki N, et al. Genetic variation in PSCA is associated with susceptibility to diffuse-type gastric cancer. *Nat Genet*. 2008;40(6):730-740. doi:10.1038/ng.152

62. Park B, Yang S, Lee J, et al. Genome-wide association of genetic variation in the PSCA gene with gastric cancer susceptibility in a Korean population. *Cancer Res Treat*. 2019;51(2):748-757. doi:10.4143/crt.2018.162

63. Abnet CC, Freedman ND, Hu N, et al. A shared susceptibility locus in PLCE1 at 10q23 for gastric adenocarcinoma and esophageal squamous cell carcinoma. *Nat Genet*. 2010;42(9):764-767. doi:10.1038/ng.649

64. Hu N, Wang Z, Song X, et al. Genome-wide association study of gastric adenocarcinoma

in Asia: a comparison of associations between cardia and non-cardia tumours. *Gut*. 2016;65:1611-1618. doi:10.1136/gutjnl-2015-309340

65. Shi Y, Hu Z, Wu C, et al. A genome-wide association study identifies new susceptibility loci for non-cardia gastric cancer at 3q13.31 and 5p13.1. *Nat Genet*. 2011;43(12):1215-1218. doi:10.1038/ng.978

66. Jin G, Ma H, Wu C, et al. Genetic variants at 6p21.1 and 7p15.3 are associated with risk of multiple cancers in Han Chinese. *Am J Hum Genet*. 2012;91(5):928-934. doi:10.1016/j.ajhg.2012.09.009

67. Wang L-D, Zhou F-Y, Li X-M, et al. Genome-wide association study of esophageal squamous cell carcinoma in Chinese subjects identifies a susceptibility locus at PLCE1. *Nat Genet*. 2010;42(9):759-763. doi:10.1038/ng.648

68. Gong X, Marisiddaiah R, Rubin LP. β-Carotene regulates expression of β-carotene 15,15′-monoxygenase in human alveolar epithelial cells. *Arch Biochem Biophys*. 2013;539(2):230-238.

69. Leung WC, Hessel S, Méplan C, et al. Two common single nucleotide polymorphisms in the gene encoding β-carotene 15,15′-monoxygenase alter β-carotene metabolism in female volunteers. *FASEB J*. 2009;23(4):1041-1053. doi:10.1096/fj.08-121962

70. Lietz G, Oxley A, Leung W, Hesketh J. Single nucleotide polymorphisms upstream from the β-Carotene 15,15’-monoxygenase gene influence provitamin a conversion efficiency in female volunteers. *J Nutr*. 2012;142(1):161S-165S. doi:10.3945/jn.111.140756

71. Kaput J, Rodriguez RL. Nutritional genomics: The next frontier in the postgenomic era. *Physiol Genomics*. 2004;16:166-177. doi:10.1152/physiolgenomics.00107.2003

72. Milne AN, Carneiro F, O’Morain C, Offerhaus GJA. Nature meets nurture: molecular genetics of gastric cancer. *Hum Genet*. 2009;126(5):615-628. doi:10.1007/s00439-009-0722-x

73. Kim J, Cho YA, Choi WJ, Jeong SH. Gene-diet interactions in gastric cancer risk: A systematic review. *World J Gastroenterol*. 2014;20(28):9600-9610. doi:10.3748/wjg.v20.i28.9600

74. Galván-Portillo M V., Cantoral A, Oñate-Ocaña LF, et al. Gastric cancer in relation to the intake of nutrients involved in one-carbon metabolism among MTHFR 677 TT carriers. *Eur J Nutr*. 2009;48(5):269-276. doi:10.1007/s00394-009-0010-5

75. Gao S, Ding L-H, Wang J-W, Li C-B, Wang Z-Y. Diet folate, DNA methylation and polymorphisms in methylenetetrahydrofolate reductase in association with the susceptibility to gastric cancer. *Asian Pac J Cancer Prev*. 2013;14(1):299-302.

76. Ko K-P, Park SK, Cho LY, et al. Soybean product intake modifies the association between

Interleukin-10 genetic polymorphisms and gastric cancer risk. *J Nutr*. 2009;139(5):1008-1012. doi:10.3945/jn.108.101865

77. Rustan AC, Drevon CA. Fatty acids: structures and properties. *Encycl Life Sci*. 2005:1-7.

78. Ellulu MS, Patimah I, Khaza'ai H, Rahmat A, Abed Y. Obesity & inflammation: The linking mechanism & the complications. *Arch Med Sci*. 2017;13(4):851-863. doi:10.5114/aoms.2016.58928

79. Patterson E, Wall R, Fitzgerald GF, Ross RP, Stanton C. Health implications of high dietary omega-6 polyunsaturated fatty acids. *J Nutr Metab*. 2012;2012:539426. doi:10.1155/2012/539426

80. WHO. Healthy diet. WHO. http://www.who.int/mediacentre/factsheets/fs394/en/. Published 2016. Accessed May 15, 2017.

81. Arab L. Biomarkers of fat and fatty acid intake. *J Nutr*. 2003;133 Suppl(3):925S-932S.

82. Ma J, Folsom AR, Shahar E, Eckfeldt JH. Plasma fatty acid composition as an indicator of habitual dietary fat intake in middle-aged adults. The Atherosclerosis Risk in Communities (ARIC) Study Investigators. *Am J Clin Nutr*. 1995;62(3):564-571.

