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Article

Prevalence of common upper gastrointestinal diseases in Chinese adults aged 18–64 years

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ABSTRACT

To investigate the prevalence of gastroesophageal reflux disease (GERD), reflux esophagitis (RE), digestive ulcer gastric ulcer (GU), duodenal ulcer (DU), and *Helicobacter pylori* infection in Chinese adults aged 18–64 years and their associated factors, a community-based cross-sectional study using a stratified multistage sampling method was conducted. A standardized questionnaire survey, the ^{13}C-urea breath test, and gastroscopy were performed. Weighted methods were used to estimate the prevalence of diseases or infection mentioned above and their risk factors. Finally, 27,637 participants aged 18–64 years were enrolled from 2017 to 2018. The prevalence (95% confidence interval) of GERD, RE, GU, DU, and *H. pylori* infection was estimated to be 10.5% (7.8%–14.2%), 5.4% (3.9%–7.3%), 2.5% (1.7%–3.7%), 4.5% (3.6%–5.4%), and 41.5% (36.7%–46.4%), respectively. The fraction of *H. pylori* infection reached 58.6% and 61.1% among the GU and DU patients, respectively. Weighted multivariable logistic regression models showed that GERD, RE, and GU shared the common risk factors of age and obesity. Dose-response relationships were observed between smoking and all four diseases, as well as alcohol consumption and GERD and *H. pylori* infection. Northwest China had the highest prevalence of GERD (23.9%), RE (8.7%), GU (7.8%), DU (7.3%), and *H. pylori* infection (63.6%); however, the southwest region had the highest prevalence of GU but the lowest of DU, RE, and *H. pylori* infection. Non-steroidal anti-inflammatory drugs were positively associated with GERD risk. On the contrary, a reduced risk of GU was observed among *H. pylori*-infected patients taking this drug. In summary, the prevalence of GERD, RE, and *H. pylori* infection still appears high in China. *H. pylori* infection eradication remains the priority to reduce the burden of peptic ulcer disease. The aging population, high prevalence of overweight or obesity, smoking, and drinking in China could explain the high burden of these diseases, thus suggesting the targeted preventive measures for upper gastrointestinal diseases in the future.

1. Introduction

Digestive diseases remain prevalent, with 2.86 billion prevalent cases, leading to 8 million deaths and 277 million disability-adjusted life years lost in 2019 [1]. Common upper gastrointestinal (GI) diseases such as peptic ulcer disease (PU), gastroesophageal reflux disease (GERD), and reflux esophagitis (RE) affect nearly 5%–10% [2], 13% [3], and 20% [4] of the worldwide population; however, there is considerable geographic variation. All these diseases share common risk factors, such as the modifiable risk factors of *Helicobacter pylori*, smoking, alcohol use, unhealthy dietary patterns, high body mass index (BMI), and non-steroidal anti-inflammatory drug (NSAID) usage. Furthermore, patients with these upper GI diseases or infected with their shared risk factor of *H. pylori* consume proton pump inhibitors or other gastric

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acid-suppressing drugs [2–7], which pose a significant financial burden on the healthcare system worldwide.

In China, previous regional studies have reported that the prevalence of PU, GERD, and RE was lower than that in the Western countries, being 6.5% [8], 5.77% [9], and 1.92% [10], respectively. With urbanization and industrialization over the past decades in China, rapid lifestyle changes, there has been an increase in the prevalence of overweight and obesity, an aging population, and advances in diagnostic methods and treatments, all of which have contributed to changes in these upper GI disease patterns in China. GBD 2019 data illustrated that the prevalence of upper digestive disease decreased from 1990 to 2017 [11]. However, there are limited studies on China's national population-based prevalence of GI diseases. Therefore, it is necessary to assess the current prevalence of those above upper GI diseases to support policy formulation and resource allocation, raise awareness of the public and policymakers, and set reasonable prevention and control targets.

Using a multistage stratified sampling method, we conducted a nationwide community-based cross-sectional study to investigate the prevalence of GERD, RE, PU (including GU and DU), and *H. pylori* infection to highlight the national burden of the four common upper GI diseases in China.

2. Materials and methods

2.1. Study population

We conducted a multistage stratified sampling approach and selected residents aged 18–64 years who lived at their current residence for at least six months within one year before the survey in the general population. We excluded those with severe cardiovascular and cerebrovascular diseases, mobility difficulties, language or mental disorders, and pregnant or lactating women.

For the sampling process (Fig. S1 online), briefly, 31 provincial regions (except Hong Kong, Macau, and Taiwan) were divided into eight regions according to the geography and dietary habits in the first stage. One or two provincial regions were randomly selected from each of the eight regions using a simple random sampling method. Then, stratified sampling was conducted, and one provincial capital or megacity, one prefecture-level city, and two rural counties were randomly sampled from each region in the second stage. Subsequently, proportional-to-size sampling was applied to choose three subdistricts or townships for each city or township at the third stage. In the fourth stage, two residential areas or villages were selected for each subdistrict or township. In the final stage, we collected the age and sex information of all the inhabitants of each selected residential area or village. Then, age- and sex-stratified sampling methods were used to enroll 144 participants who met the inclusion criteria and were randomly selected from each residential area or village according to age and sex distribution based on the 6th National Census in China from 2010. Finally, 27,648 individuals from 16 cities and 16 townships from 11 provincial regions were expected (sample size estimation is shown in Supplementary materials online). However, 11 individuals quit the survey, and 27,637 participants were selected.

The institutional review board from Peking Union Medical College Hospital led the ethical approval (S-703). Written informed consent was obtained from each participant.

2.2. Data collection

A questionnaire survey was administered by trained staff to obtain information on demographic characteristics (age, sex, nation, marital status, education, employment status, medical insurance, and economic status), lifestyle factors (diet, smoking, drinking, and labor intensity), disease and medication history, and frequency and duration of digestive symptoms within the last 12 months. Labor intensity was defined as very low (sedentary jobs), low (often standing or walking during work), moderate (mainly standing and lifting things during work), and severe (mainly heavy lifting during work). Body weight and height were measured, and BMI was calculated by dividing weight (kilograms) by the square of height (meters). NSAID usage during the past three months (yes vs. no) was defined as self-reported via a questionnaire survey.

The ^{13}C-urea breath test (^{13}C-BUT) was performed, in which the patients were required to exhale twice for collection. All exhaled breath samples were transported and processed in the central laboratory within three days. The test kits were procured from Beijing Richen-Force Science &Technology Co. Ltd.

