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Large-scale, national, family-based epidemiological study on *Helicobacter pylori* infection in China: the time to change practice for related disease prevention

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ABSTRACT

Background and aims Current practice on *Helicobacter pylori* infection mostly focuses on individual-based care in the community, but family-based *H. pylori* management has recently been suggested as a better strategy for infection control. However, the family-based *H. pylori* infection status, risk factors and transmission pattern remain to be elucidated.

Methods From September 2021 to December 2021, 10 735 families (31 098 individuals) were enrolled from 29 of 31 provinces in mainland China to examine family-based *H. pylori* infection, related factors and transmission pattern. All family members were required to answer questionnaires and test for *H. pylori* infection.

Results Among all participants, the average individual-based *H. pylori* infection rate was 40.66%, with 43.45% for adults and 20.55% for children and adolescents. Family-based infection rates ranged from 50.27% to 85.06% among the 29 provinces, with an average rate of 71.21%. In 28.87% (3099/10 735) of enrolled families, there were no infections; the remaining 71.13% (7636/10 735) of families had 1–7 infected members, and in 19.70% (1504/7636), all members were infected. Among 7961 enrolled couples, 33.21% had no infection, but in 22.99%, both were infected. Childhood infection was significantly associated with parental infection. Independent risk factors for household infection were infected family members (eg, five infected members: OR 2.72, 95% CI 1.86 to 4.00), living in highly infected areas (eg, northwest China: OR 1.83, 95% CI 1.57 to 2.13), and large families in a household (eg, family of three: OR 1.97, 95% CI 1.76 to 2.21). However, family members with higher education and income levels (OR 0.85, 95% CI 0.79 to 0.91), using serving spoons or chopsticks, more generations in a household (eg, three generations: OR 0.79, 95% CI 0.68 to 0.92), and who were younger (OR 0.57, 95% CI 0.46 to 0.70) had lower infection rates ($p<0.05$).

Conclusion Familial *H. pylori* infection rate is high in general household in China. Exposure to infected family members is likely the major source of its spread. These results provide supporting evidence for the strategic changes from *H. pylori* individual-based treatment to family-based management, and the notion has important clinical and public health implications for infection control and related disease prevention.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ On important feature of *Helicobacter pylori* is family cluster infection and intrafamilial transmission of *H. pylori* has been suggested as an important source for its spread; a family-based *H. pylori* management strategy is recently proposed for infection control, but the family-based *H. pylori* infection status, risk factors and transmission pattern remain to be evaluated.

WHAT THIS STUDY ADDS

⇒ This national wide study revealed that the family-based *H. pylori* infection rate is much higher than the individual-based infection rate in most provinces in China and stratified analyses indicated important intrafamilial transmission patterns that correlated to the incidence of infection, suggesting a major source for its spread.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The study provides supporting evidences to implement family-base *H. pylori* management to curb its intrafamilial spread in highly infected area. The results have important clinical implications in refinement of eradication strategies and impact on public health policy formulation for related disease prevention.

INTRODUCTION

Helicobacter pylori, the major cause of chronic gastritis, peptic ulcers and gastric cancer, infects around 50% of the world's population, is also closely associated with multiple extragastrointestinal diseases.[1–4] One important feature of *H. pylori* is family-cluster infections.[5 6] Accumulating evidence has demonstrated that the transmission of *H. pylori* is mainly by oral–oral, faecal–oral routes and water sources[6–8] and intrafamilial spread are common.[8–10] Within the family unit, infected parents, especially mothers, have been suggested to play an important role in its transmission, with spread also occurring between spouses and among siblings.[11–15] Therefore, treatment of whole-family *H. pylori* infection has important clinical and public health implications for related disease prevention.[16–18]

Large-scale clinical investigations[4 19–21] and international consensus reports[1–3 22] have both recommended population-wide screening and eradication of *H. pylori* for gastric cancer prevention in highly infected areas. In addition to the 'test and treat' and 'screen and treat' strategies, which are traditionally available for individual-based management of *H. pylori* infection in various infected populations,[1 2] the newly introduced 'family-based *H. pylori* infection control and management' strategy[6] in China has provided a promising and efficient avenue to curb intrafamilial spread and advanced clinical practice in managing *H. pylori* infection.