83. Miwa K, Kinami S, Miyazaki I, Hattori T. Positive association between dietary fat intake and risk of gastric stump carcinoma in rats. *Carcinogenesis*. 1996;17(9):1885-1889.

84. Wunder C, Churin Y, Winau F, et al. Cholesterol glucosylation promotes immune evasion by Helicobacter pylori. *Nat Med*. 2006;12(9):1030-1038. doi:10.1038/nm1480

85. Hollander D TA. Dietary essential fatty acids and the decline in peptic ulcer disease -a hypothesis. *Gut*. 1986;27:239-242.

86. Ä Romero CN, Medina E, Vargas J, Brenes M, Castro A DE. In vitro activity of olive oil polyphenols against Helicobacter pylori. *J Agric Food Chem*. 2007;55:680-686. doi:10.1021/jf0630217

87. Benatti P, Peluso G, Nicolai R, Calvani M. Polyunsaturated fatty acids: biochemical, nutritional and epigenetic properties. *J Am Coll Nutr*. 2004;23(4):281-302.

88. Funk CD. Prostaglandins and Leukotrienes: advances in eicosanoid biology. *Science (80-)*. 2001;294:1871-1875.

89. Park J-M, Kwon S-H, Han Y-M, et al. Omega-3 polyunsaturated fatty acids as potential chemopreventive agent for gastrointestinal cancer. *J cancer Prev*. 2013;18(3):201-208. doi:10.15430/jcp.2013.18.3.201

90. Han J, Jiang Y, Liu X, et al. Dietary fat intake and risk of gastric cancer: a meta-analysis of observational studies. *PLoS One*. 2015;10(9):e0138580. doi:10.1371/journal.pone.0138580

91. López-Carrillo L, López-Cervantes M, Ward MH, Bravo-Alvarado J, Ramírez-Espitia A. Nutrient intake and gastric cancer in Mexico. *Int J Cancer*. 1999;83(5):601-605. doi:10.1002/(SICI)1097-0215(19991126)83:5<601::AID-IJC5>3.0.CO;2-6

92. Hu J, La Vecchia C, Negri E, et al. Macronutrient intake and stomach cancer. *Cancer Causes Control*. 2015;26(6):839-847. doi:10.1007/s10552-015-0557-9

93. Wu Ae AH, Tseng C-C, Jean AE, Ae H, Bernstein L. Fiber intake and risk of adenocarcinomas of the esophagus and stomach. *Cancer Causes Control*. 2007;18(7):713-722. doi:10.1007/s10552-007-9014-8

94. Mayne ST, Risch HA, Dubrow R, et al. Nutrient intake and risk of subtypes of esophageal and gastric Cancer. *Cancer Epidemiol Biomarkers Prev*. 2001;10:1055-1062.

95. Harrison LE, Zhang Z-F, Karpeh MS, Sun M, Kurtz RC. The role of dietary factors in the intestinal and diffuse histologic subtypes of gastric adenocarcinoma. *Cancer*. 1997;80(6):1021-1028. doi:10.1002/(SICI)1097-0142(19970915)80:6<1021::AID-CNCR3>3.0.CO;2-C

96. Munoz N, Plummer M, Vivas J, et al. A case-control study of gastric cancer in Venezuela. *Int J Cancer*. 2001;93(3):417-423. doi:10.1002/ijc.1333

97. Kim HJ, Kim MK, Chang WK, Choi HS, Choi BY, Lee SS. Effect of Nutrient Intake and Helicobacter pylori Infection on Gastric Cancer in Korea: A Case-Control Study. *Nutr Cancer*. 2005;52(2):138-146. doi:10.1207/s15327914nc5202_4

98. Cornée J, Pobel D, Riboli E, Guyader M, Corn J. A case-control study of gastric cancer and nutritional factors in Marseille, France. *Eur J Epidemiol*. 1995;11:55-65.

99. Jędrychowski W, Popiela T, Steindorf K, et al. Nutrient intake patterns in gastric and colorectal cancers. *IJOMEH*. 2001;14(4):391-395.

100. Palli D, Russo A, Decarli A. Dietary patterns, nutrient intake and gastric cancer in a high-risk area of Italy. *Cancer Causes Control*. 2001;12:163-172.