Gastroscopy was performed by a trained and qualified gastroenterologist who uploaded the endoscopic images to the information collection and management system designed for the current study. The images were then subjected to blinded review by three experienced endoscopists.

Age and sex-specific response rates to the questionnaire, ^{13}C-BUT test findings, and endoscopy findings are provided in Table S1 (online). The response rates to endoscopy in participants with different GI symptoms are provided in Table S2 (online). The completeness percentage of the questionnaire, ^{13}C-BUT test, and gastroscopy in the total population was 100%, 85.1%, and 63.8%, respectively.

2.3. Diagnostic criteria for H. pylori, GERD, RE, and PU

H. pylori infection was diagnosed using the noninvasive ^{13}C-BUT test, according to the contemporary Chinese and Kyoto global consensus [12–14]. GERD and RE were diagnosed based on symptoms and gastroscopy findings, according to the contemporary Chinese and Montreal global consensus [15,16]. The diagnosis of GERD was also combined using a standardized symptom questionnaire, while individuals with alarming symptoms such as dysphagia, anemia, weight loss, bleeding, and recurrent vomiting proceeded to gastroscopy. RE and its subtypes were diagnosed based on typical GERD symptoms and abnormal endoscopic findings of erosive esophagitis [17]. Because the symptoms of PU were non-specific and had limited predictive value, a gastroscopy was performed as the gold standard for diagnosing PU, including gastric ulcer (GU) and duodenal ulcer (DU). Biopsy specimens were obtained to exclude malignant disease [2,18].

2.4. Statistical analysis

All statistical analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, USA) and SUDDAN 11 (Research Triangle Institute, Cary, USA) to account for the complex sampling design. All calculations were based on a combined weight, including sampling, nonresponse, and population weights, to represent the total population of Chinese adults (aged 18–64 years) based on Chinese population data in 2010 and the sampling scheme of our survey. Continuous variables are described as means (standard deviations) or median (p25, p75). Categorical variables are expressed as percentages. Overall and characteristic-specific age and sex standardized prevalence and their 95% confidence interval (CI) of each specific upper GI diseases were estimated. The weighted prevalence and standard error were estimated using the Taylor-linearization method appropriate for the complex survey design. A weighted Chi-square or trend test was used to test the differences in prevalence based on the different characteristics of the subjects. P-values were two-tailed, and a $P < 0.05$ was considered statistically significant. We also used weighted logistic regression based on multistage sampling to calculate odds ratios (ORs) and their 95% CIs to explore the relationship between potential risk factors and diseases. Macros to perform backward model selection (significance level for stay = 0.05) for complex survey data were used to determine the risk factors [19].

3. Results

3.1. Characteristics of the study population

A total of 27,637 individuals aged 18–64 years were included in the present study, and the characteristics of the study population are presented in Table 1. The average age was 39.7 ± 12.6 years, with 49.6% being males. A total of 27.0% reported current smoking, 10.5% reported excessive drinking, and 47.3% reported moderate or severe labor intensity. 35.0% were overweight, and 16.8% were obese. The proportion of self-report for NSAID usage was 12.7%.

3.2. Prevalence of GERD, RE, and PU by demographic characteristics

The estimated prevalence of GERD, RE, PU (including GU and DU), and *H. pylori* infection and their associations with different characteristics are shown in Tables 2 and 3.

In Chinese adults aged 18–64 years, the prevalence (95% CI) of GERD, RE, PU, and *H. pylori* infection was 10.5% (7.8%–14.2%), 5.4% (3.9%–7.3%), 6.6% (5.2%–8.2%), and 41.5% (36.7%–46.4%), respectively. Most of the participants with RE were grade A, with a prevalence (95% CI) of 3.7% (2.7%–5.1%), 1.3% (0.8%–2.1%), 0.3% (0.1%–0.7%), and 0.1% (95% CI: 0.0%–0.3%), respectively (Table S3 online).

3.2.1. Age, sex, and education level

The prevalence increased with age for GERD (18–24 years vs. 55–64 years: 6.9% vs. 13.6%, P for trend < 0.0001), RE (18–24 years vs. 55–64 years: 2.5% vs. 8.8%, P for trend = 0.0010), and GU (18–24 years vs. 55–64 years: 1.2% vs. 3.7%, P for trend < 0.0001) but not for DU and *H. pylori* infection. The phenomena were similar in males and females (Table S4 online). According to the weighted multivariable logistic regression models, age still exhibited a risk factor for GERD, RE, and GU (Table 3).

Men had a significantly greater prevalence of RE (8.1% vs. 2.5%, P = 0.0002) and DU (5.4% vs. 3.5%, P = 0.005) than women, even after adjusting for other factors (Tables 2,3). However, the multivariable models showed a significantly lower prevalence of GERD in males than females (OR = 0.70, 95% CI: 0.59–0.84).

The prevalence of GERD (15.6% for those with a primary school education or below and 7.6% for those with a junior college education or higher, P = 0.013), RE (corresponding prevalence of 5.9% and 3.3%, P = 0.026), and GU (corresponding prevalence of 3.9% and 1.3%, P = 0.047) decreased with higher education level (Table 2). In the multivariable models (Table 3), the negative associations between education level and RE and GU disappeared. However, the relationship between education and DU became significant. People with higher education levels had a greater risk of DU in the full model (junior college or higher vs. primary school education or below: OR = 1.68, 95% CI: 1.09–2.60).

3.2.2. BMI

The prevalence of GERD (P for trend = 0.007), RE (P for trend = 0.002), and *H. pylori* infection (P for trend = 0.001) increased with BMI (Table 2). The conclusion was consistent in the multivariable models (Table 3). Furthermore, a U-shaped correlation was observed between BMI and GU in the multivariable model. Compared to the individuals with normal weight, the ORs (95% CIs) for obese and underweight individuals were 1.47 (1.03–2.11) and 2.03 (0.73–5.67), respectively (Table 3).

Table 1
Characteristics of the study population.