China is one of both *H. pylori* and gastric cancer prevalent areas. The 2021 national statistics indicated that the country has a population of 1.41 billion and 494 million families, with an average family size of 2.62 persons.[23] The *H. pylori* infection rate is 49.6%,[24] and the gastric cancer incidence is 28.68/100 000.[25] Global cancer statistics in 2020[25] estimated that stomach cancer incidence and mortality were 1 089 103 and 768 793 cases worldwide, with 478 508 and 373 789 cases in China, respectively. Chronic *H. pylori* infection is considered to be the major cause of gastric cancer. Despite a few scattered reports, no large-scale family-based *H. pylori* infection survey has been performed in the general population, nor is it clear about the factors that affect *H. pylori* spread and cause disease within the household.

We aimed to determine family-based *H. pylori* infection, risk factors and transmission routes in general household in all 31 provinces in mainland China, and compare these with individual-based infection status. Investigations in this area will provide important evidence on familial *H. pylori* infection and help to formulate public health policies and refine eradication strategies for infection control and related disease prevention. Results and conclusions from the current investigation will not only benefit Chinese residents but also be valuable as a reference for other highly infected areas globally.

METHODS

Study design and family-based participant enrolment

This large-scale, national, family-based, cross-sectional survey was conducted from September 2021 to December 2021 in all 31 provinces of mainland China. The participants were cohabitants of households. The investigation adopted a non-probability (convenience) sampling method from each region, but also referred to the probability sampling for sample size calculation,[26] which showed that a sample size of 9317 would produce a two-sided 95% CI with a width equal to 0.020 when the sample infection rate is 40% (formula[26]: $n = t^2pq/d^2$; n, t, p, q and d are sample size, t value, positive rate, negative rate and acceptable error, respectively). Considering the additional bias of the convenience sampling method, we, therefore, expanded the sample size to more than 10 000 households. The sampling numbers for each region were determined based on regional population, and considering the cost, accessibility, testing facilities and COVID-19 factors. A stratified analysis of infection status was performed based on each province and geographical region of China. Because of the global COVID-19 pandemic from 2019, data from two provinces, Guangxi and Xizang (Tibet), were not available; therefore, data from only 29 of 31 provinces were analysed.

To avoid biased sample selection, enrolled families were selected from at least four different locations in a province, and could be from up to nine cities. A physician from a local tertiary hospital was assigned in each province to guide and monitor the screening and enrolment processes in communities and villages. Publicity methods included phone call, door-to-door campaigns and public posters. At least 20% of the screening sites in each province were in rural communities to ensure the inclusion of a sufficient urban and rural population comparable to the national census data.[23]

Families containing two or more family members (living together for more than 10 consecutive months per year) were invited to participate in the survey. A family could have one couple, with or without children, or more couples of different generations, or single parent with children, but with no limitation on the maximum number of persons living within a household. An infected family was defined as a household with at least one *H. pylori*-infected member. To ensure the accuracy of ^{13}C-urea breath test (^{13}C-UBT) and avoid false-negative results, the family was excluded if any member had used antibiotics within the past month, proton pump inhibitors within 2 weeks, or *H. pylori* treatment within the past 3 months. However, family members who had previously eradicated *H. pylori* beyond 3 months were eligible for inclusion. Other exclusion criteria were severe cardiac, hepatic or renal insufficiency and contraindications to performing ^{13}C-UBT.

This study was registered in the Chinese Clinical Trial Registry (www.chictr.org.cn) with registration number ChiCTR2100051229, where the protocol is freely accessible from the website after registration.

