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# BMJ Open

## Risk Factors for Gastric Cancer and Related Serological Levels in Fujian, China: Hospital-based Case-control Study

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4 **Risk Factors for Gastric Cancer and Related Serological Levels in**  
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6 **Fujian, China: Hospital-based Case-control Study**  
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35 Lan Lin and Yuan Ping have equal contribution in this study.  
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## Abstract

**OBJECTIVE** To explore the relationships between gastric cancer and serum PG I, PG II, PG I/II ratio, G-17, and *H. pylori* infection, and to investigate dietary and lifestyle risk factors for gastric cancer in Fujian Province, China.

**DESIGN** A hospital-based, 1:1 matched case-control study.

**SETTING** Patients with newly-diagnosed gastric cancer were recruited from the Fujian Provincial Hospital and the No.900 Hospital of the Joint Support Force of the Chinese People's Liberation Army between July 2014 and December 2016.

**PARTICIPANTS** A total of 180 pairs of gastric cancer patients and control subjects were recruited in the study, including 134 (74.4%) male pairs and 46 (25.6%) female pairs.

### **INVESTIGATION AND ANALYSIS MEASURES**

Serological indicators were tested with ELISA kits. Dietary, lifestyle and psychological factors were investigated through face-to-face questionnaire. Relationships between gastric cancer and these influencing factors were examined by Chi-square test and conditional logistic regression.

**RESULTS** Serum PG II and G-17 levels and *H. pylori* infection rate were higher in gastric cancer patients than in control subjects ( $P < 0.05$ ), while PG I/II ratio was lower in gastric cancer patients ( $P < 0.05$ ). Serum G-17 levels were higher in patients with corpus gastric cancer than in patients with antral gastric cancer ( $P < 0.05$ ). Serum PG II levels were higher in patients with advanced gastric cancer than in patients with early-stage cancer ( $P < 0.05$ ), however PG I/II ratio was lower in patients with advanced stage gastric cancer than in patients with early-stage cancer ( $P < 0.05$ ). Eating hot food (OR= 2.32), eating pickled vegetables (OR = 4.05), and often feel troubled (OR = 2.21) were found to significantly increase the risk of gastric cancer (all  $P < 0.05$ ), while

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3 consuming onion or garlic (OR = 0.35), drinking tea (OR = 0.26), eating  
4 fresh fruit (OR = 0.55), and high serum PG I (OR = 0.99) or PG I/II ratio  
5 (OR = 0.73) were found to be protective against gastric cancer.  
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9 **CONCLUSION** Study results showed that serum PG, G-17 and *H. pylori*  
10 antibodies could be useful indicators for early diagnosis of gastric cancer.  
11 Increase in serum G-17 level might indicate the location of gastric cancer.  
12 Increase in serum PG II level and decrease in PG I/II ratio might imply the  
13 clinical stage. Eating hot food, eating pickled vegetables, and often feel  
14 troubled may be risk factors for gastric cancer, while eating fresh fruit,  
15 eating onion or garlic, and drinking tea may be protective factors against  
16 the disease.  
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27 **Key words:** Gastric cancer, Risk factor, Pepsinogen, Gastrin, *Helicobacter*  
28 *pylori*  
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### 32 33 **Strengths and limitations of study**

34 Fujian Province, high in gastric cancer incidences, is an important research  
35 site for exploring the etiologies of gastric cancer.  
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38 This study was one of the few studies to use serum indicators as  
39 independent variables to analyze the risk factors for gastric cancer.  
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42 Strict quality control was conducted in the selection of new cases to ensure  
43 comparable results.  
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46 However, as a case-control study, recall bias was inevitable and trial  
47 studies are required for more accurate results.  
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50 Sample size of this study was not large enough, further studies will recruit  
51 more subjects.  
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## INTRODUCTION

Gastric cancer is a common malignancy in the gastric mucosa and gastric glands in the digestive tract and accounts for a high proportion of cancer deaths in China, especially in Fujian Province. According to the World Cancer Report published by the World Health Organization in 2018<sup>[1]</sup>, there were 1,033,071 new cases of gastric cancer (accounting for 5.7% of all cancer incidence) and 782,685 deaths from it (accounting for 8.2% of all cancer deaths) worldwide. Gastric cancer has high disease burdens<sup>[2]</sup>, ranking second only to lung cancer in terms of the number of deaths<sup>[1]</sup>. In China, there were 456,124 new cases of gastric cancer in 2018, accounting for 44.1% of global incidence<sup>[3]</sup>. In Fujian Province, located in southeast China, gastric cancer accounted for 12.5% of all cancer incidences in 2014<sup>[4]</sup>. Risk factors for gastric cancer such as dietary, lifestyle, and psychological factors are different across China<sup>[5-10]</sup>. The overall objectives of this study were to explore the relationship between gastric cancer and serum PG I , PG II , PG I / II ratio , G-17 and *H.pylori* infection, and to investigate the risk factors for gastric cancer in Fujian.

## METHODS

### *Study design*

This was a hospital-based, 1:1 matched case-control study, performed in accordance to the Declaration of Helsinki of the World Medical Association and approved by the Ethics Committee of the Fujian Center for Disease Control and Prevention. Informed consents were obtained from all recruited subjects. Subjects' dietary and lifestyle data were obtained through face-to-face interviews by trained investigators, and blood samples were collected for the test of serum markers.

### *Case and control groups*

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3 From July 2014 to December 2016, patients with newly-diagnosed gastric  
4 cancer were recruited from the Fujian Provincial Hospital and the No.900  
5 Hospital of the Joint Support Force of the Chinese People's Liberation  
6 Army. Control subjects were recruited simultaneously from the Medical  
7 Examination Center at the same hospital. Gastric patients and control  
8 subjects were 1:1 matched according to gender and similar age within 3  
9 years. Inclusion criteria for the gastric cancer group were: newly diagnosed  
10 of gastric cancer by gastroscopy and pathology, with no medication history  
11 of antibiotics, proton pump inhibitors, or H receptor antagonists. Patients  
12 with prior surgeries or chemotherapies were also excluded. Inclusion  
13 criteria for the control group were: no diagnosis or symptoms of chronic  
14 stomach diseases, and no mental retardation or emotional blockages. All  
15 subjects had lived in Fujian Province for more than 10 years.

### 31 ***Risk Factor Survey***

32 Data of risk factors were collected by trained investigators through  
33 face-to-face interviews with the subjects, using a consolidated  
34 questionnaire. The survey contents included general information, dietary  
35 habits(i.e., breakfast consumption, meal duration, intake frequencies of  
36 onion or garlic, spicy food, hot food, green vegetables, fresh fruit, dairy,  
37 pickled vegetables, and fish sauce), lifestyle habits (i.e., smoking, alcohol  
38 consumption, and tea consumption), and psychological factors (i.e.,  
39 personality type, adaptability, feels about life, and interpersonal skills).

### 51 ***Serum sampling***

52 A total of 5 mL of fasting venous blood was collected from each subject,  
53 and was centrifuged at 3000 r/min for 10 min to extract the serum, which  
54 was then stored at -80°C for further testing. Serum PG I, PG II, and G-17  
55 levels were tested using ELISA kits from BIOHIT, Finland (batch numbers  
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of 19PA1505, 21PB1508, and 19GC1506, respectively). Antibodies to *H. pylori* were assessed using ELISA kits from the AI Kang Company of China (lot number 201510087).

### ***Definitions and variables***

Dietary intake frequencies were classified as: never or seldom consumption (no more than once per week), occasional consumption (two to six times per week), and regular consumption (seven or more times per week). Smokers were defined as subjects who had smoked more than 100 cigarettes overall. Alcohol consumers were defined as subjects who had been drinking any alcohol at least once a week for more than six months. Tea consumers were defined as subjects who had been drinking any tea at least once a week for more than six months.

According to the calculated cut-off value, an optical density (OD) value of the sample  $>1.1 \times$  the cut-off value was considered *H. pylori*-positive, while an OD  $<0.9 \times$  the cut-off value was considered *H. pylori*-negative.

### ***Statistical analysis***

Data were inputted by the double-entry method and tested for consistency using Epidata 3.1. The SPSS version 24.0 software package was used for conducting Chi-squared tests on the demographic information, and for conducting the single and multivariate conditional logistic regression analyses on the other information to determine the odds ratio (OR) and 95% confidence interval (CI). Test significance level was set at 0.05.

## **RESULTS**

### ***Demographic information***

A total of 180 pairs of gastric cancer patients and control subjects were

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3 recruited in this study, of which 134 pairs (74.4%) were male subjects and  
4 46 pairs (25.6%) were female subjects. The average ages of the cancer  
5 group and the control group were  $61.0 \pm 10.8$  and  $60.1 \pm 10.9$  years,  
6 respectively. The two groups were not significantly different in age,  
7 marital status, education, or labor intensity (all  $P \geq 0.05$ ), however the  
8 occupation compositions were different.  
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### 17 ***Dietary habits, lifestyles and personality traits***

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19 As shown in Table 1, there were significant differences in the dietary  
20 habits between cases and controls. Lifestyles, such as smoking, alcohol  
21 consumption, and tea consumption, of the two groups were also  
22 significantly different (Table 2).  
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29 Personality types, adaptability, feelings about life, irritability, and  
30 interpersonal skills were also significantly different between cases and  
31 controls (Table 2).  
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### 37 ***Serum PG I, PG II, PG I/II ratio and G-17 levels***

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39 Serum PG I, PG II, and G-17 levels did not fit normal distributions, nor did  
40 the PG I/II ratio; therefore median values were used to indicate central  
41 tendencies and the P25 and P75 percentiles were used to indicate  
42 dispersion tendencies. Serum PG II and G-17 levels in gastric cancer  
43 patients were higher than those in the control subjects ( $P < 0.05$ ), while the  
44 PG I/II ratio was lower in the patients ( $P < 0.05$ ); PG I levels were not  
45 statistically different between the two groups. The results of the serum  
46 markers are summarized in Table 3.  
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### 57 ***H. pylori infection***

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59 As shown in Table 4, 66.67% of gastric cancer patients were *H.*  
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4 *pylori*-positive, which was significantly higher than that of the control  
5 group (54.44%,  $P < 0.05$ ). The positive rate of *H. pylori* was higher in  
6 male gastric cancer patients than in controls ( $P < 0.05$ ), however no  
7 significant differences were found between female cases and controls or  
8 among age groups ( $P > 0.05$ ).  
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### 15 ***Serological parameters with different locations of gastric cancer***

16 Serum G-17 levels were higher in patients with gastric corpus cancer than  
17 in patients with gastric antrum cancer ( $P < 0.05$ ), but not significantly  
18 different among patients with other tumor locations ( $P > 0.05$ ; Table 5).  
19 Serum PG I, PG II levels, and the PG I/II ratio were not statistically  
20 different among patients with different tumor locations ( $P > 0.05$ ; Table 5).  
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### 30 ***Serological parameters with different clinical stages of gastric cancer***