Characteristics	Total (n = 27,637)
Age (year)	39.7 ± 12.6
Age group (year)	
18–24	4283 (16.2)
25–34	5848 (21.0)
35–44	7072 (25.8)
45–54	5949 (21.3)
55–64	4485 (15.7)
Male	13,494 (49.6)
Ethnicity	
Han	25,649 (95.6)
Zhuang	373 (0.2)
Hui	641 (0.5)
Others	974 (3.7)
Location	
Megacities	6878 (7.0)
Prefecture cities	6943 (16.7)
Rural counties	13,816 (76.3)
Marital status	
Unmarried	4327 (15.2)
Married	22,719 (83.2)
Widowed	264 (0.8)
Divorce	327 (0.8)
Education level	
Primary school or below	5984 (25.0)
Junior high school	9387 (37.1)
Senior high school	6406 (21.5)
Junior college or higher	5860 (16.4)
Job category	
Mainly manual labor	12,716 (56.2)
Mainly mental work	7434 (23.1)
Manual and metal work equally	5813 (16.3)
Uncertain	1674 (4.4)
Labor intensity	
Very low	6477 (18.7)
Low	9923 (33.9)
Moderate	7809 (30.3)
Severe	3428 (17.0)
Medical insurance	
Basic medical insurance for urban workers	7871 (21.2)
Public health service	1169 (3.6)
Medical insurance for urban residents	4176 (11.4)
New rural cooperative medical insurance	14,631 (70.8)
Commercial health insurance	2083 (6.6)
Others	558 (1.8)
BMI (kg/m^2)	24.5 ± 0.1
Underweight (<18.5)	1150 (3.5)
Normal (18.5 to < 24)	12,510 (44.8)
Overweight (24 to < 28)	9612 (35.0)
Obesity (≥28)	4288 (16.8)
Smoking, pack-years	20.0 ± 18.2
Current	7479 (27.0)
Former	1141 (3.7)
Never smoking	19,016 (69.3)
Alcohol consumption (g/d)[a]	5.9 (1.0, 25.8)
Excessive drinking[b]	2854 (10.5)
Not excessive drinking	8009 (26.0)
Never drinking	16,512 (63.5)
NSAID use during the past three months	3681 (12.7)

Data are presented as mean ± standard deviation, median (p25, p75), or n (%). BMI: body mass index; NSAID: non-steroidal anti-inflammatory drug.
[a] calculated for drinkers only.
[b] Excessive drinking: >25 g/d for males and > 15 g/d for females.

Table 2
Age and sex standardized prevalence (95% CI) of GERD, reflux esophagitis, peptic ulcer, and *H. pylori* infection in Chinese adults aged 18–64 years.