Questionnaires for family members

After the programme was introduced to the community, residents were enrolled voluntarily with no specific incentive applied. All members of the family had to participate. A trained physician was onsite to guide and help the enrolment processes and fill out the questionnaire forms (online supplemental file 1). For each eligible family, members were asked to complete a questionnaire using mobile devices. The survey questionnaire contained a self-calibration system to avoid unserious answers, and household head was responsible for entering details such as family general information, the number of family members, annual household income, living area, and family sanitary and animal rearing conditions. A guardian was required to fill in personal information for children and adolescents (<18 years old), including number of siblings, parental mouth-to-mouth feeding, and the habit of holding toys in mouth. The overall questionnaire completion rate was 73.90% among all participants. Data were kept confidential and used for analysis only.

H. pylori testing for all family members

H. pylori infection was tested using a ^{13}C-UBT Kit (UREA-^{13}C breath test Heliforce kits, Beijing Richen-Force Science & Technology, Beijing, China) for all enrolled family members, following the manufacturer's instructions. The sensitivity and specificity of the assay were 95.52% and 94.74%, respectively, according to the manufacturer's introduction. A delta over baseline (DOB) of ≥4.0 was considered positive for *H. pylori*, and a DOB<4.0 was considered negative.

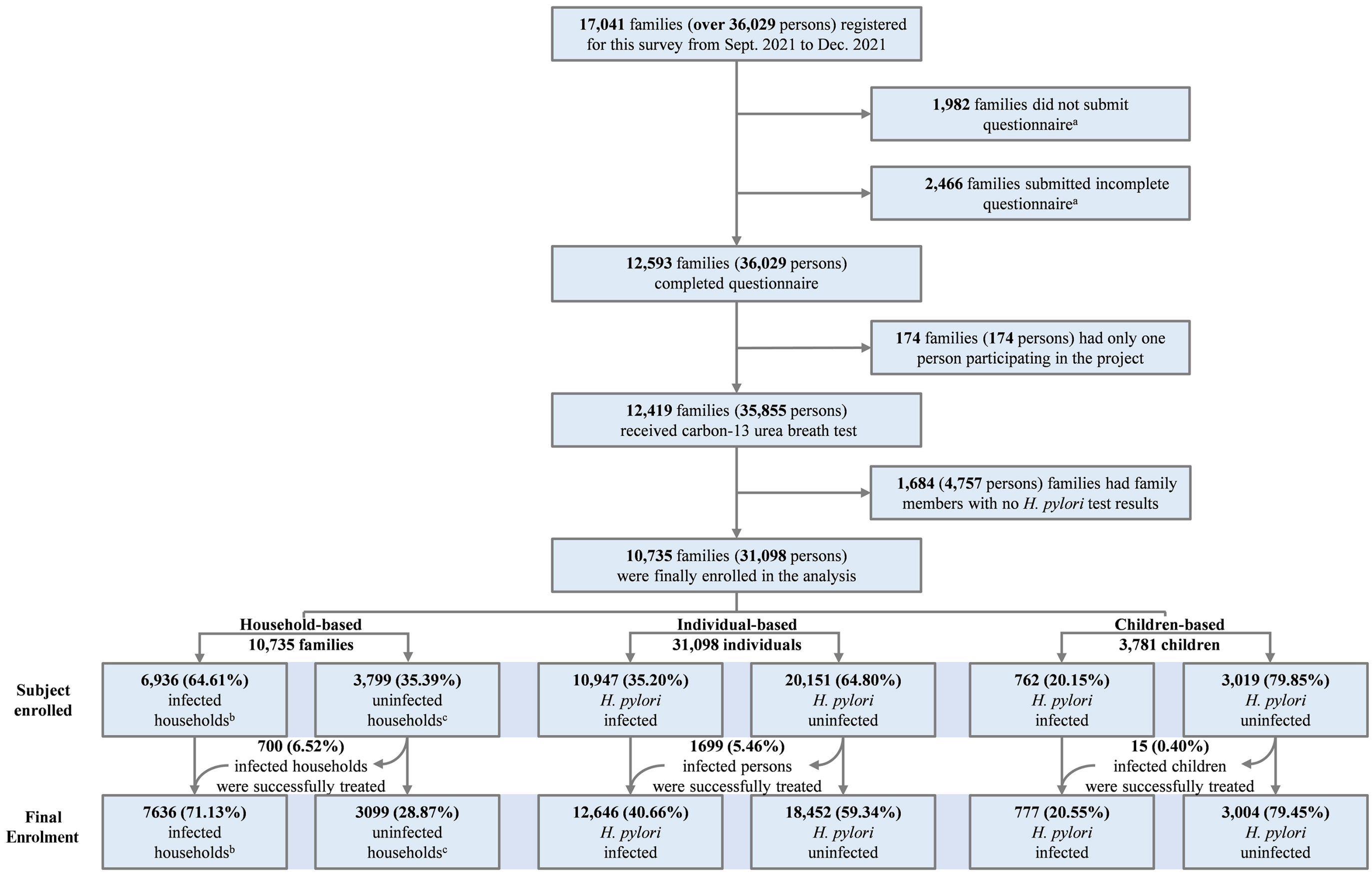

Figure 1 Flow chart of household and individual enrolment processes. (A) These households failed to submit, or submitted incomplete questionnaires, the exact number of family members in these households were not available. (B) Infected household is defined as a household with at least one *Helicobacter pylori*-infected family member. (C) Uninfected household is defined as a household without any *H. pylori*-infected family member.

Statistical analysis