101. O ’doherty MG, Freedman ND, Hollenbeck AR, et al. Association of dietary fat intakes with risk of esophageal and gastric cancer in the NIH-AARP Diet and Health study. *Int J Cancer*. 2012;131(6):1376-1387. doi:10.1002/ijc.27366

102. Lucenteforte E, Bosetti C, Gallus S, et al. Macronutrients, fatty acids and cholesterol intake and stomach cancer risk. *Ann Oncol*. 2009;20:1434-1438. doi:10.1093/annonc/mdp009

103. Qiu J-L, Chen K, Zheng J-N, Wang J-Y, Zhang L-J, Sui L-M. Nutritional factors and gastric cancer in Zhoushan Islands, China. *World J Gastroenterol*. 2005;11(28):4311-4316. doi:10.3748/WJG.V11.I28.4311

104. Kuriki K, Wakai K, Matsuo K, et al. Gastric cancer risk and erythrocyte composition of

docosahexaenoic acid with anti- inflammatory effects. *Cancer Epidemiol Biomarkers Prev*. 2007;16(11):2406-2415. doi:10.1158/1055-9965.EPI-07-0655

105. Chajès V, Jenab M, Romieu I, Ferrari P, Dahm CC, Overvad K et al., Chajès V, Jenab M, et al. Plasma phospholipid fatty acid concentrations and risk of gastric adenocarcinomas in the European Prospective Investigation into Cancer and Nutrition (EPIC-EURGAST). *Am J Clin Nutr*. 2011;94(5):1304-1313. doi:10.3945/ajcn.110.005892

106. Hanukoglu I. Steroidogenic enzymes: Structure, function, and role in regulation of steroid hormone biosynthesis. *J Steroid Biochem Mol Biol*. 1992;43(8):779-804. doi:10.1016/0960-0760(92)90307-5

107. Kimura Y, Sumiyoshi M. High-fat, high-sucrose, and high-cholesterol diets accelerate tumor growth and metastasis in tumor-bearing Mice. *Nutr Cancer*. 2007;59(2):207-216. doi:10.1080/01635580701499537

108. Llaverias G, Danilo C, Mercier I, et al. Role of cholesterol in the development and progression of breast cancer. *Am J Pathol*. 2011;178(1):402-412. doi:10.1016/J.AJPATH.2010.11.005

109. Du Q, Wang Q, Fan H, et al. Dietary cholesterol promotes AOM-induced colorectal cancer through activating the NLRP3 inflammasome. *Biochem Pharmacol*. 2016;105:42-54. doi:10.1016/J.BCP.2016.02.017

110. Liang JQ, Teoh N, Xu L, et al. Dietary cholesterol promotes steatohepatitis related hepatocellular carcinoma through dysregulated metabolism and calcium signaling. *Nat Commun*. 2018;9(1):4490. doi:10.1038/s41467-018-06931-6

111. McGee DJ, George AE, Trainor EA, Horton KE, Hildebrandt E, Testerman TL. Cholesterol enhances Helicobacter pylori resistance to antibiotics and LL-37. *Antimicrob Agents Chemother*. 2011;55(6):2897-2904. doi:10.1128/AAC.00016-11

112. Gonzalez CA, Riboli E, Badosa J, et al. Nutritional factors and gastric cancer in Spain. *Am J Epidemiol*. 1994;139(5):466-473.

113. Lissowska J, Gail MH, Pee D, et al. Diet and stomach cancer risk in Warsaw, Poland. *Nutr Cancer*. 2004;48(2):149-159. doi:10.1207/s15327914nc4802_4

114. Wulaningsih W, Garmo H, Holmberg L, et al. Serum lipids and the risk of gastrointestinal malignancies in the swedish AMORIS study. *J Cancer Epidemiol*. 2012;2012:792034. doi:10.1155/2012/792034

115. Borena W, Stocks T, Jonsson H, et al. Serum triglycerides and cancer risk in the metabolic syndrome and cancer (Me-Can) collaborative study. *Cancer Causes Control*. 2011;22(2):291-299. doi:10.1007/s10552-010-9697-0

116. Kitahara CM, Berrington de González A, Freedman ND, et al. Total cholesterol and cancer

risk in a large prospective study in Korea. *J Clin Oncol*. 2011;29(12):1592-1598. doi:10.1200/JCO.2010.31.5200

117. Iso H, Ikeda A, Inoue M, Sato S, Tsugane S. Serum cholesterol levels in relation to the incidence of cancer: The JPHC study cohorts. *Int J Cancer*. 2009;125(11):2679-2686. doi:10.1002/ijc.24668

118. WHO. *The World Health Report 2002: Reducing Risks, Promoting Healthy Life*.; 2002. doi:10.1080/1357628031000116808

119. Gary R. Beecher. Overview of dietary flavonoids: nomenclature, occurrence and intake. *J Nutr*. 2003;133(10):3248S-3254S. doi:10.3945/ajcn.113.060186.Am

120. Chun OK, Chung SJ, Song WO. Estimated dietary flavonoid intake and major food sources of U.S. adults. *J Nutr*. 2007;137(5):1244-1252.