	GERD (*n* = 27,637)	Reflux esophagitis (*n* = 17,632)	Gastric ulcer (*n* = 17,632)	Duodenal ulcer (*n* = 17,632)	Peptic ulcer (*n* = 17,632)	*H. pylori* infection (*n* = 22,485)
Overall	10.5 (7.8–14.2)	5.4 (3.9–7.3)	2.5 (1.7–3.7)	4.5 (3.6–5.4)	6.6 (5.2–8.2)	41.5 (36.7–46.4)
Age group (year)						
18–24	6.9 (5.1–9.3)	2.5 (1.4–4.2)	1.2 (0.5–2.4)	4.4 (2.9–6.4)	5.3 (3.8–7.4)	37.5 (30.4–45.2)
25–34	8.7 (6.1–12.1)	4.2 (2.8–5.9)	2.5 (1.4–3.9)	5.0 (3.6–6.9)	7.2 (5.2–9.8)	41.7 (35.3–48.3)
35–44	10.6 (7.6–14.7)	5.3 (3.8–7.4)	2.3 (1.4–3.5)	4.1 (2.9–5.5)	5.9 (4.5–7.9)	42.6 (38.3–47.0)
45–54	12.8 (9.2–17.6)	6.4 (4.3–9.4)	3.0 (1.8–4.6)	4.6 (3.2–6.4)	7.1 (5.2–9.6)	42.8 (38.1–47.7)
55–64	13.6 (10.0–18.3)	8.8 (5.8–13.2)	3.7 (2.9–4.6)	4.2 (3.3–5.4)	7.3 (6.2–8.5)	42.2 (37.1–47.4)
P for trend	<0.0001	0.001	<0.0001	0.699	0.051	0.199
Sex						
Male	10.3 (7.5–14.0)	8.1 (6.0–11.0)	3.0 (1.7–4.9)	5.4 (4.4–6.5)	7.8 (6.0–10.2)	41.6 (37.3–46.1)
Female	10.8 (8.0–14.4)	2.5 (1.7–3.7)	2.0 (1.4–2.8)	3.5 (2.6–4.6)	5.2 (4.1–6.5)	41.4 (36.0–47.0)
P for difference	0.310	0.0002	0.180	0.005	0.017	0.840
Education level						
Primary school or below	15.6 (11.4–21.1)	5.9 (4.4–8.0)	3.9 (2.2–6.5)	3.7 (2.4–5.5)	6.9 (4.5–10.6)	41.8 (34.1–49.8)
Junior high school	10.6 (8.2–13.6)	6.2 (4.7–8.2)	2.3 (1.4–3.4)	4.7 (3.8–5.6)	6.5 (5.3–8.0)	44.2 (38.9–49.6)
Senior high school	6.7 (4.7–9.5)	4.8 (2.7–7.9)	2.2 (1.1–3.8)	4.3 (3.5–5.3)	6.1 (4.9–7.6)	38.9 (35.3–42.6)
Junior college or higher	7.6 (5.5–10.5)	3.3 (1.9–5.4)	1.3 (0.8–2.1)	5.5 (3.4–8.7)	6.6 (4.4–9.6)	38.3 (33.3–43.6)
P for trend	0.013	0.026	0.045	0.307	0.767	0.220
Marital status						
Unmarried	7.1 (5.1–9.7)	3.2 (1.8–5.2)	1.4 (0.67–2.7)	5.0 (3.4–6.9)	6.0 (4.6–7.9)	35.2 (28.8–42.1)
Married	11.1 (8.2–14.9)	5.8 (4.2–7.9)	2.7 (1.8–3.9)	4.4 (3.5–5.4)	6.6 (5.3–8.3)	42.7 (37.9–47.7)
Widowed	15.7 (6.9–31.9)	5.8 (3.0–10.7)	6.1 (1.6–21.0)	5.3 (1.9–13.6)	9.5 (3.9–21.5)	41.4 (28.3–55.9)
Divorce	19.0 (12.9–27.2)	6.3 (2.9–13.1)	2.0 (0.5–5.0)	2.2 (0.63–5.2)	3.8 (1.6–7.5)	42.0 (34.0–50.3)
P for difference	0.003	0.007	0.079	0.466	0.382	0.034
BMI (kg/m^2)						
Underweight (<18.5)	8.7 (6.7–11.2)	2.8 (1.0–6.1)	3.9 (0.6–12.3)	4.7 (2.2–8.7)	8.5 (4.1–16.7)	34.8 (27.5–42.8)
Normal (18.5 to < 24)	9.8 (6.5–14.5)	4.7 (3.1–6.7)	2.3 (1.4–3.6)	4.6 (3.5–5.9)	6.9 (5.2–9.1)	39.8 (33.2–46.9)
Overweight (24 to < 28)	11.3 (8.8–14.5)	5.9 (4.2–8.2)	2.5 (1.9–3.3)	4.6 (3.7–5.5)	5.7 (4.4–7.5)	43.7 (40.0–48.0)
Obesity (≥28)	11.6 (9.0–14.9)	6.6 (4.7–9.3)	2.8 (1.7–4.3)	3.9 (2.8–5.4)	6.5 (5.5–7.8)	43.0 (40.0–46.1)
P for trend	0.007	0.002	0.820	0.354	0.486	0.001
Smoking status						
Non-smoker	9.6 (7.1–13.0)	3.8 (2.6–5.4)	1.9 (1.3–2.8)	3.9 (3.1–4.9)	5.6 (4.5–6.9)	41.1 (36.1–46.3)
≤15 pack-years	11.4 (8.3–15.5)	7.5 (5.3–10.4)	6.9 (2.2–4.4)	5.2 (3.8–7.2)	7.6 (5.9–9.7)	41.9 (36.7–47.4)
>15 pack-years	13.8 (9.9–18.8)	10.6 (7.7–14.4)	4.6 (2.5–7.6)	6.1 (4.4–8.4)	10.0 (6.9–14.1)	42.7 (38.3–47.1)
P for trend	0.004	<0.0001	0.010	0.017	0.004	0.095
Drinking status[a]						
Never drinking	9.4 (6.4–13.5)	4.2 (2.7–6.1)	2.4 (1.5–3.7)	4.2 (3.3–5.2)	6.2 (4.8–8.0)	40.5 (35.2–45.9)
Without excessive	11.8 (9.0–15.3)	6.7 (4.9–9.1)	2.7 (1.5–4.3)	5.6 (4.4–7.0)	7.7 (5.8–10.1)	42.6 (37.2–48.1)
Excessive	14.2 (11.8–17.0)	9.4 (6.8–12.9)	2.8 (2.0–3.7)	3.6 (2.7–4.7)	5.9 (5.1–6.9)	44.6 (41.4–47.9)
P for trend	0.001	<0.0001	0.361	0.004	0.160	0.024
Labor intensity						
Very low	9.2 (7.3–11.6)	4.9 (3.7–6.3)	1.9 (1.3–2.8)	4.2 (2.4–6.8)	5.8 (3.8–8.7)	39.2 (34.9–43.6)
Low	7.6 (5.5–10.6)	3.9 (2.4–6.0)	2.2 (1.4–3.1)	4.1 (3.3–4.9)	5.9 (4.9–7.1)	38.5 (35.4–41.7)
Moderate	11.4 (8.4–15.3)	6.6 (4.7–9.1)	2.3 (1.3–3.7)	4.6 (3.7–5.6)	6.5 (5.1–8.4)	43.2 (38.4–48.1)
Severe	16.2 (11.4–22.4)	6.8 (5.1–9.0)	4.2 (2.5–6.8)	5.3 (3.6–7.8)	8.6 (5.8–12.5)	46.6 (36.5–57.1)
P for trend	0.041	0.015	0.0006	0.410	0.190	0.003 (0.129)
Location						
Megacities	9.3 (5.2–16.0)	6.2 (5.0–7.6)	3.8 (0.5–12.9)	5.6 (3.8–8.1)	8.8 (4.5–16.5)	42.0 (37.9–46.3)
Prefecture cities	10.2 (6.7–15.3)	4.5 (3.7–5.4)	1.8 (0.9–3.4)	3.3 (2.5–4.3)	4.8 (3.4–6.6)	38.9 (31.7–46.6)
Rural counties	10.7 (7.3–15.5)	5.5 (3.7–8.2)	2.6 (1.5–4.1)	4.6 (3.6–5.8)	6.7 (5.1–8.9)	42.0 (35.6–48.8)
P for difference	0.910	0.036	0.064	0.005	0.961	0.659

Data are presented as percentage (95% CI). CI: confidence interval; GERD: gastroesophageal reflux disease; *H. pylori*: *Helicobacter pylori*; BMI: body mass index.
[a] Excessive: >25 g/d for males and > 15 g/d for females.

3.2.3. Smoking and drinking status

In the univariate and multivariable analyses, a linear association was observed between smoking and all diseases in our study except for *H. pylori* infection (Tables 2,3). The prevalence of GERD, RE, GU, and DU for those who smoked > 15 pack-years reached 13.8%, 10.6%, 4.6%, and 6.1%, respectively. Similarly, the univariate analysis demonstrated a linear dose–response relationship between drinking status and GERD (*P* for trend = 0.001), RE (*P* for trend < 0.0001), DU (*P* for trend = 0.004), and *H. pylori* infection (*P* for trend = 0.024) but not GU (Table 2). However, only the prevalence of GERD and *H. pylori* infection was observed to be increased with alcohol consumption in the multivariable models. Compared

Table 3
Multivariable analysis for the risk factors of the four diseases and *H. pylori* infection.