31 As shown in Table 6, serum PG II levels in patients with advanced gastric  
32 cancer were higher than in patients with early-stage gastric cancer  
33 ( $P < 0.05$ ). However, the PG I/II ratio was lower in patients with advanced  
34 cancer than in patients with early-stage disease ( $P < 0.05$ ). Serum PG I and  
35 G-17 levels were not significantly different between the two different  
36 clinical stages ( $P > 0.05$ ).  
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### 47 ***Multivariate analysis***

48 Multivariate conditional logistic regression analysis was performed with  
49 gastric cancer as the independent variable, and the dietary/lifestyle habits,  
50 psychological factors, serum PG I level, serum PG II level, PG I/II ratio,  
51 serum G-17 level, and *H. pylori* infection as dependent variables. As  
52 shown in Table 7, eating hot food, consumption of pickled vegetables, and  
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4 often feel troubled may be risk factors for gastric cancer. However, the  
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6 consumption of fresh fruit, onion or garlic, drinking tea, and elevated  
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8 serum PG I levels and PG I/II ratio might be protective factors for gastric  
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10 cancer. Other factors examined in this study had no statistically significant  
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12 effect on gastric cancer ( $P > 0.05$ ).  
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## 17 18 **DISCUSSION**

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20 Overall, this study has found that gastric cancer was related to several  
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22 dietary and lifestyle factors, the changes in serum PG I/II ratio and G-17,  
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24 and the infection rate of *H. pylori*.  
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28 Multivariate conditional logistic regression analysis indicated that the  
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30 consumption of pickled vegetables may be a risk factor for gastric cancer.  
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32 Pickles are high in salt and may damage the gastric mucosa, reduce gastric  
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34 acid secretion, and inhibit the synthesis of prostaglandin E, which  
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36 enhances gastric mucosa resistance<sup>[11]</sup>. In addition, pickles contain high  
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38 amount of nitrate and nitrite, which can be converted to N-nitrosamide, a  
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40 carcinogen, under gastric acid conditions<sup>[12]</sup>. In an area with high incidence  
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42 of gastric cancer in northwest China's Gansu Province<sup>[13]</sup>, where people  
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44 often consume pickled vegetables as substitutions of fresh vegetables in  
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46 winters, 65%-75% of pickles had detectable levels of nitrite and all had  
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48 tested positive for nitrate; and the levels of nitrite and nitrate in the gastric  
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50 juice were significantly higher in people often consume pickled vegetables  
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52 than in people who seldom consume pickled vegetables. Nitrate and nitrite  
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54 levels in the gastric juice were associated with the frequency of pickle  
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56 intake, which in turn was associated with gastric cancer. This study also  
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3 found that regular pickle intake (seven or more times per week) increased  
4 the risk of gastric cancer (OR = 4.05; 95% CI: 2.01–8.02).  
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9 Study results also indicated that tea consumption was a protective factor  
10 against gastric cancer. Tie Guanyin, one of the most popular teas in Fujian,  
11 is rich in tea polyphenols. Tea polyphenols can act as strong antioxidants  
12 to effectively remove free radicals. They can also regulate carcinogen  
13 metabolizing enzymes, inhibit the nitrosation reactions, block the  
14 expression of tumor genes, enhance immunity, and therefore act as potent  
15 anti-cancer agents<sup>[14]</sup>. However, a meta-analysis of 12 cohort studies from  
16 China, Japan, and America suggested that drinking green tea ( $\geq 5$  cups per  
17 day) was not correlated with the incidence of gastric cancer ( $P > 0.05$ )<sup>[15]</sup>.  
18 Stratified sex analyses showed that drinking  $\geq 5$  cups of green tea per day  
19 was a protective factor against gastric cancer in females, but not in  
20 males<sup>[15]</sup>. In this study, results showed that drinking tea lowered the risk of  
21 gastric cancer (OR = 0.26, 95% CI: 0.10–0.67), confirming the results  
22 shown by Li-Na Mu, et al<sup>[16]</sup>. Our findings also indicated that drinking tea  
23 may be an independent protective factor against gastric cancer, however  
24 other factors, such as the type of tea and the water temperature, might  
25 affect this relationship and warrant further investigation.  
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45 As the medical model shifts from "biomedical" to "bio-psycho-social"  
46 paradigm, the relationship between psychological factors and tumor  
47 gradually catches the attention of numerous scholars in recent years. A  
48 meta-analysis including 5,265 cases of gastric cancer and 12,539 controls  
49 from 22 domestic studies found that long-term stress had adverse effects  
50 on gastric cancer (merged OR of 2.91, 95% CI: 2.03–4.19)<sup>[17]</sup>. Another  
51 study showed that psychological factors were associated with the incidence  
52 of gastric cancer and that history of metal stimulus increased the risk of  
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3 gastric cancer significantly (OR = 1.74, 95% CI: 1.11–2.74)<sup>[18]</sup>. People who  
4 often feel anxious/irritable or experience hardships in life have altered  
5 hormone levels, which in turn affect their immune system. In particular,  
6 epinephrine and norepinephrine are released under stress or anxiety,  
7 causing decrease in natural killer cells, reduction in immunity functions  
8 and acceleration in the initiation and progression of malignancies<sup>[19]</sup>.  
9 Similar to previous studies, this study also found that often feel troubled  
10 was related to gastric cancer (OR = 2.21, 95% CI: 1.23–3.98) in our  
11 subjects.  
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23 Recent studies indicated that low serum PG I and PG I/II ratio were  
24 strongly associated with gastric cancer, while the relationship between PG  
25 II and gastric cancer was not as obvious. PG I is primarily secreted by  
26 chief cells and mucous neck cells in the fundic glands, whereas PG II is  
27 secreted by all gastric glands and the proximal duodenal mucosa<sup>[20]</sup>. When  
28 chronic *H. pylori* infection with chronic atrophic gastritis (CAG) extends  
29 from antrum to corpus of stomach, chief cells are replaced by pyloric  
30 glands. Therefore, the concentration of serum PG I will decrease due to  
31 damaged secretion ability of gastric mucosa, however the secretion of PG  
32 II remains, resulting in a lowered PGI/II ratio, which would reflect the  
33 severity of CAG. Patients with premalignant lesions, such as CAG or  
34 dysplasia, have considerable higher risks for developing gastric cancer.  
35 Our previous study<sup>[21]</sup> explored the changes of serum PG levels in different  
36 gastric cancer states. Results found significant differences in serum PG I ,  
37 PG II , and PGI/II ratio among the control group, the atrophic gastritis  
38 group, and the gastric cancer group (all  $P < 0.001$ ). Serum PG I level was  
39 lower in the gastric cancer group than in the other two groups, and was  
40 also lower in the atrophic gastritis group than in the control group, both  
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3 differences were statistically significant ( $P < 0.05$ ). Serum PGI/II ratio in the  
4 gastric cancer group was lower than in the control group and the atrophic  
5 gastritis group, and was also lower in the atrophic gastritis group than in  
6 the control group, both differences were statistically significant ( $P < 0.05$ ).  
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8 In a study in Japan including 10,996 healthy residents who had underwent  
9 gastroscop examinations and tested for serum PG, the incidence of gastric  
10 cancer was higher in subjects with lower serum PG I levels and PG I/II  
11 ratios<sup>[22]</sup>. In our study, single conditional logistic regression results showed  
12 that serum PG II was higher in gastric cancer patients than in control  
13 subjects ( $P < 0.05$ ), PG I/II ratio was lower in gastric cancer patients than in  
14 control subjects ( $P < 0.05$ ), and PG I levels in the two groups were not  
15 significantly different ( $P > 0.05$ ), which was in agreement with the study  
16 conducted by Cao, et al.<sup>[23]</sup>. Moreover, our results showed that after  
17 controlling for other risk factors, decreased levels of serum PG I and PG  
18 I/II ratios might be independent risk factors for gastric cancer, which was  
19 in agreement with the results of a nested case-control study conducted by  
20 Kurilovich, et al.<sup>[24]</sup>.

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40 Qin Cao et al<sup>[25]</sup>. found that serum PG I and PG II levels were lower in  
41 patients with advanced-stage gastric cancer than in those with early-stage  
42 disease ( $P < 0.05$ ), which was consistent with the results observed in the  
43 elderly gastric cancer patients (aged  $>60$  years) by Wei Huang, et al<sup>[26]</sup>. In  
44 this study, serum PG II levels were significantly higher in advanced stage  
45 gastric cancer patients than those with early-stage disease ( $P < 0.05$ ), PG  
46 I/II ratio was significantly lower in advanced stage gastric cancer patients  
47 ( $P < 0.05$ ). These results demonstrated that serum PG II level and PG I/II  
48 ratio were different at different clinical stages of gastric cancer. Therefore,  
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3 the elevation of serum PG II levels and reduced PG I/II ratio may be  
4 indicators of the clinical stages of gastric cancer.  
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9 Gastrin, a peptide hormone synthesized and secreted by the G cells of the  
10 pyloric antrum of the stomach, was first discovered in 1906<sup>[27]</sup>, and is now  
11 well known for its multiple subtypes<sup>[28]</sup>. 90% of the intra-corporeal gastrin  
12 is G-17, which is one of the main forms in gastrin circulation, and the  
13 change of which can indicate the impairment of gastric mucosa  
14 functions<sup>[29]</sup>. Li Wang et al. <sup>[30]</sup> had used immunohistochemical method to  
15 detect serum G-17, and found it had increased concentrations in superficial  
16 gastritis, para-cancerous tissues and gastric cancer cells. In addition, serum  
17 G-17 levels were found to be higher in patients with pre-operative gastric  
18 cancer than in healthy controls ( $P < 0.05$ ), and were also elevated in  
19 patients with advanced clinical stage of gastric cancer<sup>[31]</sup>.  
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33 Our finding was coincided with the study conducted by Rui-Xin Lin, et al.,  
34 that serum G-17 in patients with gastric cancer was higher than in the  
35 controls ( $P < 0.05$ ) <sup>[32]</sup>. This indicated that increased serum G-17 levels  
36 were associated with gastric cancer and hypergastrinemia. In terms of the  
37 potential mechanism of action, animal experiments with overexpressed  
38 G-17 indicated that gastrin could influence gastric carcinogenesis<sup>[33]</sup>.  
39 Serum G-17 levels were found to be higher in patients with gastric corpus  
40 cancer than in patients with gastric cancer in other locations ( $P < 0.05$ ),  
41 which was similar to the findings described by Hu et al<sup>[34]</sup>. This may be  
42 related to the the vagus nerve's depressive effect on G-17 secretion. Serum  
43 G-17 levels were more clearly elevated when cancer invaded the gastric  
44 body, which could damage the vagus nerve and inhibit G-17 secretion<sup>[35]</sup>.  
45 Therefore, our results suggested that changes in serum G-17 levels in  
46 gastric cancer patients may be indicative of cancer location.  
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*H. pylori* infection was a risk factor for gastric cancer. The International Agency for Research on Cancer (IARC) formally identified *H. pylori* as Class I carcinogen in 1994. In addition, a 7.8-year prospective study of 1,526 Japanese patients with gastric diseases showed that patients with *H. pylori* infection had diseases such as gastric atrophy, intestinal metaplasia, as well as precancerous lesions<sup>[36]</sup>. Moreover, a study conducted in Changle City, Fujian Province, China, showed that although patients with precancerous gastric lesions were unable to avoid gastric cancer, *H. pylori* eradication could reduce the risk of gastric cancer in people without precancerous lesions<sup>[37]</sup>. The *H. pylori* infection rate in the control group in the current study was 54.4%, which was close to the number found in natural population (54.76%)<sup>[38]</sup>. However, the infection rate in gastric cancer patients was 66.7%, similar to the results observed by Xue-Yuan Cao, et al<sup>[39]</sup>, suggesting that *H. pylori* infection was more common in gastric cancer patients. In addition, the *H. pylori* infection rate in the gastric cancer group was significantly higher than in the control group in male subjects ( $P < 0.05$ ), whereas no such difference was observed in females, which might be associated with a lower prevalence of *H. pylori* infection in women<sup>[40]</sup>.