121. Bawaked RA, Schröder H, Barba LR, et al. Dietary flavonoids of Spanish youth: intakes, sources, and association with the Mediterranean diet. *PeerJ*. 2017;5:e3304. doi:10.7717/peerj.3304

122. Li G, Zhu Y, Zhang Y, Lang J, Chen Y, Ling W. Estimated daily flavonoid and stilbene intake from fruits, vegetables, and nuts and associations with lipid profiles in Chinese adults. *JAND*. 2013;113:786-794. doi:10.1016/j.jand.2013.01.018

123. Xu M, Chen Y-M, Huang J, et al. Flavonoid intake from vegetables and fruits is inversely associated with colorectal cancer risk: a case–control study in China. *Br J Nutr*. 2016;116:1275-1287. doi:10.1017/S0007114516003196

124. Zamora-Ros R, Knaze V, Luján-Barroso L, et al. Differences in dietary intakes, food sources and determinants of total flavonoids between Mediterranean and non-Mediterranean countries participating in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. *Br J Nutr*. 2013;109:1498-1507. doi:10.1017/S0007114512003273

125. Zamora-Ros R, Rabassa M, Llorach R, Gonzaíez CA, Andres-Lacueva C. Application of dietary phenolic biomarkers in epidemiology: past, present, and future. *J Agric Food Chem*. 2012;60:6648-6657. doi:10.1021/jf204742e

126. Ren W, Qiao Z, Wang H, Zhu L, Zhang L. Flavonoids: Promising anticancer agents. *Med Res Rev*. 2003;23(4):519-534. doi:10.1002/med.10033

127. Luo Y, Yu H, Yang Y, et al. A flavonoid compound from Chrysosplenium nudicaule inhibits growth and induces apoptosis of the human stomach cancer cell line SGC-7901. *Pharm Biol*. 2016;54(7):1133-1139. doi:10.3109/13880209.2015.1055634

128. Skiba MA, Szendzielorz K, Mazur B, Król W. The inhibitory effect of flavonoids on interleukin-8 release by human gastric adenocarcinoma (AGS) cells infected with cag PAI

(+) Helicobacter pylori. *Cent Eur J Immunol*. 2016;3(3):229-235. doi:10.5114/ceji.2016.63119

129. Shen X, Si Y, Wang Z, Wang J, Guo Y, Zhang X. Quercetin inhibits the growth of human gastric cancer stem cells by inducing mitochondrial-dependent apoptosis through the inhibition of PI3K/Akt signaling. *Int J Mol Med*. 2016;38(2):619-626. doi:10.3892/ijmm.2016.2625

130. Ohno T, Ohtani M, Suto H, et al. Effect of green tea catechins on gastric mucosal dysplasia in insulin-gastrin mice. *Oncol Rep*. 2016;35(6):3241-3247. doi:10.3892/or.2016.4717

131. Garcia-Closas R, Gonzalez CA, Agudo A, Riboli E. Intake of specific carotenoids and flavonoids and the risk of gastric cancer in Spain. *Cancer Causes Control*. 1999;10(1):71-75.

132. Lagiou P, Samoli E, Lagiou A, et al. Flavonoids, vitamin C and adenocarcinoma of the stomach. *Cancer Causes Control*. 2004;15(1):67-72. doi:10.1023/B:CACO.0000016619.18041.b0

133. Petrick JL, Steck SE, Bradshaw PT, et al. Dietary intake of flavonoids and oesophageal and gastric cancer: incidence and survival in the United States of America (USA). *Br J Cancer*. 2015;112:1291-1300. doi:10.1038/bjc.2015.25

134. Woo HD, Lee JJY, Choi IJ, et al. Dietary flavonoids and gastric cancer risk in a Korean population. *Nutrients*. 2014;6(11):4961-4973. doi:10.3390/nu6114961

135. Zamora-Ros R, Agudo A, Lujan-Barroso L, et al. Dietary flavonoid and lignan intake and gastric adenocarcinoma risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. *Am J Clin Nutr*. 2012;96(6):1398-1408. doi:10.3945/ajcn.112.037358

136. Fang X, Wei J, He X, et al. *Landscape of Dietary Factors Associated with Risk of Gastric Cancer: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies*. Vol 51. Elsevier Ltd; 2015:2820-2832. doi:10.1016/j.ejca.2015.09.010

137. Wang T, Cai H, Sasazuki S, et al. Fruit and vegetable consumption, *Helicobacter pylori* antibodies, and gastric cancer risk: A pooled analysis of prospective studies in China, Japan, and Korea. *Int J Cancer*. 2017;140(3):591-599. doi:10.1002/ijc.30477