	GERD	Reflux esophagitis	Gastric ulcer	Duodenal ulcer	*H. pylori* infection
Region					
Northeast	0.44 (0.32–0.60)	0.55 (0.36–0.83)	0.13 (0.07–0.24)	0.50 (0.35–0.71)	0.48 (0.39–0.60)
LRYR	0.26 (0.21–0.32)	0.66 (0.46–0.95)	0.25 (0.12–0.51)	0.68 (0.35–1.32)	0.42 (0.33–0.53)
BTH	0.41 (0.33–0.52)	0.40 (0.27–0.61)	0.17 (0.08–0.33)	0.58 (0.34–1.00)	0.41 (0.33–0.52)
LMRYR	0.57 (0.38–0.85)	1.00 (0.70–1.42)	0.25 (0.13–0.45)	0.57 (0.38–0.86)	0.48 (0.39–0.59)
MRYR	0.16 (0.12–0.23)	0.24 (0.11–0.54)	0.35 (0.19–0.66)	0.67 (0.44–1.01)	0.29 (0.22–0.39)
South China	0.28 (0.24–0.34)	0.80 (0.59–1.10)	0.25 (0.15–0.41)	1.33 (0.94–1.88)	0.29 (0.22–0.37)
Northwest	Reference	Reference	Reference	Reference	Reference
Southwest	0.38 (0.27–0.53)	0.28 (0.20–0.40)	0.78 (0.49–1.24)	0.77 (0.54–1.09)	0.14 (0.11–0.18)
Age group (year)					
18–24	Reference	Reference	Reference		
25–34	1.16 (0.94–1.43)	1.63 (0.89–2.98)	1.88 (0.92–3.85)		
35–44	1.34 (1.09–1.64)	2.13 (1.26–3.60)	1.69 (0.86–3.34)		
45–54	1.56 (1.23–1.97)	2.67 (1.37–5.21)	2.14 (1.06–4.30)		
55–64	1.58 (1.22–2.04)	3.69 (2.21–6.15)	2.69 (1.26–5.75)		
Male vs. female	0.70 (0.59–0.84)	2.97 (2.35–3.75)		1.42 (1.05–1.92)	
Education level					
Primary school or below	Reference			Reference	
Junior high school	0.74 (0.63–0.87)			1.31 (1.02–1.68)	
Senior high school	0.56 (0.47–0.67)			1.23 (0.92–1.64)	
Junior college or higher	0.64 (0.52–0.78)			1.68 (1.09–2.60)	
Marital status					
Unmarried					
Married					1.38 (1.19–1.60)
Widowed					1.33 (0.82–2.15)
Divorce					1.31 (0.91–1.87)
BMI (kg/m^2)					
Underweight (<18.5)	1.00 (0.74–1.34)	0.72 (0.31–1.65)	2.03 (0.73–5.67)		0.85 (0.71–1.02)
Normal (18.5 to < 24)	Reference	Reference	Reference		Reference
Overweight (24 to < 28)	1.12 (0.97–1.28)	1.16 (0.93–1.44)	1.13 (0.82–1.54)		1.16 (1.04–1.29)
Obesity (≥28)	1.16 (1.00–1.35)	1.35 (1.07–1.71)	1.47 (1.03–2.11)		1.11 (0.98–1.26)
Smoking status					
Non-smoker	Reference	Reference	Reference	Reference	
≤15 pack-years	1.33 (1.08–1.63)	1.26 (1.01–1.58)	1.68 (1.17–2.40)	1.16 (0.82–1.63)	
>15 pack-years	1.28 (1.07–1.53)	1.29 (1.01–1.65)	1.97 (1.31–2.98)	1.60 (1.04–2.46)	
Drinking status					
Never drinking	Reference				Reference
Without excessive	1.36 (1.16–1.59)				1.04 (0.94–1.14)
Excessive[a]	1.77 (1.44–2.16)				1.16 (1.01–1.33)
Location					
Megacities		1.45 (0.99–2.13)	2.16 (1.26–3.71)	1.64 (1.13–2.38)	
Prefecture cities		Reference	Reference	Reference	
Rural counties		1.44 (1.06–1.94)	1.34 (0.94–1.9)	1.39 (1.01–1.91)	
H. pylori infection					
(−)		Reference	Reference	Reference	
(+)		0.58 (0.46–0.74)	2.03 (1.41–2.92)	2.29 (1.63–3.23)	
Undetected		0.99 (0.79–1.25)	1.18 (0.83–1.68)	1.88 (1.23–2.87)	
NASID usage					
(−)	Reference				
(+)	1.40 (1.19–1.64)				

Data are presented as odds ratio (95% CI). GERD: gastroesophageal reflux disease; *H. pylori*: *Helicobacter pylori*; BMI: body mass index; LRYR: lower reaches of the Yangtze River; BTH: Beijing-Tianjin-Hebei region; LMRYR: lower or middle reaches of the Yellow River; MRYR: Middle reaches of the Yangtze River; NSAID: non-steroidal anti-inflammatory drug.
[a] Excessive: >25 g/day for males and > 15 g/day for females.

to never drinking, the adjusted ORs (95% CIs) for excessive drinking were 1.77 (1.44–2.16) and 1.16 (1.01–1.33) for GERD and *H. pylori* infection, respectively.

3.2.4. Geographic and economic development level

Geographic variations in the age and sex-standardized prevalence were found (Table 4), with the highest prevalence of GERD (23.9%), RE (8.7%), GU (7.8%), DU (7.3%), and *H. pylori* infection (63.6%) observed in Northwest China and the lowest or near lowest prevalence of GERD (4.5%), RE (2.6%), GU (2.4%) and Du (4.2%) observed in the middle reaches of the Yangtze River (MRYR) region. Comparable to the MRYR region, the Beijing-Tianjin-Hebei region also had the lowest prevalence of RE, GU, and DU. Interestingly, the southwest region had the second-highest prevalence of GU but the lowest or nearly the lowest prevalence of DU, RE, and *H. pylori* infection. Multivariable regression models also

Table 4
Age and sex standardized prevalence (95% CI) of GERD, reflux esophagitis, peptic ulcer, and *H. pylori infection* in Chinese adults aged 18–64 years in different regions.

	GERD (*n* = 27,637)	Reflux esophagitis (*n* = 17,632)	Gastric ulcer (*n* = 17,632)	Duodenal ulcer (*n* = 17,632)	*H. pylori* infection (*n* = 22,485)
Region					
Northeast	12.1 (10.6–13.8)	5.3 (4.5–6.2)	1.0 (0.2–2.9)	3.4 (2.7–4.2)	46.2 (42.8–49.7)
LRYR	6.9 (4.8–9.9)	6.6 (4.8–9.2)	1.9 (0.6–4.3)	4.6 (2.6–7.6)	43.0 (37.4–48.9)
BTH	10.9 (7.0–16.5)	4.3 (2.1–7.7)	1.3 (0.9–1.9)	4.0 (1.5–8.5)	42.8 (41.5–44.0)
LMRYR	14.0 (7.5–24.5)	8.7 (4.3–16.9)	1.8 (0.8–3.5)	3.7 (2.1–6.1)	46.5 (44.2–48.9)
MRYR	4.5 (2.0–8.5)	2.6 (0.1–12.9)	2.4 (1.1–4.6)	4.2 (3.3–5.2)	34.4 (32.3–36.6)
South China	8.1 (7.0–9.4)	7.1 (4.4–11.4)	1.6 (1.1–2.4)	7.4 (4.9–11.1)	33.2 (27.2–39.8)
Northwest	23.9 (21.7–26.2)	8.7 (8.2–9.3)	7.8 (4.5–13.2)	7.3 (6.6–8.1)	63.6 (59.9–67.1)
Southwest	12.0 (6.6–20.8)	3.2 (2.0–4.9)	5.1 (3.8–6.7)	4.0 (2.4–6.3)	20.0 (15.7–25.2)
P for difference	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

CI: confidence interval; GERD: gastroesophageal reflux disease; *H. pylori*: *Helicobacter pylori*; LRYR: lower reaches of the Yangtze River; BTH: Beijing-Tianjin-Hebei region; LMRYR: lower or middle reaches of the Yellow River; MRYR: Middle reaches of the Yangtze River.

supported the significant regional variation in the prevalence of the four diseases and *H. pylori* infection (Table 3).