There were some strengths in this study. Firstly, Fujian Province is an area with high incidence of gastric cancer in China. According to the report of Fujian Province, the incidence of gastric cancer collected from tumor registration areas in Fujian Province in 2017 was 31.68/100,000, accounting for 12.47% of all new cancer cases, ranking the third in cancer incidence; gastric cancer mortality rate was 25.90/100,000, accounting for 14.74% of all cancer deaths, also ranking the third in cancer deaths. Therefore, Fujian is an important research site for exploring the causes of

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3 gastric cancer. Secondly, strict quality control was conducted in this study  
4 in the selection of new cases to make sure the results be comparable.  
5 Taking into account the effects of proton pump inhibitors and H receptor  
6 antagonists on serum markers, patients who had taken these drugs within a  
7 week before recruiting were excluded. With strictly controlling the quality  
8 of selected cases, the difficulty in obtaining cases also increased. Thirdly,  
9 this study was one of the few studies to use serum indicators as  
10 independent variables to explore the risk factors for gastric cancer.  
11 However, several limitations should be considered. First, for a case-control  
12 study, the causal association between dietary/lifestyle habits and gastric  
13 cancer could not be precisely identified. Second, the consumptions of  
14 alcohol, tea, and pickled vegetables were self-reported. Subjects often had  
15 difficulties in recalling food consumptions and it was also hard to estimate  
16 the accurate amount of consumption. Therefore, recall bias and  
17 misclassification bias were inevitable. Randomized Control Trial studies  
18 shall be conducted for more accurate results. Third, the sample size was  
19 relatively small. China has high incidence of gastric cancer and provides  
20 favorable conditions for studying it. We plan to expand the sample size in  
21 our further researches on gastric cancer.  
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### 44 **Conclusion**

45 In conclusion, this study indicated that serum PG and G-17 levels, as well  
46 as the detection of *H. pylori* antibodies, could be useful indicators of  
47 gastric cancer location and cancer stage. Elevation of serum G-17 levels  
48 may be indicative of the gastric cancer location, while the increase in the  
49 PG II level and the reduction in the PG I/II ratio may imply the clinical  
50 stage. Poor dietary habits, salty food, and often feel troubled may be risk  
51 factors for gastric cancer, while eating fresh fruit, onion or garlic, and  
52 drinking tea may help protect against this disease.  
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## Footnotes

**Contributions:** Lan Lin and Ping Yuan are joint first authors. Kui-cheng Zheng and Wen Wang obtained funding. Kui-cheng Zheng designed the study. Lan Lin drafted the manuscript. Ping Yuan contributed to the interpretation of the results and critical revision of the manuscript for important intellectual content. Wen Wang, Si-han Wu, Liang-xiang Huang collected the data. Bing-shan Wu and Tie-hui Chen detected serological indicators. Xiao-qing Li analyzed the data. All authors have read and approved the final manuscript. Kui-cheng Zheng and Lin Cai are the study guarantors.

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**Competing interests:** We have read and understood BMJ policy on declaration of interests and declare that we have no competing interests.

**Patient consent:** Not required.

**Ethical approval:** This study was approved by the ethical reviews

committee at Fujian Center for Disease Control and Prevention.

**Data sharing:** Data are stored in Fujian Center for Disease Control and Prevention, No.76 Jintai Road, Gulou District, Fuzhou, China. Data are available upon request to Kui-cheng Zheng; Email address: zkcfcjcdc@sina.com.

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**Table 1 Single conditional logistic regression analysis on dietary factors, *n*(%)**

Factor	Frequency*	Cases	Control	<i>P</i>	OR	95% CI
<b>Breakfast consumption</b>	+	112 (62.22)	153 (85.00)		1.00	
	++	38 (21.11)	18 (10.00)	<0.01	2.84	(1.54,5.25)
	+++	30 (16.67)	9 (5.00)	<0.01	4.78	(2.10,10.87)
<b>Meal duration</b>	≥20 min	24 (13.33)	46 (25.56)		1.00	
	10–20 min	50 (27.78)	70 (38.89)	0.393	1.32	(0.70,2.52)
	<20 min	106 (58.89)	64 (35.56)	<0.01	2.97	(1.63,5.40)
<b>Onion or garlic</b>	+	73 (40.56)	49 (27.22)		1.00	
	++	66 (36.67)	56 (31.11)	0.29	0.74	(0.42,1.30)
	+++	41 (22.78)	75 (41.67)	<0.01	0.36	(0.21,0.63)
<b>Spicy food</b>	+	104 (57.78)	125 (69.44)		1.00	
	++	45 (25.00)	48 (26.67)	0.71	1.11	(0.64,1.93)
	+++	31 (17.22)	7 (3.89)	<0.01	5.95	(2.28,15.53)
<b>Hot food</b>	+	76 (42.22)	114 (63.33)		1.00	
	++	47 (26.11)	47 (26.11)	0.25	1.35	(0.81,2.27)
	+++	57 (31.67)	19 (10.56)	<0.01	5.63	(2.72,11.66)
<b>Green vegetables</b>	+	35 (19.44)	15 (8.33)		1.00	
	++	70 (38.9)	46 (25.56)	0.34	0.71	(0.36,1.43)
	+++	75 (41.67)	119 (66.11)	<0.01	0.29	(0.15,0.56)
<b>Fresh fruit</b>	+	115 (63.89)	43 (23.89)		1.00	
	++	42 (23.33)	78 (43.33)	<0.01	0.20	(0.11,0.37)
	+++	23 (12.78)	59 (32.78)	<0.01	0.16	(0.08,0.32)
<b>Dairy</b>	+	133 (73.89)	82 (45.56)		1.00	
	++	32 (17.78)	53 (29.44)	<0.01	0.28	(0.15,0.53)
	+++	15 (8.33)	45 (25.00)	<0.01	0.17	(0.08,0.36)
<b>Pickled vegetables</b>	+	55 (30.56)	125 (69.44)		1.00	
	++	65 (36.11)	45 (25.00)	<0.01	2.67	(1.60,4.49)
	+++	60 (33.33)	10 (5.56)	<0.01	15.27	(5.91,39.49)
<b>Fish sauce</b>	+	109 (60.56)	135 (75.00)		1.00	
	++	30 (16.67)	32 (17.78)	0.96	1.02	(0.56,1.83)
	+++	41 (22.78)	13 (7.22)	<0.01	3.81	(1.89,7.65)

\* “+”, never or seldom consuming; “++”, sometimes consuming; “+++”, regularly consuming.

**Table 2 Single conditional logistic regression analysis on lifestyle habits and personality factors, *n*(%)**

Factors	classified	Cases	Controls	<i>P</i>	OR	95% CI
Smoker	No	89 (49.44)	116 (64.44)		1.00	
	Yes	91 (50.56)	64 (35.56)	0.01	2.67	(1.51,4.77)
Alcohol consumption	No	118 (65.56)	140 (77.78)		1.00	
	Yes	62 (34.44)	40 (22.22)	0.01	1.85	(1.15,2.98)
Tea consumption	No	132 (73.33)	102 (56.67)		1.00	
	Yes	48 (26.67)	78 (43.33)	0.01	0.43	(0.23,0.71)
Personality type	Type A	98 (54.44)	78 (43.33)		1.00	
	Intermediate	36 (20.00)	41 (22.78)	0.15	0.66	(0.38,1.15)
	Type B	46 (25.56)	61 (33.89)	0.04	0.59	(0.36,0.97)
Adaptability	Easy	56 (31.11)	61 (33.89)		1.00	
	Between	72 (40.00)	91 (50.56)	0.58	0.88	(0.55,0.41)
	Difficult	52 (28.89)	28 (15.56)	0.03	1.93	(1.08,3.45)
How feel about life	Feel happy	33 (18.33)	63 (35.00)		1.00	
	Feel troubled	71 (39.44)	78 (43.33)	0.03	1.85	(1.06,3.22)
	Often feel troubled	76 (42.22)	39 (21.67)	<0.01	4.16	(2.21,7.86)
Irritable	No	84 (46.67)	110 (61.11)		1.00	
	Yes	96 (53.33)	70 (38.89)	0.04	2.00	(1.25,3.20)
Interpersonal skills	Good	70 (38.89)	96 (53.33)		1.00	
	General	86 (47.78)	75 (41.67)	0.06	1.53	(0.10,2.38)
	Poor	24 (13.33)	9 (5.00)	0.00	3.79	(1.57,9.12)

**Table 3 Comparisons of serum PG I , PG II , PG I/II ratio and G-17 between cases and controls, M(p25,p75)**

Type	Total (n)	PG I ( $\mu\text{g/L}$ )	PG II ( $\mu\text{g/L}$ )	PG I/II ratio	G-17 (pmol/L)
Cases	180	115.56 (68.84,177.47)	17.85 (10.58,8.74)	6.58 (4.95,8.48)	7.62 (3.96,14.24)
Controls	180	117.69 (89.83,145.32)	11.19 (7.45,17.37)	9.60 (7.35,13.45)	3.54 (2.24,7.13)
<i>Z</i>	—	<b>0.26</b>	<b>5.48</b>	<b>8.06</b>	<b>6.01</b>
<i>P</i>	—	<b>0.78</b>	<b>&lt;0.01</b>	<b>&lt;0.01</b>	<b>&lt;0.01</b>