Ordinal categorical variables were compared using Wilcoxon rank-sum test or Kruskal-Wallis H test. Unordered categorical variables were compared using the χ^2 test or Fisher's exact test where appropriate. Continuous variables were summarised as mean±SD and compared using the Wilcoxon rank-sum test. All variables on univariate analysis with $p<0.10$ were included in the multivariate logistic regression analysis (stepwise, sls=0.10, sle=0.05) to investigate associations between risk factors and *H. pylori* infection. ORs and 95% CIs were calculated. A $p<0.05$ was considered statistically significant.

Role of the funding sources

The funders of this study had no role in study design, data collection, data analysis, data interpretation, report writing or decision to submit the manuscript.

RESULTS

General information of enrolled families and individuals

Family enrollment information is shown in figure 1. A total of 17 041 families registered, but only 10 735 families were enrolled, and 31 098 participants from 10 735 households were finally analysed. Evaluation of demographic information between current study population and the seventh national census data of China showed that the study population was comparable to the national data (online supplemental table 1).[23] The mean age of the study population was 43.49 years; 13 478 (43.34%) participants were male, and 17 620 (56.66%) were female; 24 092 (77.47%) were married; 3781 (12.16%) were children and adolescents. Of the participants, 12 646 (40.66%) were infected by *H. pylori*, and 1699 (13.44%) had received successful treatment; another 10 947 (35.20%) participants were infected cases newly identified. The average household size of the 10 735 enrolled families was 2.90 persons; 7636 (71.13%) families had at least one infected person. The overall average individual-based *H. pylori* infection rate was 40.66%; with 43.45% for adult, and 20.55% for children and adolescents. A significant association between age and *H. pylori* infection was observed in different age groups, and the highest infection rates were between ages 31 and 70 years (figure 2A).

Household *H. pylori* infection status and risk factors

Table 1 shows the household member infection information and risk factors of the 10 735 enrolled families; to further identify the detailed familial infection status, stratified information is presented in figure 2B,C. Among the 10 735 families, 5305 (49.42%) were two-person families, and 123 (1.15 %) were seven-member families; 28.87% of families had no infection, but in 14.01% of families, all members were infected. The remaining 6132 (57.12%) families had 1–6 infected members (figure 2B).