The lowest prevalence of RE (4.5%), GU (1.8%), and DU (3.3%) was found among the residents living in the prefecture cities, followed by rural counties (RE: 5.5%, GU: 2.6%, DU: 4.6%), and the highest among the residents in megacities (RE: 6.2%, GU: 3.8%, DU: 5.6%). The conclusion remained consistent in the multivariable models (Table 3). The correlation between economic development level, GERD, and *H. pylori* infection was not discovered.

3.3. H. Pylori infection, NSAID usage, and their associations with GERD, RE, and PU

Fig. 1 shows the prevalence of GERD, RE, GU, and PU according to *H. pylori* infection status and NSAID usage. A higher prevalence of GU (3.8% vs. 1.9%) and DU (6.3% vs. 2.9%) but a lower prevalence of RE (4.2% vs. 5.9%) in those with current *H. pylori* infection than the uninfected was observed. NSAID usage was only found to be associated with the risk of GERD (14.4% vs. 10.0%). The conclusion remained consistent in the multivariable models (Table 3). Furthermore, we conducted a joint analysis of NSAIDs and *H. pylori* infection (Fig. 1). Among the *H. pylori*-infected participants, those who used NSAIDs had a lower prevalence of GU (3.0% vs. 3.9%) but a greater prevalence of DU (7.5% vs. 6.2%) than those who did not use NSAIDs.

Moreover, we analyzed the proportions of *H. pylori* infection in subjects diagnosed with GERD, RE, GU, and DU (Table 5). Among the GERD, RE, GU, and DU patients, 43.7%, 35.2%, 58.6%, and 61.1% had *H. pylori* infection, respectively. The percentage of *pylori*-positive GU was significantly greater in men than in women (64.7% vs. 50.6%, $P = 0.008$). Among the DU patients, symptomatic patients had a greater percentage of *H. pylori*-positive than the asymptomatic patients (70.9% vs. 51.9%, $P = 0.007$). Furthermore, younger DU patients had a higher proportion of *pylori*-positive than the olders. However, we did not observe a difference in the proportion of *pylori* infection between symptomatic and asymptomatic GU patients.

4. Discussion

4.1. Overall prevalence

This nationwide community-based cross-sectional study investigated the prevalence of *H. pylori* infection and *H. pylori*-associated upper GI diseases in China. Similar to the global trend [20], the *H. pylori* infection rate continuously decreased from 63.8% in 1983–1994 to 46.7% after 2006 in China [21]. However, a considerably high prevalence (41.5%) of *H. pylori* infection in Chinese adults aged 18–64 years still appeared, thus indicating a 576.8 million *H. pylori*-positive population in China based on 2015 census data. *H. pylori* infection is closely related to gastric cancer risk. In 2019, the National Clinical Medical Research Center for Digestive Diseases and the National Early Gastrointestinal Cancer Prevention and Treatment Canter Alliance published a consensus on eradicating *H. pylori* and preventing and controlling gastric cancer in China [22]. However, China does not have sufficient healthcare policies to eradicate this infection.

Globally, a decrease in *H. pylori*-positive PU has been accompanied by an increase in GERD and RE [23] and a decreasing trend in the prevalence of PU [11]. Our study also demonstrated a positive correlation between *H. pylori* infection and DU and GU but a negative correlation between the infection and RE. However, our study reported a prevalence of GERD of 10.5%, which was higher than a pooled rate of 4.16% in China (ten studies involving 36,887 individuals) and lower than 14.0% worldwide between 1947 and 2018 [24].

A similar trend was observed for RE. The prevalence of RE that was reported in our study (5.4%, 95% CI: 3.9%–7.3%) was higher than that reported in a previous report in 1997 (1.2%) but lower than that reported in some countries (for example, 11.8% in Italy) [10]. Furthermore, patients with RE grades C and D accounted for 0.3% of the total population; additionally, approximately 4.2 million patients had severe RE based on the people in China, emphasizing the importance of preventing RE.

Additionally, the prevalence of PU in Chinese adults aged 18–64 years was 6.6% (2.5% for GU and 4.5% for DU), which is higher than the worldwide prevalence reported by GBD 2019 [11]. The reason could be that GBD data were estimated by the model based on secondary data, most of which did not use endoscopy to diagnose PU.

4.2. H. Pylori infection and NSAID usage

Globally, especially among Western countries, causes other than *H. pylori* infection have become responsible for PU. A national hospital-based study in the United States showed that the proportions of *H. pylori*-positive GU (17% vs. 14%) and DU (25% vs. 21%) declined from 2009 through 2018 [25]. However, 58.6% of the GU and 61.1% of the DU patients in our population were still *H. pylori*-positive. Especially among asymptomatic GU patients, the proportion reached 62.5%, suggesting that controlling *H. pylori* infection is still the priority for preventing PU in Chinese adults.