Note: PG is pepsinogen, and G-17 is Gastrin-17



**Table 4. Comparison of the *H. pylori* positive rates between cases and controls, *n*(%)**

Type	Cases	Controls	$\chi^2$	<i>P</i>
<b>Total</b>	120(66.67)	98(54.44)	5.63	0.02
<b>Gender</b>				
<b>Male</b>	94(52.22)	77(42.78)	4.88	0.03
<b>Female</b>	26(14.44)	21(11.67)	0.97	0.33
<b><math>\chi^2</math></b>	2.65	1.20		
<b><i>P</i></b>	0.10	0.27		
<b>Age, years</b>				
<b>&lt;50</b>	20(11.11)	16(8.89)	0.86	0.36
<b>50–65</b>	51(28.33)	42(23.33)	3.16	0.08
<b>≥65</b>	49(27.22)	40 (22.22)	1.57	0.21
<b><math>\chi^2</math></b>	<b>0.55</b>	<b>1.28</b>		
<b><i>P</i></b>	<b>0.76</b>	<b>0.53</b>		

**Table 5. Comparison of the serological parameters among patients with different locations of gastric cancer, M(p25,p75)**

Location	Cases (n)	PG I ( $\mu\text{g/L}$ )	PG II ( $\mu\text{g/L}$ )	PG I/II ratio	Gastrin-17 (pmol/L)
<b>Cardia</b>	19	116.15 (61.42,182.66)	17.27 (11.74, 28.83)	6.41 (5.09, 8.01)	6.35 (2.36, 10.75)
<b>Fundus</b>	17	81.26 (53.44, 197.57)	20.72 (9.32, 33.06)	5.22 (3.29, 8.41)	8.14 (3.85, 12.50)
<b>Gastric corpus</b>	55	118.23 (66.41, 175.04)	19.43 (12.25, 28.94)	5.69 (3.78, 8.23)	12.00 (6.58, 19.74)
<b>Gastric antrum</b>	70	118.65 (78.87, 173.66)	16.79 (10.42, 27.49)	7.05 (5.45, 9.07)	6.12 (3.84, 12.67)
<b>Gastric angle</b>	19	116.00 (68.13, 195.76)	15.89 (7.39, 29.28)	7.25 (5.63, 8.10)	6.44 (2.58, 14.81)
<b><math>\chi^2</math></b>		<b>1.58</b>	<b>1.59</b>	<b>7.41</b>	<b>10.79</b>
<b><i>P</i></b>		<b>0.81</b>	<b>0.81</b>	<b>0.12</b>	<b>0.03</b>

Note: PG is pepsinogen

**Table 6. Comparison of the serological parameters in patients with different clinical stages of gastric cancer, M(p25,p75)**

Clinical stage	Cases (n)	PG I ( $\mu\text{g/L}$ )	PG I I ( $\mu\text{g/L}$ )	PG I/II ratio	Gastrin-17 (pmol/L)
Early	49	93.07 (68.39, 171.64)	13.81 (7.42, 23.92)	6.95 (5.71, 9.73)	5.93 (2.85, 12.75)
Advanced	131	118.23 (69.43, 181.24)	19.43 (12.51, 30.41)	6.10 (4.50, 8.03)	8.19 (4.29, 14.39)
<b>Z</b>		<b>0.88</b>	<b>2.33</b>	<b>2.43</b>	<b>1.75</b>
<b>P</b>		<b>0.38</b>	<b>0.02</b>	<b>0.02</b>	<b>0.08</b>

Note: PG is pepsinogen

**Table 7. Multivariate conditional logistic regression analysis.**

Factors	$\beta$	S.E.	Wald	P	OR	95% CI
Hot food	0.84	0.31	7.63	0.006	2.32	(1.28,4.23)
Onion or garlic	-1.05	0.33	10.11	0.001	0.35	(0.18,0.67)
Fresh fruit	-0.60	0.29	4.34	0.037	0.55	(0.31,0.97)
Pickled vegetables	1.39	0.35	15.44	<0.001	4.05	(2.01,8.03)
Tea consumption	-1.35	0.49	7.77	0.005	0.26	(0.10,0.67)
Often feel troubled	0.79	0.30	7.03	0.008	2.21	(1.23,3.98)
PG I	-0.01	0.00	3.96	0.047	0.99	(0.99,1.00)
PG I/II ratio	-0.32	0.07	20.82	<0.001	0.73	(0.63,0.83)

# Reporting checklist for genetic association study.

Based on the STREGA guidelines.

## Instructions to authors

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		Page
	Reporting Item	Number
<b>Title and abstract</b>		
Title	<a href="#">#1a</a> Indicate the study's design with a commonly used term in the title or the abstract	1

1	Abstract	<a href="#">#1b</a>	Provide in the abstract an informative and balanced	2-3
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3				
4			summary of what was done and what was found	
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6	<b>Background/rationale</b>			
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10		<a href="#">#2</a>	Explain the scientific background and rationale for the	3-4
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12			investigation being reported	
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15	<b>Objectives</b>			
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18		<a href="#">#3</a>	State specific objectives, including any prespecified	2
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20			hypotheses. State if the study is the first report of a	
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22			genetic association, a replication effort, or both.	
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26	<b>Study design</b>			
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29		<a href="#">#4</a>	Present key elements of study design early in the paper	2
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32	<b>Setting</b>			
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35		<a href="#">#5</a>	Describe the setting, locations, and relevant dates,	2
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37			including periods of recruitment, exposure, follow-up,	
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39			and data collection	
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43	<b>Eligibility criteria</b>			
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46		<a href="#">#6a</a>	Cohort study – Give the eligibility criteria, and the	4
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48			sources and methods of selection of participants.	
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50			Describe methods of follow-up. Case-control study –	
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53			Give the eligibility criteria, and the sources and methods	
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55			of case ascertainment and control selection. Give the	
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57			rationale for the choice of cases and controls. Cross-	
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sectional study – Give the eligibility criteria, and the sources and methods of selection of participants. Give information on the criteria and methods for selection of subsets of participants from a larger study, when relevant.

Variables	<p><a href="#">#6b</a> Cohort study – For matched studies, give matching criteria and number of exposed and unexposed. Case-control study – For matched studies, give matching criteria and the number of controls per case.</p>	n/a
Data sources/measurement	<p><a href="#">#7a</a> Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</p> <p><a href="#">#7b</a> Clearly define genetic exposures (genetic variants) using a widely-used nomenclature system. Identify variables likely to be associated with population stratification (confounding by ethnic origin).</p> <p><a href="#">#8a</a> For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for exposed and unexposed groups if applicable.</p>	4 5 4

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23	<b>Bias</b>		
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26		<a href="#">#8b</a>	Describe laboratory methods, including source and 5
27			storage of DNA, genotyping methods and platforms
28			(including the allele calling algorithm used, and its
29			version), error rates and call rates. State the laboratory /
30			centre where genotyping was done. Describe
31			comparability of laboratory methods if there is more than
32			one group. Specify whether genotypes were assigned
33			using all of the data from the study simultaneously or in
34			smaller batches.
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1	<a href="#">#12a</a>	Describe all statistical methods, including those used to	5
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9	<a href="#">#12b</a>	Describe any methods used to examine subgroups and	n/a
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14	<a href="#">#12c</a>	Explain how missing data were addressed	n/a
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17	<a href="#">#12d</a>	If applicable, explain how loss to follow-up was	n/a
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19		addressed	
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23	<a href="#">#12e</a>	Describe any sensitivity analyses	n/a
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26	<a href="#">#12f</a>	State whether Hardy-Weinberg equilibrium was	n/a
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28		considered and, if so, how.	
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31	<a href="#">#12g</a>	Describe any methods used for inferring genotypes or	n/a
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42	<a href="#">#12i</a>	Describe any methods used to address multiple	n/a
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44		comparisons or to control risk of false positive findings.	
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47	<a href="#">#12j</a>	Describe any methods used to address and correct for	n/a
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49		relatedness among subjects	
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53	<b>Participants</b>		
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56	<a href="#">#13a</a>	Report numbers of individuals at each stage of study—	5-6
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58		eg numbers potentially eligible, examined for eligibility,	
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confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable. Report numbers of individuals in whom genotyping was attempted and numbers of individuals in whom genotyping was successful.

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21	<b>Descriptive data</b>		
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24		<a href="#">#14a</a> Give characteristics of study participants (eg	5-6
25		demographic, clinical, social) and information on	
26		exposures and potential confounders. Give information	
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42		<a href="#">#14c</a> Cohort study – Summarize follow-up time, e.g. average	n/a
43		and total amount.	
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47	<b>Outcome data</b>		
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50		<a href="#">#15</a> Cohort study Report numbers of outcome events or	5-6
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1 genotype category over time Case-control study –  
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 3 Report numbers in each exposure category, or  
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 5 summary measures of exposure. Give information  
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 7 separately for cases and controls . Report numbers in  
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 9 each genotype category. Cross-sectional study – Report  
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 11 numbers of outcome events or summary measures.  
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 13 Give information separately for exposed and unexposed  
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 15 groups if applicable. Report outcomes (phenotypes) for  
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 17 each genotype category  
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## 22 Main results

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 25 [#16a](#) Give unadjusted estimates and, if applicable, 6  
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 27 confounder-adjusted estimates and their precision (eg,  
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 29 95% confidence interval). Make clear which  
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 31 confounders were adjusted for and why they were  
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 33 included  
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 37 [#16b](#) Report category boundaries when continuous variables n/a  
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 39 were categorized  
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 42 [#16c](#) If relevant, consider translating estimates of relative risk n/a  
 43  
 44 into absolute risk for a meaningful time period  
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 48 [#16d](#) Report results of any adjustments for multiple 6  
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 50 comparisons  
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## 53 Other analyses

1		<a href="#">#17a</a>	Report other analyses done—e.g., analyses of	n/a
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11		<a href="#">#17c</a>	Report other analyses done—e.g., analyses of	n/a
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17	<b>Key results</b>			
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20		<a href="#">#18</a>	Summarise key results with reference to study	5-6
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26	<b>Limitations</b>			
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29		<a href="#">#19</a>	Discuss limitations of the study, taking into account	11
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31			sources of potential bias or imprecision. Discuss both	
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33			direction and magnitude of any potential bias.	
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37	<b>Interpretation</b>			
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40		<a href="#">#20</a>	Give a cautious overall interpretation considering	7-11
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44			from similar studies, and other relevant evidence.	
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47	<b>Generalisability</b>			
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50		<a href="#">#21</a>	Discuss the generalisability (external validity) of the	7-11
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52			study results	
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56	<b>Funding</b>			
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1                                    [#22](#)    Give the source of funding and the role of the funders            11  
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9    None The STREGA checklist is distributed under the terms of the Creative Commons Attribution  
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For peer review only

# BMJ Open

## Risk Factors for Gastric Cancer and Related Serological Levels in Fujian, China: Hospital-based Case-control Study

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Manuscript ID	bmjopen-2020-042341.R1
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Date Submitted by the Author:	11-Aug-2020
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<b>Primary Subject Heading</b>:	Epidemiology
Secondary Subject Heading:	Gastroenterology and hepatology, Public health
Keywords:	Epidemiology < ONCOLOGY, PREVENTIVE MEDICINE, Gastrointestinal tumours < ONCOLOGY

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4 **Risk Factors for Gastric Cancer and Related Serological Levels in**  
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6 **Fujian, China: Hospital-based Case-control Study**  
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35 PY and LL have equal contribution in this study.  
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## Abstract

**OBJECTIVE** To explore the relationships between gastric cancer and serum PG I, PG II, PG I/II ratio, G-17, and *H. pylori* infection, and to investigate dietary and lifestyle risk factors for gastric cancer in Fujian Province, China.