138. González CA, Jakszyn P, Pera G, et al. Meat Intake and Risk of Stomach and Esophageal Adenocarcinoma Within the European Prospective Investigation Into Cancer and Nutrition (EPIC). *JNCI J Natl Cancer Inst*. 2006;98(5):345-354. doi:10.1093/jnci/djj071

139. Hu FB. Dietary pattern analysis: A new direction in nutritional epidemiology. *Curr Opin Lipidol*. 2002;13(1):3-9. doi:10.1097/00041433-200202000-00002

140. van den Brandt PA, Schulpen M. Mediterranean diet adherence and risk of postmenopausal

breast cancer: results of a cohort study and meta-analysis. *Int J Cancer*. 2017;140(10):2220-2231. doi:10.1002/ijc.30654

141. Sedaghat F, Heidari Z, Jalali S, Doustmohammadian A, Ehteshami M, Rashidkhani B. Healthy Eating Index 2010 and Breast Cancer Risk. *Nutr Cancer*. 2018;70(6):860-866. doi:10.1080/01635581.2018.1490781

142. Nguyen S, Li H, Yu D, et al. Adherence to dietary recommendations and colorectal cancer risk: results from two prospective cohort studies. *Int J Epidemiol*. 2020;49(1):270-280. doi:10.1093/ije/dyz118

143. Petimar J, Smith-Warner SA, Fung TT, et al. Recommendation-based dietary indexes and risk of colorectal cancer in the Nurses' Health Study and Health Professionals Follow-up Study. *Am J Clin Nutr*. 2018;108(5):1092-1103. doi:10.1093/ajcn/nqy171

144. Li WQ, Park Y, Wu JW, et al. Index-based Dietary Patterns and Risk of Esophageal and Gastric Cancer in a Large Cohort Study. *Clin Gastroenterol Hepatol*. 2013;11(9):1130-1136.e2. doi:10.1016/j.cgh.2013.03.023

145. Ma Y, Yang W, Simon TG, et al. Dietary Patterns and Risk of Hepatocellular Carcinoma Among U.S. Men and Women. *Hepatology*. 2019;70(2):577-586. doi:10.1002/hep.30362

146. Anic GM, Park Y, Subar AF, Schap TE, Reedy J. Index-based dietary patterns and risk of lung cancer in the NIH-AARP diet and health study. *Eur J Clin Nutr*. 2016;70(1):123-129. doi:10.1038/ejcn.2015.122

147. Schulpen M, Peeters PH, van den Brandt PA. Mediterranean diet adherence and risk of esophageal and gastric cancer subtypes in the Netherlands Cohort Study. *Gastric Cancer*. 2019;22(4):663-674. doi:10.1007/s10120-019-00927-x

148. Jakszyn P, Bueno-de-mesquita HB, Palli D, et al. Adherence to a Mediterranean diet and risk of gastric adenocarcinoma within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study 1 – 3. *Am J Clin Nutr*. 2010;91(1):381-390. doi:10.3945/ajcn.2009.28209.Subjects

149. Stojanovic J, Giraldi L, Arzani D, et al. Adherence to Mediterranean diet and risk of gastric cancer: Results of a case-control study in Italy. *Eur J Cancer Prev*. 2017;26(6):491-496. doi:10.1097/CEJ.0000000000000371

150. Praud D, Bertuccio P, Bosetti C, Turati F, Ferraroni M, La Vecchia C. Adherence to the Mediterranean diet and gastric cancer risk in Italy. *Int J Cancer*. 2014;134(12):2935-2941. doi:10.1002/ijc.28620

151. Castelló A, Fernández de Larrea N, Martín V, et al. High adherence to the Western, Prudent, and Mediterranean dietary patterns and risk of gastric adenocarcinoma: MCC-Spain study. *Gastric Cancer*. 2018;21(3):372-382. doi:10.1007/s10120-017-0774-x

152. Huang Y, Han R-Q, Teng Z, Zhou J-Y, Tao R, Yu H. Incidence, mortality and survival in rural areas of stomach cancer during 2003-2012 in Jiangsu Province, China. *Chinese J Dis Control Prev*. 2017;21(5):482-486.

153. Zhao J-K, Wu M, Kim CH, et al. Jiangsu Four Cancers Study: a large case–control study of lung, liver, stomach, and esophageal cancers in Jiangsu Province, China. *Eur J cancer Prev*. 2017;26(4):357-364. doi:10.1097/CEJ.0000000000000262

154. Garza-González E, Perez-Perez GI, Maldonado-Garza HJ, Bosques-Padilla FJ. A review of Helicobacter pylori diagnosis, treatment, and methods to detect eradication. *World J Gastroenterol*. 2014;20(6):1438-1449. doi:10.3748/wjg.v20.i6.1438

155. Baecker A. Geographic variability and the association of flavonoids, glycemic index, and related single nucleotide polymorphisms with liver cancer. 2017.