NSAIDs cause approximately 10% of the PU worldwide [26]. However, we did not observe significant correlations between NSAIDs and PU but rather between NSAIDs and GERD. The reason for this effect may be the low percentage of NSAID usage in our study population (only 12.7%). Consistent with a hospital-based study [27], our study demonstrated a reduced risk of GU but not

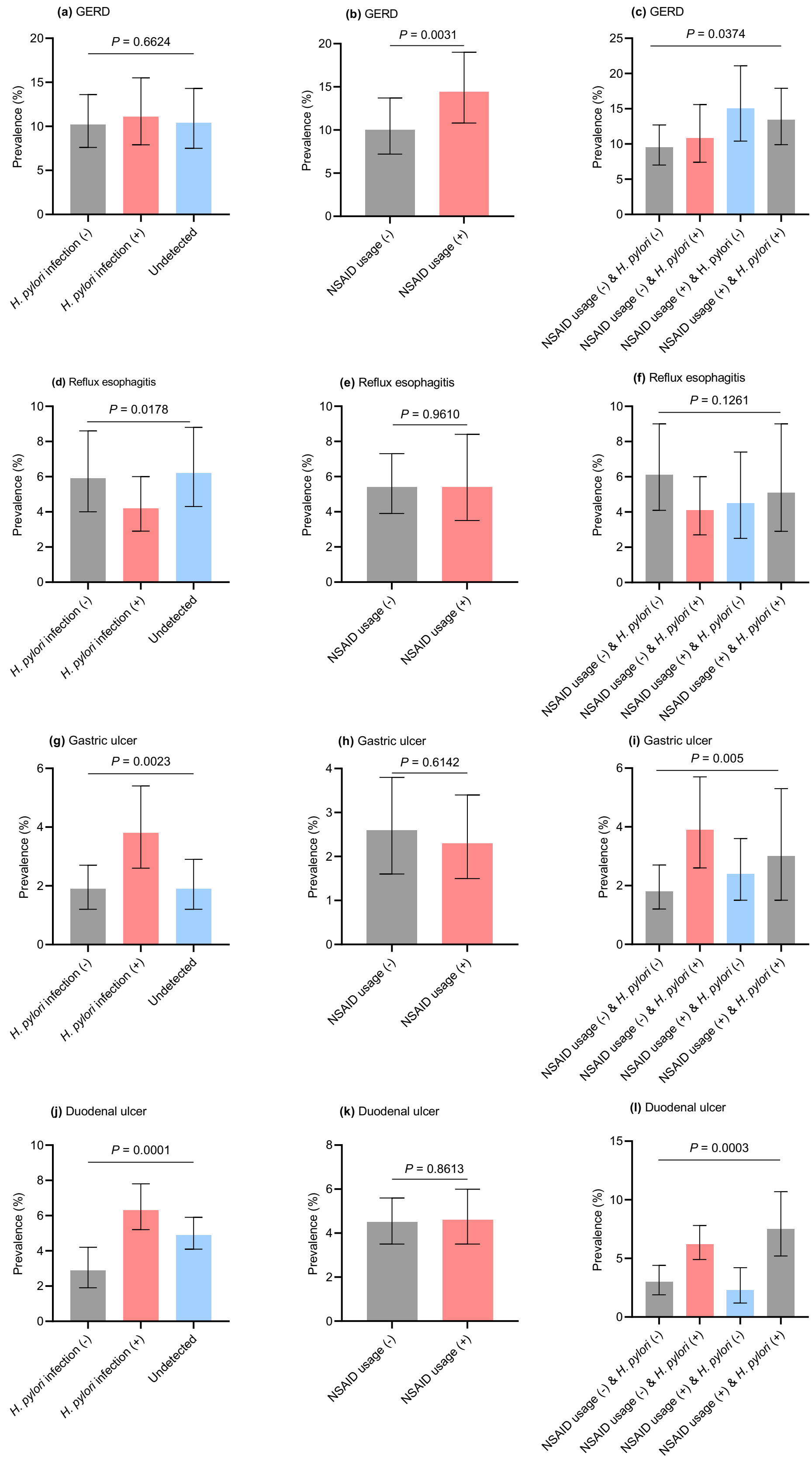

Fig. 1. The prevalence of GERD, reflux esophagitis, gastric ulcer, and duodenal ulcer by *H. pylori* infection and NSAID usage. (a–c) GERD. (d–f) Reflux esophagitis. (g–i) Gastric ulcer. (j–l) Duodenal ulcer. GERD: gastroesophageal reflux disease; *H. pylori*: *Helicobacter pylori*; NSAID: non-steroidal anti-inflammatory drug.

Table 5
Proportion (95% CI) of *H. pylori* infection among the participants with gastric ulcer, duodenal ulcer, GERD, and reflux esophagitis with different characteristics.

	GERD (%)	*P*-value	Reflux esophagitis (%)	*P*-value	Gastric ulcer (%)	*P*-value	Duodenal ulcer (%)	*P*-value
Total	43.7 (35.6–52.1)		35.2 (25.8–45.9)		58.6 (50.5–66.3)		61.1 (49.6–71.4)	
Symptomatic	43.7 (35.6–52.1)	–	35.2 (25.8–45.9)	–	55.9 (46.6–64.8)	0.384	70.9 (65.8–75.5)	0.007
Asymptotic	–		–		62.5 (48.8–74.4)		51.9 (34.6–68.8)	
Uncertain	–		–		35.3 (26.3–45.5)		44.2 (13.1–80.6)	
Age (year)								
18–34	44.3 (33.8–55.3)	0.913	29.7 (17.1–46.4)	0.357	66.4 (48.1–80.8)	0.256	65.5 (48.3–79.4)	0.028
35–44	41.5 (30.6–53.3)		37.7 (26.1–50.9)		55.3 (34.6–74.3)		68.7 (56.5–78.8)	
45–64	44.4 (36.8–52.3)		35.7 (26.1–46.5)		56.8 (47.8–65.4)		53.6 (40.4–66.3)	
Sex								
Male	45.1 (35.5–55.0)	0.438	33.9 (24.9–44.2)	0.211	64.7 (58.5–70.4)	0.008	56.4 (43.2–68.8)	0.053
Female	42.2 (34.5–50.4)		39.6 (26.9–53.9)		50.6 (40.2–61.0)		69.0 (59.9–76.9)	

–: not applicable. CI: confidence interval; GERD: gastroesophageal reflux disease; *H. pylori*: *Helicobacter pylori*.

DU among *H. pylori*-infected patients taking NSAIDs, suggesting that the rational use of NSAIDs might decrease the risk of PU.

4.3. Demographic characteristics-related burden

Inconsistent with other studies based on a population encompassing all ages [28], we did not observe a significant association between age and *H. pylori* infection in the 18–64 age group. However, the prevalence of GERD, RE, and GU increased with age in Chinese adults, which is consistent with some findings [24,29] but not others [30]. As China is rapidly moving towards an aging society, the absolute cases of GERD, RE, and GU will continue to increase.

Additionally, males had a greater age-standardized prevalence of DU and RE but a lower prevalence of GERD in the study population, which is consistent with the global sex-related burden of PU [11]. The sex difference between GU and DU needs to be confirmed.