**DESIGN** A hospital-based, 1:1 matched case-control study.

**SETTING** Patients with newly-diagnosed gastric cancer were recruited from the Fujian Provincial Hospital and the No.900 Hospital of the Joint Support Force of the Chinese People's Liberation Army between July 2014 and December 2016.

**PARTICIPANTS** A total of 180 pairs of gastric cancer patients and control subjects were recruited in the study, including 134 (74.4%) male pairs and 46 (25.6%) female pairs.

**INVESTIGATION AND ANALYSIS MEASURES** Serological indicators were tested with ELISA kits. Dietary, lifestyle and psychological factors were investigated through face-to-face questionnaire. Relationships between gastric cancer and these influencing factors were examined by Chi-square test and conditional logistic regression.

**RESULTS** Serum PG II and G-17 levels and *H. pylori* infection rate were higher in gastric cancer patients than in control subjects ( $P < 0.05$ ), while PG I/II ratio was lower in gastric cancer patients ( $P < 0.05$ ). Serum G-17 levels were higher in patients with corpus gastric cancer than in patients with antral gastric cancer ( $P < 0.05$ ). Serum PG II levels were higher in patients with advanced gastric cancer than in patients with early-stage cancer ( $P < 0.05$ ), however, PG I/II ratio was lower in patients with advanced stage gastric cancer than in patients with early-stage cancer ( $P < 0.05$ ). Eating hot food (OR= 2.32), eating pickled vegetables (OR = 4.05), and often feel troubled (OR = 2.21) were found to significantly increase the risk of gastric cancer (all  $P < 0.05$ ), while

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3 consuming onion or garlic (OR = 0.35), drinking tea (OR = 0.26), eating  
4 fresh fruit (OR = 0.55), and high serum PG I (OR = 0.99) or PG I/II ratio  
5 (OR = 0.73) were found to be protective against gastric cancer.  
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9 **CONCLUSION** Study results showed that serum PG, G-17 and *H. pylori*  
10 antibodies could be useful indicators for early diagnosis of gastric cancer.  
11 Increase in serum G-17 level might indicate the location of gastric cancer.  
12 Increase in serum PG II level and decrease in PG I/II ratio might imply the  
13 clinical stage. Eating hot food, eating pickled vegetables, and often feel  
14 troubled may be risk factors for gastric cancer, while eating fresh fruit,  
15 eating onion or garlic, and drinking tea may be protective factors against  
16 the disease.  
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27 **Key words:** Gastric cancer, Risk factor, Pepsinogen, Gastrin, *Helicobacter*  
28 *pylori*  
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### 32 33 **Strengths and limitations of study**

34 Fujian Province, high in gastric cancer incidences, is an important research  
35 site for exploring the etiologies of gastric cancer.  
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38 This study was one of the few studies to use serum indicators as  
39 independent variables to analyze the risk factors for gastric cancer.  
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42 Strict quality control was conducted in the selection of new cases to ensure  
43 comparable results.  
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46 However, as a case-control study, recall bias was inevitable and trial  
47 studies are required for more accurate results.  
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50 Sample size of this study was not large enough, further studies will recruit  
51 more subjects.  
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## INTRODUCTION

Gastric cancer is a common malignancy in the gastric mucosa and gastric glands in the digestive tract and accounts for a high proportion of cancer deaths in China, especially in Fujian Province. According to the World Cancer Report published by the World Health Organization in 2018<sup>[1]</sup>, there were 1,033,071 new cases of gastric cancer (accounting for 5.7% of all cancer incidence) and 782,685 deaths from it (accounting for 8.2% of all cancer deaths) worldwide. Gastric cancer has high disease burdens<sup>[2]</sup>, ranking second only to lung cancer in terms of the number of deaths<sup>[1]</sup>. In China, there were 456,124 new cases of gastric cancer in 2018, accounting for 44.1% of global incidence<sup>[3]</sup>. In Fujian Province, located in southeast China, gastric cancer accounted for 12.5% of all cancer incidences in 2014<sup>[4]</sup>. Risk factors for gastric cancer such as dietary, lifestyle, and psychological factors are different across China<sup>[5-10]</sup>. The overall objectives of this study were to explore the relationship between gastric cancer and serum PG I , PG II , PG I / II ratio , G-17 and *H.pylori* infection, and to investigate the risk factors for gastric cancer in Fujian.

## METHODS

### *Study design*

This was a hospital-based, 1:1 matched case-control study, performed in accordance to the Declaration of Helsinki of the World Medical Association and approved by the Ethics Committee of the Fujian Center for Disease Control and Prevention. Informed consents were obtained from all recruited subjects. Subjects' dietary and lifestyle data were obtained through face-to-face interviews by trained investigators, and blood samples were collected for the test of serum markers.

### *Case and control groups*

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3 From July 2014 to December 2016, patients with newly-diagnosed gastric  
4 cancer were recruited from the Fujian Provincial Hospital and the No.900  
5 Hospital of the Joint Support Force of the Chinese People's Liberation  
6 Army. Control subjects were recruited simultaneously from the Medical  
7 Examination Center at the same hospital. Gastric patients and control  
8 subjects were 1:1 matched according to gender and similar age within 3  
9 years. Inclusion criteria for the gastric cancer group were: newly diagnosed  
10 of gastric cancer by gastroscopy and pathology, with no medication history  
11 of antibiotics, proton pump inhibitors, or H receptor antagonists. Patients  
12 with prior surgeries or chemotherapies were also excluded. Inclusion  
13 criteria for the control group were: no diagnosis or symptoms of chronic  
14 stomach diseases, and no mental retardation or emotional blockages. All  
15 subjects had lived in Fujian Province for more than 10 years.

### 31 ***Risk Factor Survey***

32 Data of risk factors were collected by trained investigators through  
33 face-to-face interviews with the subjects, using a consolidated  
34 questionnaire. The survey contents included general information, dietary  
35 habits(i.e., breakfast consumption, meal duration, intake frequencies of  
36 onion or garlic, spicy food, hot food, green vegetables, fresh fruit, dairy,  
37 pickled vegetables, and fish sauce), lifestyle habits (i.e., smoking, alcohol  
38 consumption, and tea consumption), and psychological factors (i.e.,  
39 personality type, adaptability, feels about life, and interpersonal skills).

### 51 ***Serum sampling***

52 A total of 5 mL of fasting venous blood was collected from each subject,  
53 and was centrifuged at 3000 r/min for 10 min to extract the serum, which  
54 was then stored at -80°C for further testing. Serum PG I, PG II, and G-17  
55 levels were tested using ELISA kits from BIOHIT, Finland (batch numbers  
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of 19PA1505, 21PB1508, and 19GC1506, respectively). Antibodies to *H. pylori* were assessed using ELISA kits from the AI Kang Company of China (lot number 201510087).

### ***Definitions and variables***

Dietary intake frequencies were classified as: never or seldom consumption (no more than once per week), occasional consumption (two to six times per week), and regular consumption (seven or more times per week). Smokers were defined as subjects who had smoked more than 100 cigarettes overall. Alcohol consumers were defined as subjects who had been drinking any alcohol at least once a week for more than six months. Tea consumers were defined as subjects who had been drinking any tea at least once a week for more than six months.

According to the calculated cut-off value, an optical density (OD) value of the sample  $>1.1 \times$  the cut-off value was considered *H. pylori*-positive, while an OD  $<0.9 \times$  the cut-off value was considered *H. pylori*-negative.

### ***Statistical analysis***

Data were inputted by the double-entry method and tested for consistency using Epidata 3.1. The SPSS version 24.0 software package was used for conducting Chi-squared tests on the demographic information, and for conducting the single and multivariate conditional logistic regression analyses on the other information to determine the odds ratio (OR) and 95% confidence interval (CI). Test significance level was set at 0.05.

### ***Patient and public involvement***

Dr Kazuo Aoki, a Japanese expert, was involved in designing the study due to the growing concern among people with Gastric Cancer both in

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Japan and China. This study was undertaken in the two hospitals with the First-class at Grade 3 in Fujian province in order to ensure the quality of research and access to adequate and widely sourced cases. The findings of this study will be published to inform the public about the risk factors for gastric cancer and some of the inspection results were fed back to the subjects through the form of inspection report.

## RESULTS

### *Demographic information*

A total of 180 pairs of gastric cancer patients and control subjects were recruited in this study, of which 134 pairs (74.4%) were male subjects and 46 pairs (25.6%) were female subjects. The average ages of the cancer group and the control group were  $61.0 \pm 10.8$  and  $60.1 \pm 10.9$  years, respectively. The two groups were not significantly different in age, marital status, education, or labor intensity (all  $P \geq 0.05$ ), however the occupation compositions were different.

### *Dietary habits, lifestyles and personality traits*

As shown in Table 1, there were significant differences in the dietary habits between cases and controls. Lifestyles, such as smoking, alcohol consumption, and tea consumption, of the two groups were also significantly different (Table 2).

Personality types, adaptability, feelings about life, irritability, and interpersonal skills were also significantly different between cases and controls (Table 2).