156. Yang Y, Wang X, Leong P, et al. New Chinese dietary guidelines: healthy eating patterns and food-based dietary recommendations. *Asia Pac J Clin Nutr*. 2018;27(4):908-913. doi:10.6133/apjcn.072018.03

157. Greenland S. Bayesian perspectives for epidemiological research. II. Regression analysis. *Int J Epidemiol*. 2007;36:195-202. doi:10.1093/ije/dyl289

158. Willett WC, Howe GR, Kushi LH. Adjustment for total energy intake in epidemiologic studies. *Am J Clin Nutr*. 1997;65(4 Suppl):1220S-1228S; discussion 1229S-1231S.

159. Willett W. *Nutritional Epidemiology*. Third. New York: Oxford University Press; 2012.

160. Vanderweele TJ, Knol MJ. A tutorial on interaction. *Epidemiol Methods*. 2014;3(1):33-72. doi:10.1515/em-2013-0005

161. Wang A, Arah OA. G-Computation Demonstration in Causal Mediation Analysis. doi:10.1007/s10654-015-0100-z

162. VanderWeele TJ, Vansteelandt S. Odds ratios for mediation analysis for a dichotomous outcome. *Am J Epidemiol*. 2010;172(12):1339-1348. doi:10.1093/aje/kwq332

163. Valeri L, VanderWeele TJ. Mediation analysis allowing for exposure–mediator interactions and causal interpretation: Theoretical assumptions and implementation with SAS and SPSS macros. *Psychol Methods*. 2013;18(2):137-150. doi:10.1037/a0031034

164. Yuan Y-Q, Li F, Dong R-H, et al. The Development of a Chinese Healthy Eating Index and Its Application in the General Population. *Nutrients*. 2017;9(9):977. doi:10.3390/nu9090977

165. *2015-2020 Dietary Guidelines for Americans, 8th Edition*. https://health.gov/dietaryguidelines/2015/guidelines/. Accessed September 19, 2019.

166. Consortium IS. Common polygenic variation contributes to risk of schizophrenia that overlaps with bipolar disorder. *Nature*. 2009;460(7256):748-752. doi:10.1038/nature08185

167. Mu L-N, Lu Q-Y, Yu S-Z, et al. Green tea drinking and multigenetic index on the risk of stomach cancer in a Chinese population. *Int J cancer*. 2005;116(6):972-983. doi:10.1002/ijc.21137

168. Tsubura A, Yuri T, Yoshizawa K, Uehara N, Takada H. Role of fatty acids in malignancy and visual impairment: epidemiological evidence and experimental studies. *Histol Histopathol*. 2009;24(2):223-234. doi:10.14670/HH-24.223

169. Ji B-T, Chow W-H, Yang G, et al. Dietary habits and stomach cancer in Shanghai, China. *Int J Cancer*. 1998;76(5):659-664. doi:10.1002/(SICI)1097-0215(19980529)76:5<659::AID-IJC8>3.0.CO;2-P

170. Thiébaut ACM, Chajès V, Gerber M, et al. Dietary intakes of ω-6 and ω-3 polyunsaturated fatty acids and the risk of breast cancer. *Int J Cancer*. 2009;124(4):924-931. doi:10.1002/ijc.23980

171. Serini S, Calviello G. Long-chain omega-3 fatty acids and cancer: any cause for concern? *Curr Opin Clin Nutr Metab Care*. 2018;21(2):83-89. doi:10.1097/MCO.0000000000000439

172. Tall AR, Yvan-Charvet L. Cholesterol, inflammation and innate immunity. *Nat Rev Immunol*. 2015;15(2):104-116. doi:10.1038/nri3793

173. Jung MK, Jeon SW, Cho CM, et al. Hyperglycaemia, hypercholesterolaemia and the risk for developing gastric dysplasia. *Dig Liver Dis*. 2008;40:361-365. doi:10.1016/j.dld.2007.12.002

174. Bo Y, Sun J, Wang M, Ding J, Lu Q, Yuan L. Dietary flavonoid intake and the risk of digestive tract cancers: a systematic review and meta- analysis. *Sci Rep*. 2016;6(1):24836. doi:10.1038/srep24836

175. Bertuccio P, Alicandro G, Rota M, et al. Citrus fruit intake and gastric cancer: the Stomach cancer Pooling (StoP) project consortium. *Int J Cancer*. 2019;144(12):2936-2944. doi:10.1002/ijc.32046

176. Zhang J, Wu D, Vikash, et al. Hesperetin induces the apoptosis of gastric cancer cells via activating mitochondrial pathway by increasing reactive oxygen species. *Dig Dis Sci*. 2015;60(10):2985-2995. doi:10.1007/s10620-015-3696-7