Multivariable regression models detected only a significant correlation between marriage status and *H. pylori* infection, consistent with a nationwide study in China [28]. Compared to unmarried individuals, married participants had a higher risk of *H. pylori* infection, suggesting the benefit of a family-based strategy for *H. pylori* infection screening and treatment [31].

4.4. Obesity

Comparable to the China National Nutrition Surveys in 2015–2019 [32], the weighted prevalence of overweight or obesity in our population was 51.8%. The relationship between obesity and PU has remained controversial [33–38] due to the different study designs, diagnostic methods, and whether *H. pylori* infection and NSAID use are considered. GERD, RE, and GU (but not DU) were found to share the common obesity risk factor in Chinese adults. Meanwhile, being overweight was independently associated with *H. pylori* infection, which is consistent with the findings of a systematic review that included nine eligible studies and 27,111 Chinese adults [39]. GI hormones, insulin resistance, and the immune response are the underlying mechanisms [40–42] for these findings.

4.5. Smoking and drinking

In our population, linear dose–response relationships were found between GERD, RE, GU, and DU and smoking. The potential mechanism of pathophysiology includes cigarette smoking causing direct mucosal injury, thus increasing the risk of *H. pylori* infection and allowing for the reflux of harmful duodenal contents into the stomach [43]. Excessive drinking was also correlated with a higher prevalence of GERD and *H. pylori* infection, consistent with the findings of a study in the Republic of Korea [29]. Although the age-standardized prevalence of smoking and drinking has declined during the past decades, there is still a high prevalence of smoking and drinking in China [44–46], which could explain the increased prevalence of GERD and RE.

4.6. Geographical disparity

Differences in the regional prevalence of the four diseases and *H. pylori* infection should be noted. The northwestern region, including the five provincial regions of Ningxia, Xinjiang, Qinghai, Gansu, and Nei Mongol, had the highest prevalence of *H. pylori* infection. In contrast, Southwest China, including Yunnan, Guizhou, and Chongqing, had the lowest *H. pylori* infection rate (20.0%). Our results were consistent with the national family-based epidemiology on *H. pylori* infection in China [28], which reported a province-specific infection rate. Similarly, the northwestern region had the highest prevalence of GERD, GU, and DU, which was partially explained by *H. pylori* infection and clustered risk factors of *H. pylori* infection upper GI disease.

Brown et al. [47] explained that the higher prevalence of *H. pylori* infection in rural China in 2002 was partly due to infrequent handwashing before meals, crowding, and washing/bathing in a pond or ditch. However, our study did not observe a significant association between economic development and infection rate, suggesting that improving hygiene and living standards in China is insufficient to decrease *H. pylori* infection. However, variations based on urbanization were observed in the prevalence of RE, GU, and DU, even after adjusting for covariates. People living in megacities or rural counties had a greater risk of the abovementioned three diseases, which may be attributable to psychological stress and poor living conditions, respectively.

4.7. Strengths of the study

This study had several strengths. First, this was the first nationwide representative survey to use endoscopy to diagnose PU, which provided reliable data on the prevalence of PU in the Chinese mainland. Second, we diagnosed each individual with *H. pylori* infection and *H. pylori*-related upper GI diseases. This enabled us to explore the shared risk factors of the above diseases.

4.8. Limitations of the study

Our study has several limitations. First, although the response rates for the questionnaire and ^{13}UBT test reached 100.0% and 85.1%, respectively, for endoscopy, it was only 63.8%. Further analysis showed that the participants with GI symptoms have a higher response rate than those without, which may lead to overestimating the prevalence of these diseases. However, compared to other studies that reported a response rate of 32.7%–73.3% with small sample sizes ranging from 1533 to 3148 [8], the response rate of endoscopy in the present study is acceptable. Second, we did not obtain information about dietary patterns and sanitary living conditions, which reduced our ability to explain geographic variations. Third, due to the study's cross-sectional design, the causality of the risk factor for *H. pylori* infection and associated upper GI diseases could not be determined. Fourth, we did not report the prevalence of atrophic gastritis, whose diagnosis should be confirmed by histopathology because obtaining pathological specimens in field investigation is not feasible.

4.9. Conclusions

In conclusion, the prevalence of *H. pylori* infection and *H. pylori*-associated upper GI diseases of GERD, RE, GU, and DU still appeared high in Chinese adults aged 18–64 years compared to worldwide. The aging population, high prevalence of overweight or obesity, smoking, and drinking in China could explain the high burden of these diseases. In contrast to the developed countries, *H. pylori* infection eradication remains the priority for reducing the burden of PU. Furthermore, the discrepancy in the prevalence of *H. pylori* infection, GERD, RE, GU, and DU among the different regions suggests the different clustered effects of risk factors among the different areas. A well-designed cohort study is warranted to provide insights into possible etiologies and solid evidence for strategy formulation for managing upper GI diseases.

Conflict of interest

The authors declare that they have no conflict of interest.

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Authors contribution

Jiaming Qian, Hui Li, Hong Yang, and Li Wang contributed to the conceptualization. Jiaming Qian, Hong Yang, Hui Li, Li Wang, and Limin Wang contributed to the methodology. Hong Yang, Mei Zhang, Zhengjing Huang, Yuanyuan Sun, Wenbo Li, Chun Li, Xuzhen Qin, Yanhong Wang, Xiao Zhang, Zhenping Zhao, Limin Wang, and Jiaming Qian contributed to the epidemiological investigation. Yuanyuan Sun, and Yanhong Wang, contributed to the data management. Yuanyuan Sun and Li Wang contributed to the statistical analysis. Hong Yang contributed to the writing of the original manuscript. Li Wang, Jiaming Qian, and Limin Wang contributed to the review and editing of the manuscript and to the decision to submit the manuscript. Li Wang contributed to the visualization. Jiaming Qian, Hong Yang, and Limin Wang contributed to the project administration. Jiaming Qian contributed to the funding acquisition. All of the authors critically reviewed and approved the final version. All of the authors had full access to the data in the study and had final responsibility for the decision to submit for publication.

Data availability

The data underlying this study are available from the corresponding author upon reasonable request.

Appendix A. Supplementary materials

Supplementary materials to this article can be found online at https://doi.org/10.1016/j.scib.2024.07.048.

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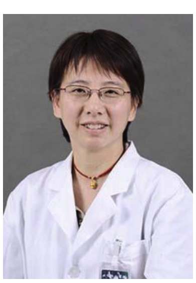

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