### *Serum PG I, PG II, PG I/II ratio and G-17 levels*

Serum PG I, PG II, and G-17 levels did not fit normal distributions, nor did

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3 the PG I/II ratio; therefore median values were used to indicate central  
4 tendencies and the P25 and P75 percentiles were used to indicate  
5 dispersion tendencies. Serum PG II and G-17 levels in gastric cancer  
6 patients were higher than those in the control subjects ( $P < 0.05$ ), while the  
7 PG I/II ratio was lower in the patients ( $P < 0.05$ ); PG I levels were not  
8 statistically different between the two groups. The results of the serum  
9 markers are summarized in Table 3.  
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### 19 ***H. pylori infection***

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21 As shown in Table 4, 66.67% of gastric cancer patients were *H.*  
22 *pylori*-positive, which was significantly higher than that of the control  
23 group (54.44%,  $P < 0.05$ ). The positive rate of *H. pylori* was higher in  
24 male gastric cancer patients than in controls ( $P < 0.05$ ), however no  
25 significant differences were found between female cases and controls or  
26 among age groups ( $P > 0.05$ ).  
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### 36 ***Serological parameters with different locations of gastric cancer***

37 Serum G-17 levels were higher in patients with gastric corpus cancer than  
38 in patients with gastric antrum cancer ( $P < 0.05$ ), but not significantly  
39 different among patients with other tumor locations ( $P > 0.05$ ; Table 5).  
40 Serum PG I, PG II levels, and the PG I/II ratio were not statistically  
41 different among patients with different tumor locations ( $P > 0.05$ ; Table 5).  
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### 50 ***Serological parameters with different clinical stages of gastric cancer***

51 As shown in Table 6, serum PG II levels in patients with advanced gastric  
52 cancer were higher than in patients with early-stage gastric cancer  
53 ( $P < 0.05$ ). However, the PG I/II ratio was lower in patients with advanced  
54 cancer than in patients with early-stage disease ( $P < 0.05$ ). Serum PG I and  
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3 G-17 levels were not significantly different between the two different  
4 clinical stages ( $P > 0.05$ ).  
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### 10 ***Multivariate analysis***

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12 Multivariate conditional logistic regression analysis was performed with  
13 gastric cancer as the independent variable, and the dietary/lifestyle habits,  
14 psychological factors, serum PG I level, serum PG II level, PG I/II ratio,  
15 serum G-17 level, and *H. pylori* infection as dependent variables. As  
16 shown in Table 7, eating hot food, consumption of pickled vegetables, and  
17 often feel troubled may be risk factors for gastric cancer. However, the  
18 consumption of fresh fruit, onion or garlic, drinking tea, and elevated  
19 serum PG I levels and PG I/II ratio might be protective factors for gastric  
20 cancer. Other factors examined in this study had no statistically significant  
21 effect on gastric cancer ( $P > 0.05$ ).  
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### 40 **DISCUSSION**

41 Overall, this study has found that gastric cancer was related to several  
42 dietary and lifestyle factors, the changes in serum PG I/II ratio and G-17,  
43 and the infection rate of *H. pylori*.  
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50 Multivariate conditional logistic regression analysis indicated that the  
51 consumption of pickled vegetables may be a risk factor for gastric cancer.  
52 Pickles are high in salt and may damage the gastric mucosa, reduce gastric  
53 acid secretion, and inhibit the synthesis of prostaglandin E, which  
54 enhances gastric mucosa resistance<sup>[11]</sup>. In addition, pickles contain high  
55 amount of nitrate and nitrite, which can be converted to N-nitrosamide, a  
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3 carcinogen, under gastric acid conditions<sup>[12]</sup>. In an area with high incidence  
4 of gastric cancer in northwest China's Gansu Province<sup>[13]</sup>, where people  
5 often consume pickled vegetables as substitutions of fresh vegetables in  
6 winters, 65%-75% of pickles had detectable levels of nitrite and all had  
7 tested positive for nitrate; and the levels of nitrite and nitrate in the gastric  
8 juice were significantly higher in people often consume pickled vegetables  
9 than in people who seldom consume pickled vegetables. Nitrate and nitrite  
10 levels in the gastric juice were associated with the frequency of pickle  
11 intake, which in turn was associated with gastric cancer. This study also  
12 found that regular pickle intake (seven or more times per week) increased  
13 the risk of gastric cancer (OR = 4.05; 95% CI: 2.01–8.02).  
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28 Study results also indicated that tea consumption was a protective factor  
29 against gastric cancer. Tie Guanyin, one of the most popular teas in Fujian,  
30 is rich in tea polyphenols. Tea polyphenols can act as strong antioxidants  
31 to effectively remove free radicals. They can also regulate carcinogen  
32 metabolizing enzymes, inhibit the nitrosation reactions, block the  
33 expression of tumor genes, enhance immunity, and therefore act as potent  
34 anti-cancer agents<sup>[14]</sup>. However, a meta-analysis of 12 cohort studies from  
35 China, Japan, and America suggested that drinking green tea ( $\geq 5$  cups per  
36 day) was not correlated with the incidence of gastric cancer ( $P > 0.05$ )<sup>[15]</sup>.  
37 Stratified sex analyses showed that drinking  $\geq 5$  cups of green tea per day  
38 was a protective factor against gastric cancer in females, but not in  
39 males<sup>[15]</sup>. In this study, results showed that drinking tea lowered the risk of  
40 gastric cancer (OR = 0.26, 95% CI: 0.10–0.67), confirming the results  
41 shown by Li-Na Mu, et al<sup>[16]</sup>. Our findings also indicated that drinking tea  
42 may be an independent protective factor against gastric cancer, however  
43 other factors, such as the type of tea and the water temperature, might  
44 affect this relationship and warrant further investigation.  
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5 As the medical model shifts from "biomedical" to "bio-psycho-social"  
6 paradigm, the relationship between psychological factors and tumor  
7 gradually catches the attention of numerous scholars in recent years. A  
8 meta-analysis including 5,265 cases of gastric cancer and 12,539 controls  
9 from 22 domestic studies found that long-term stress had adverse effects  
10 on gastric cancer (merged OR of 2.91, 95% CI: 2.03–4.19)<sup>[17]</sup>. Another  
11 study showed that psychological factors were associated with the incidence  
12 of gastric cancer and that history of metal stimulus increased the risk of  
13 gastric cancer significantly (OR = 1.74, 95% CI: 1.11–2.74)<sup>[18]</sup>. People who  
14 often feel anxious/irritable or experience hardships in life have altered  
15 hormone levels, which in turn affect their immune system. In particular,  
16 epinephrine and norepinephrine are released under stress or anxiety,  
17 causing decrease in natural killer cells, reduction in immunity functions  
18 and acceleration in the initiation and progression of malignancies<sup>[19]</sup>.  
19 Similar to previous studies, this study also found that often feel troubled  
20 was related to gastric cancer (OR = 2.21, 95% CI: 1.23–3.98) in our  
21 subjects.  
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41 Recent studies indicated that low serum PG I and PG I/II ratio were  
42 strongly associated with gastric cancer, while the relationship between PG  
43 II and gastric cancer was not as obvious. PG I is primarily secreted by  
44 chief cells and mucous neck cells in the fundic glands, whereas PG II is  
45 secreted by all gastric glands and the proximal duodenal mucosa<sup>[20]</sup>. When  
46 chronic *H. pylori* infection with chronic atrophic gastritis (CAG) extends  
47 from antrum to corpus of stomach, chief cells are replaced by pyloric  
48 glands. Therefore, the concentration of serum PG I will decrease due to  
49 damaged secretion ability of gastric mucosa, however the secretion of PG  
50 II remains, resulting in a lowered PGI/II ratio, which would reflect the  
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3 severity of CAG. Patients with premalignant lesions, such as CAG or  
4 dysplasia, have considerable higher risks for developing gastric cancer.  
5 Our previous study<sup>[21]</sup> explored the changes of serum PG levels in different  
6 gastric cancer states. Results found significant differences in serum PG I ,  
7 PG II , and PGI/II ratio among the control group, the atrophic gastritis  
8 group, and the gastric cancer group (all  $P < 0.001$ ). Serum PG I level was  
9 lower in the gastric cancer group than in the other two groups, and was  
10 also lower in the atrophic gastritis group than in the control group, both  
11 differences were statistically significant ( $P < 0.05$ ). Serum PGI/II ratio in the  
12 gastric cancer group was lower than in the control group and the atrophic  
13 gastritis group, and was also lower in the atrophic gastritis group than in  
14 the control group, both differences were statistically significant ( $P < 0.05$ ) .  
15 In a study in Japan including 10,996 healthy residents who had underwent  
16 gastroscop examinations and tested for serum PG, the incidence of gastric  
17 cancer was higher in subjects with lower serum PG I levels and PG I/II  
18 ratios<sup>[22]</sup>. In our study, single conditional logistic regression results showed  
19 that serum PG II was higher in gastric cancer patients than in control  
20 subjects ( $P < 0.05$ ), PG I/II ratio was lower in gastric cancer patients than in  
21 control subjects ( $P < 0.05$ ), and PG I levels in the two groups were not  
22 significantly different ( $P > 0.05$ ), which was in agreement with the study  
23 conducted by Cao, et al.<sup>[23]</sup>. Moreover, our results showed that after  
24 controlling for other risk factors, decreased levels of serum PG I and PG  
25 I/II ratios might be independent risk factors for gastric cancer, which was  
26 in agreement with the results of a nested case-control study conducted by  
27 Kurilovich, et al.<sup>[24]</sup>.

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Qin Cao et al<sup>[25]</sup>. found that serum PG I and PG II levels were lower in  
patients with advanced-stage gastric cancer than in those with early-stage