177. Bao L, Liu F, Guo H, et al. Naringenin inhibits proliferation, migration, and invasion as well as induces apoptosis of gastric cancer SGC7901 cell line by downregulation of AKT pathway. *Tumor Biol*. 2016;37(8):11365-11374. doi:10.1007/s13277-016-5013-2

178. Bornschein J, Malfertheiner P. Gastric carcinogenesis. *Langenbeck's Arch Surg*.

2011;396(6):729-742. doi:10.1007/s00423-011-0810-y

179. Ekström AM, Serafini M, Nyrén O, Wolk A, Bosetti C, Bellocco R. Dietary quercetin intake and risk of gastric cancer: results from a population-based study in Sweden. *Ann Oncol*. 2011;22(2):438-443. doi:10.1093/annonc/mdq390

180. Hollman PCH, Cassidy A, Comte B, et al. The biological relevance of direct antioxidant effects of polyphenols for cardiovascular health in humans is not established. *J Nutr*. 2011;141(5):989S-1009S. doi:10.3945/jn.110.131490

181. Na H-K, Lee JY. Molecular basis of alcohol-related gastric and colon cancer. *Int J Mol Sci*. 2017;18(6):1116. doi:10.3390/ijms18061116

182. Kim J, Kang M, Lee J-S, Inoue M, Sasazuki S, Tsugane S. Fermented and non-fermented soy food consumption and gastric cancer in Japanese and Korean populations: A meta-analysis of observational studies. *Cancer Sci*. 2011;102(1):231-244. doi:10.1111/j.1349-7006.2010.01770.x

183. Furihata C, Ohta H, Katsuyama T. Cause and effect between concentration-dependent tissue damage and temporary cell proliferation in rat stomach mucosa by NaCl, a stomach tumor promoter. *Carcinogenesis*. 1996;17(3):401-406.

184. Arts IC, Hollman PC. Polyphenols and disease risk in epidemiologic studies. *Am J Clin Nutr*. 2005;81(1):317S-325S. doi:10.1093/ajcn/81.1.317S

185. Yao LH, Jiang YM, Shi J, et al. Flavonoids in food and their health benefits. *Plant Foods Hum Nutr*. 2004;59:113-122.

186. Pourfarzi F, Whelan A, Kaldor J, Malekzadeh R. The role of diet and other environmental factors in the causation of gastric cancer in Iran-A population based study. *Int J Cancer*. 2009;125(8):1953-1960. doi:10.1002/ijc.24499

187. Hertog MGL, Hollman PCH, Katan MB, Kromhout D. Intake of potentially anticarcinogenic flavonoids and their determinants in adults in the Netherlands. *Nutr Cancer*. 1993;20:21-29. doi:10.1080/01635589309514267

188. Cassidy A, Minihane A-M. The role of metabolism (and the microbiome) in defining the clinical efficacy of dietary flavonoids. *Am J Clin Nutr*. 2017;105(1):10-22. doi:10.3945/ajcn.116.136051

189. Bednarek AK, Keck-Waggoner CL, Daniel RL, et al. WWOX, the FRA16D gene, behaves as a suppressor of tumor growth. *Cancer Res*. 2001;61(22):8068-8073.

190. Bartel DP. MicroRNAs: Genomics, Biogenesis, Mechanism, and Function. *Cell*. 2004;116(2):281-297. doi:10.1016/S0092-8674(04)00045-5

191. Zhu W, Zhao J, He J, et al. Genetic variants in the MicroRNA biosynthetic pathway Gemin3

and Gemin4 are associated with a risk of cancer: a meta-analysis. *PeerJ*. 2016;4:e1724. doi:10.7717/peerj.1724

192. Manicum T, Ni F, Ye Y, Fan X, Chen B-C. Prognostic values of E2F mRNA expression in human gastric cancer. *Biosci Rep*. 2018;38(6):BSR20181264. doi:10.1042/BSR20181264

193. Katoh M, Katoh M. Notch signaling in gastrointestinal tract (Review). *Int J Oncol*. 2007;30(1):247-251. doi:10.3892/ijo.30.1.247

194. Kolligs FT, Bommer G, Göke B. Wnt/beta-catenin/Tcf signaling: A critical pathway in gastrointestinal tumorigenesis. *Digestion*. 2002;66(3):131-144. doi:10.1159/000066755

195. Saitoh T, Mine T, Katoh M. Up-regulation of WNT8B mRNA in human gastric cancer. *Int J Oncol*. 2002;20(2):343-348.

196. Cybulski C, Górski B, Huzarski T, et al. CHEK2 is a multiorgan cancer susceptibility gene. *Am J Hum Genet*. 2004;75(6):1131-1135. doi:10.1086/426403

197. Teodorczyk U, Cybulski C, Wokołorczyk D, et al. The risk of gastric cancer in carriers of CHEK2 mutations. *Fam Cancer*. 2013;12(3):473-478. doi:10.1007/s10689-012-9599-2