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3 disease ( $P < 0.05$ ), which was consistent with the results observed in the  
4 elderly gastric cancer patients (aged  $>60$  years) by Wei Huang, et al<sup>[26]</sup>. In  
5 this study, serum PG II levels were significantly higher in advanced stage  
6 gastric cancer patients than those with early-stage disease ( $P < 0.05$ ), PG  
7 I/II ratio was significantly lower in advanced stage gastric cancer patients  
8 ( $P < 0.05$ ). These results demonstrated that serum PG II level and PG I/II  
9 ratio were different at different clinical stages of gastric cancer. Therefore,  
10 the elevation of serum PG II levels and reduced PG I/II ratio may be  
11 indicators of the clinical stages of gastric cancer.  
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24 Gastrin, a peptide hormone synthesized and secreted by the G cells of the  
25 pyloric antrum of the stomach, was first discovered in 1906<sup>[27]</sup>, and is now  
26 well known for its multiple subtypes<sup>[28]</sup>. 90% of the intra-corporeal gastrin  
27 is G-17, which is one of the main forms in gastrin circulation, and the  
28 change of which can indicate the impairment of gastric mucosa  
29 functions<sup>[29]</sup>. Li Wang et al. <sup>[30]</sup> had used immunohistochemical method to  
30 detect serum G-17, and found it had increased concentrations in superficial  
31 gastritis, para-cancerous tissues and gastric cancer cells. In addition, serum  
32 G-17 levels were found to be higher in patients with pre-operative gastric  
33 cancer than in healthy controls ( $P < 0.05$ ), and were also elevated in  
34 patients with advanced clinical stage of gastric cancer<sup>[31]</sup>.  
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48 Our finding was coincided with the study conducted by Rui-Xin Lin, et al.,  
49 that serum G-17 in patients with gastric cancer was higher than in the  
50 controls ( $P < 0.05$ ) <sup>[32]</sup>. This indicated that increased serum G-17 levels  
51 were associated with gastric cancer and hypergastrinemia. In terms of the  
52 potential mechanism of action, animal experiments with overexpressed  
53 G-17 indicated that gastrin could influence gastric carcinogenesis<sup>[33]</sup>.  
54 Serum G-17 levels were found to be higher in patients with gastric corpus  
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3 cancer than in patients with gastric cancer in other locations ( $P < 0.05$ ),  
4 which was similar to the findings described by Hu et al<sup>[34]</sup>. This may be  
5 related to the the vagus nerve's depressive effect on G-17 secretion. Serum  
6 G-17 levels were more clearly elevated when cancer invaded the gastric  
7 body, which could damage the vagus nerve and inhibit G-17 secretion<sup>[35]</sup>.  
8 Therefore, our results suggested that changes in serum G-17 levels in  
9 gastric cancer patients may be indicative of cancer location.  
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19 *H. pylori* infection was a risk factor for gastric cancer. The International  
20 Agency for Research on Cancer (IARC) formally identified *H. pylori* as  
21 Class I carcinogen in 1994. In addition, a 7.8-year prospective study of  
22 1,526 Japanese patients with gastric diseases showed that patients with *H.*  
23 *pylori* infection had diseases such as gastric atrophy, intestinal metaplasia,  
24 as well as precancerous lesions<sup>[36]</sup>. Moreover, a study conducted in  
25 Changle City, Fujian Province, China, showed that although patients with  
26 precancerous gastric lesions were unable to avoid gastric cancer, *H. pylori*  
27 eradication could reduce the risk of gastric cancer in people without  
28 precancerous lesions<sup>[37]</sup>. The *H. pylori* infection rate in the control group in  
29 the current study was 54.4%, which was close to the number found in  
30 natural population (54.76%)<sup>[38]</sup>. However, the infection rate in gastric  
31 cancer patients was 66.7%, similar to the results observed by Xue-Yuan  
32 Cao, et al<sup>[39]</sup>, suggesting that *H. pylori* infection was more common in  
33 gastric cancer patients. In addition, the *H. pylori* infection rate in the  
34 gastric cancer group was significantly higher than in the control group in  
35 male subjects ( $P < 0.05$ ), whereas no such difference was observed in  
36 females, which might be associated with a lower prevalence of *H. pylori*  
37 infection in women<sup>[40]</sup>.  
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There were some strengths in this study. Firstly, Fujian Province is an area

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3 with high incidence of gastric cancer in China. According to the report of  
4 Fujian Province, the incidence of gastric cancer collected from tumor  
5 registration areas in Fujian Province in 2017 was 31.68/100,000,  
6 accounting for 12.47% of all new cancer cases, ranking the third in cancer  
7 incidence; gastric cancer mortality rate was 25.90/100,000, accounting for  
8 14.74% of all cancer deaths, also ranking the third in cancer deaths.  
9 Therefore, Fujian is an important research site for exploring the causes of  
10 gastric cancer. Secondly, strict quality control was conducted in this study  
11 in the selection of new cases to make sure the results be comparable.  
12 Taking into account the effects of proton pump inhibitors and H receptor  
13 antagonists on serum markers, patients who had taken these drugs within a  
14 week before recruiting were excluded. With strictly controlling the quality  
15 of selected cases, the difficulty in obtaining cases also increased. Thirdly,  
16 this study was one of the few studies to use serum indicators as  
17 independent variables to explore the risk factors for gastric cancer.  
18 However, several limitations should be considered. First, for a case-control  
19 study, the causal association between dietary/lifestyle habits and gastric  
20 cancer could not be precisely identified. Second, the consumptions of  
21 alcohol, tea, and pickled vegetables were self-reported. Subjects often had  
22 difficulties in recalling food consumptions and it was also hard to estimate  
23 the accurate amount of consumption. Therefore, recall bias and  
24 misclassification bias were inevitable. Randomized Control Trial studies  
25 shall be conducted for more accurate results. Third, the sample size was  
26 relatively small. China has high incidence of gastric cancer and provides  
27 favorable conditions for studying it. We plan to expand the sample size in  
28 our further researches on gastric cancer.  
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### 57 ***Conclusion***

58 In conclusion, this study indicated that serum PG and G-17 levels, as well  
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3 as the detection of *H. pylori* antibodies, could be useful indicators of  
4 gastric cancer location and cancer stage. Elevation of serum G-17 levels  
5 may be indicative of the gastric cancer location, while the increase in the  
6 PG II level and the reduction in the PG I/II ratio may imply the clinical  
7 stage. Poor dietary habits, salty food, and often feel troubled may be risk  
8 factors for gastric cancer, while eating fresh fruit, onion or garlic, and  
9 drinking tea may help protect against this disease.  
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24 assistance from the hospital staff in collecting blood samples.  
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### 31 **Footnotes**

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33 **Contributions:** PY and LL are joint first authors. KZ and WW obtained  
34 funding. KZ designed the study. LL drafted the manuscript. PY contributed  
35 to the interpretation of the results and critical revision of the manuscript for  
36 important intellectual content. WW, SW, LH collected the data. BW and T  
37 C detected serological indicators. XL analyzed the data. All authors have  
38 read and approved the final manuscript. KZ and LC are the study  
39 guarantors.  
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**Competing interests:** We have read and understood BMJ policy on declaration of interests and declare that we have no competing interests.

**Patient consent:** All subjects signed the informed consent form.

**Ethical approval:** This study was approved by the ethical reviews committee at Fujian Center for Disease Control and Prevention.

**Data sharing:** Data are stored in Fujian Center for Disease Control and Prevention, No.76 Jintai Road, Gulou District, Fuzhou, China. Data are available upon request to Kui-cheng Zheng; Email address: zkcfdc@sina.com.

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**Table 1 Single conditional logistic regression analysis on dietary factors, *n*(%)**

Factor	Frequency*	Cases	Control	<i>P</i>	OR	95% CI
<b>Breakfast consumption</b>	+	112 (62.22)	153 (85.00)		1.00	
	++	38 (21.11)	18 (10.00)	<0.01	2.84	(1.54,5.25)
	+++	30 (16.67)	9 (5.00)	<0.01	4.78	(2.10,10.87)
<b>Meal duration</b>	≥20 min	24 (13.33)	46 (25.56)		1.00	
	10–20 min	50 (27.78)	70 (38.89)	0.393	1.32	(0.70,2.52)
	<20 min	106 (58.89)	64 (35.56)	<0.01	2.97	(1.63,5.40)
<b>Onion or garlic</b>	+	73 (40.56)	49 (27.22)		1.00	
	++	66 (36.67)	56 (31.11)	0.29	0.74	(0.42,1.30)
	+++	41 (22.78)	75 (41.67)	<0.01	0.36	(0.21,0.63)
<b>Spicy food</b>	+	104 (57.78)	125 (69.44)		1.00	
	++	45 (25.00)	48 (26.67)	0.71	1.11	(0.64,1.93)
	+++	31 (17.22)	7 (3.89)	<0.01	5.95	(2.28,15.53)
<b>Hot food</b>	+	76 (42.22)	114 (63.33)		1.00	
	++	47 (26.11)	47 (26.11)	0.25	1.35	(0.81,2.27)
	+++	57 (31.67)	19 (10.56)	<0.01	5.63	(2.72,11.66)
<b>Green vegetables</b>	+	35 (19.44)	15 (8.33)		1.00	
	++	70 (38.9)	46 (25.56)	0.34	0.71	(0.36,1.43)
	+++	75 (41.67)	119 (66.11)	<0.01	0.29	(0.15,0.56)
<b>Fresh fruit</b>	+	115 (63.89)	43 (23.89)		1.00	
	++	42 (23.33)	78 (43.33)	<0.01	0.20	(0.11,0.37)
	+++	23 (12.78)	59 (32.78)	<0.01	0.16	(0.08,0.32)
<b>Dairy</b>	+	133 (73.89)	82 (45.56)		1.00	
	++	32 (17.78)	53 (29.44)	<0.01	0.28	(0.15,0.53)
	+++	15 (8.33)	45 (25.00)	<0.01	0.17	(0.08,0.36)
<b>Pickled vegetables</b>	+	55 (30.56)	125 (69.44)		1.00	
	++	65 (36.11)	45 (25.00)	<0.01	2.67	(1.60,4.49)
	+++	60 (33.33)	10 (5.56)	<0.01	15.27	(5.91,39.49)
<b>Fish sauce</b>	+	109 (60.56)	135 (75.00)		1.00	
	++	30 (16.67)	32 (17.78)	0.96	1.02	(0.56,1.83)
	+++	41 (22.78)	13 (7.22)	<0.01	3.81	(1.89,7.65)

\* “+”, never or seldom consuming; “++”, sometimes consuming; “+++”, regularly consuming.

**Table 2 Single conditional logistic regression analysis on lifestyle habits and personality factors, *n*(%)**

Factors	classified	Cases	Controls	<i>P</i>	OR	95% CI
Smoker	No	89 (49.44)	116 (64.44)		1.00	
	Yes	91 (50.56)	64 (35.56)	0.01	2.67	(1.51,4.77)
Alcohol consumption	No	118 (65.56)	140 (77.78)		1.00	
	Yes	62 (34.44)	40 (22.22)	0.01	1.85	(1.15,2.98)
Tea consumption	No	132 (73.33)	102 (56.67)		1.00	
	Yes	48 (26.67)	78 (43.33)	0.01	0.43	(0.23,0.71)
Personality type	Type A	98 (54.44)	78 (43.33)		1.00	
	Intermediate	36 (20.00)	41 (22.78)	0.15	0.66	(0.38,1.15)
	Type B	46 (25.56)	61 (33.89)	0.04	0.59	(0.36,0.97)
Adaptability	Easy	56 (31.11)	61 (33.89)		1.00	
	Between	72 (40.00)	91 (50.56)	0.58	0.88	(0.55,0.41)
	Difficult	52 (28.89)	28 (15.56)	0.03	1.93	(1.08,3.45)
How feel about life	Feel happy	33 (18.33)	63 (35.00)		1.00	
	Feel troubled	71 (39.44)	78 (43.33)	0.03	1.85	(1.06,3.22)
	Often feel troubled	76 (42.22)	39 (21.67)	<0.01	4.16	(2.21,7.86)
Irritable	No	84 (46.67)	110 (61.11)		1.00	
	Yes	96 (53.33)	70 (38.89)	0.04	2.00	(1.25,3.20)
Interpersonal skills	Good	70 (38.89)	96 (53.33)		1.00	
	General	86 (47.78)	75 (41.67)	0.06	1.53	(0.10,2.38)
	Poor	24 (13.33)	9 (5.00)	0.00	3.79	(1.57,9.12)