198. Xu D, Shao W, Jiang Y, Wang X, Liu Y, Liu X. FTO expression is associated with the occurrence of gastric cancer and prognosis. *Oncol Rep*. 2017;38(4):2285-2292. doi:10.3892/or.2017.5904

199. Yazdani U, Terman JR. The semaphorins. *Genome Biol*. 2006;7(3):211. doi:10.1186/gb-2006-7-3-211

200. Gurrapu S, Tamagnone L. Transmembrane semaphorins: Multimodal signaling cues in development and cancer. *Cell Adhes Migr*. 2016;10(6):675-691. doi:10.1080/19336918.2016.1197479

201. Wing MR, Bourdon DM, Harden TK. PLC-epsilon: a shared effector protein in Ras-, Rho-, and G alpha beta gamma-mediated signaling. *Mol Interv*. 2003;3(5):273-280. doi:10.1124/mi.3.5.273

202. Chen Q, Wang Y, Xu Y, Lin H, Xue F, Chen X. Correlation between PLCE1 rs2274223 variant and digestive tract cancer: A meta-analysis. *Mol Genet Genomic Med*. 2019;7(4):e00589. doi:10.1002/mgg3.589

203. Kirkpatrick KL, Mokbel K. The significance of human telomerase reverse transcriptase (hTERT) in cancer. *Eur J Surg Oncol*. 2001;27(8):754-760. doi:10.1053/ejso.2001.1151

204. Bayram S, Ülger Y, Sümbül AT, et al. Polymorphisms in human telomerase reverse transcriptase (hTERT) gene and susceptibility to gastric cancer in a Turkish population: Hospital-based case–control study. *Gene*. 2016;585(1):84-92. doi:10.1016/J.GENE.2016.03.030

205. Zhang J, Ju H, Gao J-R, et al. Polymorphisms in human telomerase reverse transcriptase (hTERT) gene, gene- gene and gene-smoking interaction with susceptibility to gastric cancer in Chinese Han population. *Oncotarget*. 2017;8(12):20235-20243. doi:10.18632/oncotarget.15664

206. Rafnar T, Sulem P, Besenbacher S, et al. Genome-wide significant association between a sequence variant at 15q15.2 and lung cancer risk. *Cancer Res*. 2011;71(4):1356-1361. doi:10.1158/0008-5472.CAN-10-2852

207. Park SL, Cheng I, Haiman CA. Genome-wide association studies of cancer in diverse populations. *Cancer Epidemiol Biomarkers Prev*. 2018;27(4):405-417. doi:10.1158/1055-9965.EPI-17-0169

208. Zhou Y, Wang T, Meng Q, Zhai S. Association of carotenoids with risk of gastric cancer: A meta-analysis. *Clin Nutr*. 2016;35(1):109-116. doi:10.1016/J.CLNU.2015.02.003

209. Qian C, Liu F, Ye B, Zhang X, Liang Y, Yao J. Notch4 promotes gastric cancer growth through activation of Wnt1/β-catenin signaling. *Mol Cell Biochem*. 2015;401(1-2):165-174. doi:10.1007/s11010-014-2304-z

210. Gambhir S, Vyas D, Hollis M, Aekka A, Vyas A. Nuclear factor kappa B role in inflammation associated gastrointestinal malignancies. *World J Gastroenterol*. 2015;21(11):3174-3183. doi:10.3748/wjg.v21.i11.3174

211. Karin M, Delhase M. The IκB kinase (IKK) and NF-κB: key elements of proinflammatory signalling. *Semin Immunol*. 2000;12(1):85-98. doi:10.1006/SMIM.2000.0210

212. Li D, Wu C, Cai Y, Liu B. Association of NFKB1 and NFKBIA gene polymorphisms with susceptibility of gastric cancer. *Tumor Biol*. 2017;39(7):1010428317717107. doi:10.1177/1010428317717107

213. Shen Z, Li C, Zhang K, et al. The up-regulation of miR-300 in gastric cancer and its effects on cells malignancy. *Int J Clin Exp Med*. 2015;8(5):6773-6783.

214. Yang F, Oz HS, Barve S, de Villiers WJS, McClain CJ, Varilek GW. The Green Tea Polyphenol (−)-Epigallocatechin-3-Gallate Blocks Nuclear Factor-κB Activation by Inhibiting IκB Kinase Activity in the Intestinal Epithelial Cell Line IEC-6. *Mol Pharmacol*. 2001;60(3):528-533.

215. McColl KEL, Watabe H, Derakhshan MH. Sporadic gastric cancer; a complex interaction of genetic and environmental risk factors. *Am J Gastroenterol*. 2007;102(9):1893-1895. doi:10.1111/j.1572-0241.2007.01417.x