**Table 3 Comparisons of serum PG I , PG II, PG I/II ratio and G-17 between cases and controls, M(p25,p75)**

Type	Total (n)	PG I ( $\mu\text{g/L}$ )	PG II ( $\mu\text{g/L}$ )	PG I/II ratio	G-17 (pmol/L)
Cases	180	115.56 (68.84,177.47)	17.85 (10.58,8.74)	6.58 (4.95,8.48)	7.62 (3.96,14.24)
Controls	180	117.69 (89.83,145.32)	11.19 (7.45,17.37)	9.60 (7.35,13.45)	3.54 (2.24,7.13)
<i>Z</i>	—	<b>0.26</b>	<b>5.48</b>	<b>8.06</b>	<b>6.01</b>
<i>P</i>	—	<b>0.78</b>	<b>&lt;0.01</b>	<b>&lt;0.01</b>	<b>&lt;0.01</b>

Note: PG is pepsinogen, and G-17 is Gastrin-17

**Table 4. Comparison of the H. pylori positive rates between cases and controls, n(%)**

Type	Cases	Controls	$\chi^2$	<i>P</i>
<b>Total</b>	120(66.67)	98(54.44)	5.63	0.02
<b>Gender</b>				
<b>Male</b>	94(52.22)	77(42.78)	4.88	0.03
<b>Female</b>	26(14.44)	21(11.67)	0.97	0.33
<b><math>\chi^2</math></b>	2.65	1.20		
<b><i>P</i></b>	0.10	0.27		
<b>Age, years</b>				
<b>&lt;50</b>	20(11.11)	16(8.89)	0.86	0.36
<b>50–65</b>	51(28.33)	42(23.33)	3.16	0.08
<b>≥65</b>	49(27.22)	40 (22.22)	1.57	0.21
<b><math>\chi^2</math></b>	<b>0.55</b>	<b>1.28</b>		
<b><i>P</i></b>	<b>0.76</b>	<b>0.53</b>		

**Table 5. Comparison of the serological parameters among patients with different locations of gastric cancer, M(p25,p75)**

Location	Cases (n)	PG I ( $\mu\text{g/L}$ )	PG II ( $\mu\text{g/L}$ )	PG I/II ratio	Gastrin-17 (pmol/L)
<b>Cardia</b>	19	116.15 (61.42,182.66)	17.27 (11.74, 28.83)	6.41 (5.09, 8.01)	6.35 (2.36, 10.75)
<b>Fundus</b>	17	81.26 (53.44, 197.57)	20.72 (9.32, 33.06)	5.22 (3.29, 8.41)	8.14 (3.85, 12.50)
<b>Gastric corpus</b>	55	118.23 (66.41, 175.04)	19.43 (12.25, 28.94)	5.69 (3.78, 8.23)	12.00 (6.58, 19.74)
<b>Gastric antrum</b>	70	118.65 (78.87, 173.66)	16.79 (10.42, 27.49)	7.05 (5.45, 9.07)	6.12 (3.84, 12.67)
<b>Gastric angle</b>	19	116.00 (68.13, 195.76)	15.89 (7.39, 29.28)	7.25 (5.63, 8.10)	6.44 (2.58, 14.81)
<b><math>\chi^2</math></b>		<b>1.58</b>	<b>1.59</b>	<b>7.41</b>	<b>10.79</b>
<b><i>P</i></b>		<b>0.81</b>	<b>0.81</b>	<b>0.12</b>	<b>0.03</b>

Note: PG is pepsinogen

**Table 6. Comparison of the serological parameters in patients with different clinical stages of gastric cancer, M(p25,p75)**

Clinical stage	Cases (n)	PG I ( $\mu\text{g/L}$ )	PG I I ( $\mu\text{g/L}$ )	PG I/II ratio	Gastrin-17 (pmol/L)
Early	49	93.07 (68.39, 171.64)	13.81 (7.42, 23.92)	6.95 (5.71, 9.73)	5.93 (2.85, 12.75)
Advanced	131	118.23 (69.43, 181.24)	19.43 (12.51, 30.41)	6.10 (4.50, 8.03)	8.19 (4.29, 14.39)
<b>Z</b>		<b>0.88</b>	<b>2.33</b>	<b>2.43</b>	<b>1.75</b>
<b>P</b>		<b>0.38</b>	<b>0.02</b>	<b>0.02</b>	<b>0.08</b>

Note: PG is pepsinogen

**Table 7. Multivariate conditional logistic regression analysis.**

Factors	$\beta$	S.E.	Wald	P	OR	95% CI
Hot food	0.84	0.31	7.63	0.006	2.32	(1.28,4.23)
Onion or garlic	-1.05	0.33	10.11	0.001	0.35	(0.18,0.67)
Fresh fruit	-0.60	0.29	4.34	0.037	0.55	(0.31,0.97)
Pickled vegetables	1.39	0.35	15.44	<0.001	4.05	(2.01,8.03)
Tea consumption	-1.35	0.49	7.77	0.005	0.26	(0.10,0.67)
Often feel troubled	0.79	0.30	7.03	0.008	2.21	(1.23,3.98)
PG I	-0.01	0.00	3.96	0.047	0.99	(0.99,1.00)
PG I/II ratio	-0.32	0.07	20.82	<0.001	0.73	(0.63,0.83)

# Reporting checklist for genetic association study.

Based on the STREGA guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STREGA reporting guidelines, and cite them as:

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		Page
	Reporting Item	Number
<b>Title and abstract</b>		
Title	<a href="#">#1a</a> Indicate the study's design with a commonly used term in the title or the abstract	1

1	Abstract	<a href="#">#1b</a>	Provide in the abstract an informative and balanced	2-3
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4			summary of what was done and what was found	
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6	<b>Background/rationale</b>			
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10		<a href="#">#2</a>	Explain the scientific background and rationale for the	3-4
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15	<b>Objectives</b>			
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18		<a href="#">#3</a>	State specific objectives, including any prespecified	2
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20			hypotheses. State if the study is the first report of a	
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26	<b>Study design</b>			
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29		<a href="#">#4</a>	Present key elements of study design early in the paper	2
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35		<a href="#">#5</a>	Describe the setting, locations, and relevant dates,	2
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43	<b>Eligibility criteria</b>			
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46		<a href="#">#6a</a>	Cohort study – Give the eligibility criteria, and the	4
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48			sources and methods of selection of participants.	
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sectional study – Give the eligibility criteria, and the sources and methods of selection of participants. Give information on the criteria and methods for selection of subsets of participants from a larger study, when relevant.

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23	<b>Variables</b>		
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26		<a href="#">#8b</a>	Describe laboratory methods, including source and 5
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29			version), error rates and call rates. State the laboratory /
30			centre where genotyping was done. Describe
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1	<a href="#">#12a</a>	Describe all statistical methods, including those used to	5
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14	<a href="#">#12c</a>	Explain how missing data were addressed	n/a
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17	<a href="#">#12d</a>	If applicable, explain how loss to follow-up was	n/a
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26	<a href="#">#12f</a>	State whether Hardy-Weinberg equilibrium was	n/a
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53	<b>Participants</b>		
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56	<a href="#">#13a</a>	Report numbers of individuals at each stage of study—	5-6
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confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable. Report numbers of individuals in whom genotyping was attempted and numbers of individuals in whom genotyping was successful.

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21	<b>Descriptive data</b>		
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36		<a href="#">#14b</a>	Indicate number of participants with missing data for n/a
37			
38			each variable of interest
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40			
41			
42		<a href="#">#14c</a>	Cohort study – Summarize follow-up time, e.g. average n/a
43			
44			and total amount.
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46			
47	<b>Outcome data</b>		
48			
49			
50		<a href="#">#15</a>	Cohort study Report numbers of outcome events or 5-6
51			
52			summary measures over time. Give information
53			separately for exposed and unexposed groups if
54			applicable. Report outcomes (phenotypes) for each
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1 genotype category over time Case-control study –  
 2 Report numbers in each exposure category, or  
 3 summary measures of exposure. Give information  
 4 separately for cases and controls . Report numbers in  
 5 each genotype category. Cross-sectional study – Report  
 6 numbers of outcome events or summary measures.  
 7 Give information separately for exposed and unexposed  
 8 groups if applicable. Report outcomes (phenotypes) for  
 9 each genotype category  
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## 22 Main results

- 23  
 24  
 25 [#16a](#) Give unadjusted estimates and, if applicable, 6  
 26 confounder-adjusted estimates and their precision (eg,  
 27 95% confidence interval). Make clear which  
 28 confounders were adjusted for and why they were  
 29 included  
 30  
 31  
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 36  
 37 [#16b](#) Report category boundaries when continuous variables n/a  
 38 were categorized  
 39  
 40  
 41  
 42 [#16c](#) If relevant, consider translating estimates of relative risk n/a  
 43 into absolute risk for a meaningful time period  
 44  
 45  
 46  
 47  
 48 [#16d](#) Report results of any adjustments for multiple 6  
 49 comparisons  
 50  
 51

## 52 Other analyses

1		<a href="#">#17a</a>	Report other analyses done—e.g., analyses of	n/a
2				
3			subgroups and interactions, and sensitivity analyses	
4				
5				
6		<a href="#">#17b</a>	Report other analyses done—e.g., analyses of	n/a
7				
8			subgroups and interactions, and sensitivity analyses	
9				
10				
11		<a href="#">#17c</a>	Report other analyses done—e.g., analyses of	n/a
12				
13			subgroups and interactions, and sensitivity analyses	
14				
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16				
17	<b>Key results</b>			
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19				
20		<a href="#">#18</a>	Summarise key results with reference to study	5-6
21			objectives	
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26	<b>Limitations</b>			
27				
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29		<a href="#">#19</a>	Discuss limitations of the study, taking into account	11
30			sources of potential bias or imprecision. Discuss both	
31			direction and magnitude of any potential bias.	
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36	<b>Interpretation</b>			
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39		<a href="#">#20</a>	Give a cautious overall interpretation considering	7-11
40			objectives, limitations, multiplicity of analyses, results	
41			from similar studies, and other relevant evidence.	
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47	<b>Generalisability</b>			
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49				
50		<a href="#">#21</a>	Discuss the generalisability (external validity) of the	7-11
51			study results	
52				
53				
54				
55				
56	<b>Funding</b>			
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1                                    [#22](#)    Give the source of funding and the role of the funders            11  
2  
3  
4                                    for the present study and, if applicable, for the original  
5  
6                                    study on which the present article is based  
7

8  
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