A stratified presentation of the correlation between family size and family member infection is presented in figure 2C. Among the 7636 infected families, 4051 (53.05%) had only one infected member. In 1504 (19.7%) families, all members were infected, and the remaining 2081 (27.25%) families had 2–6 infected

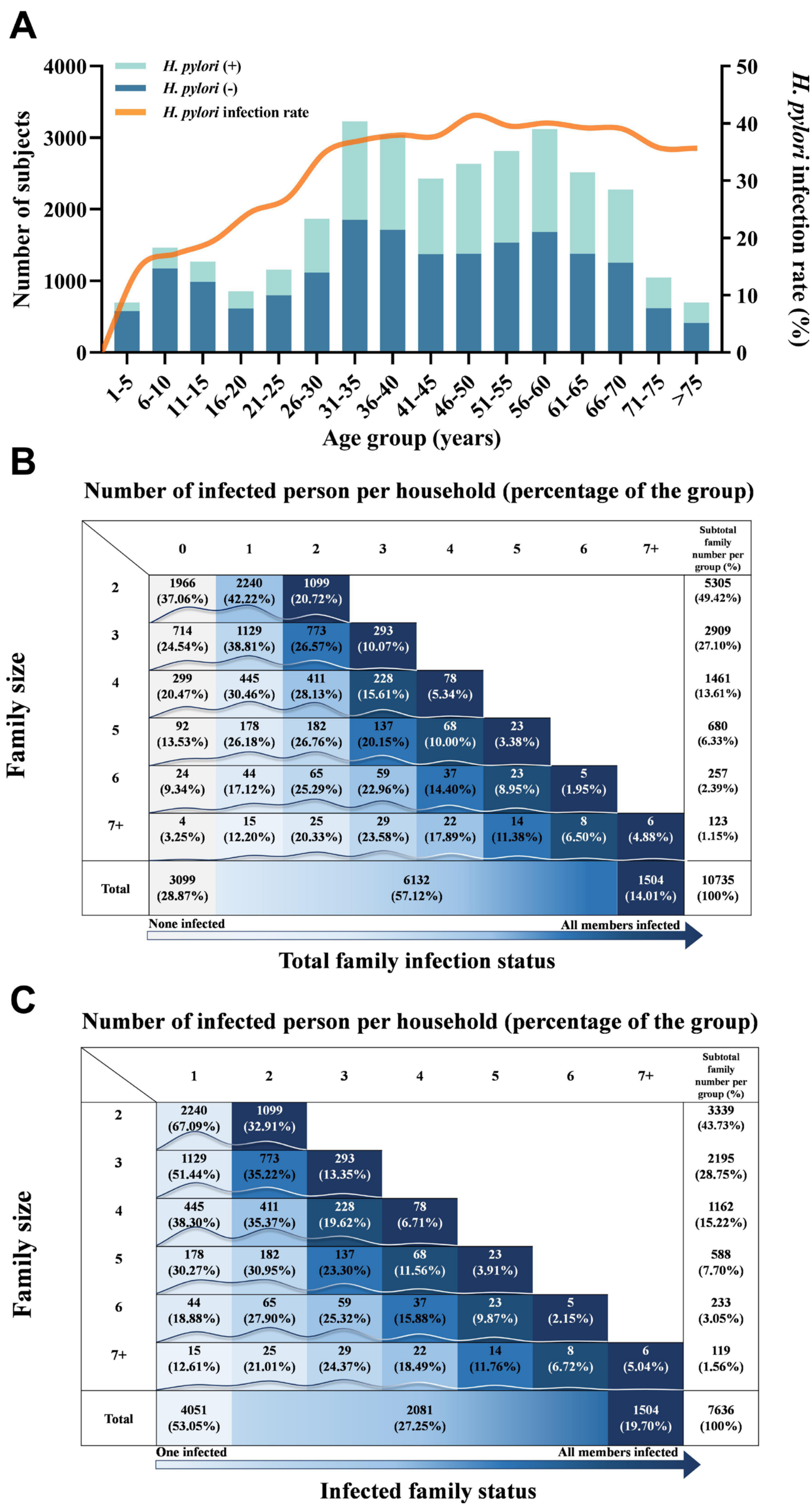

Figure 2 *Helicobacter pylori* infection status of the enrolled families. (A) *H. pylori* infection status of enrolled participants and their infection rates in different age groups. Left y axis represents the number of participants enrolled, and right y axis represents the percentage of their infection rates, x axis indicates different age groups. (B, C) figure 2B indicates *H. pylori* infection status of 10 735 enrolled families, and figure 2C indicates stratified 7636 *H. pylori*-infected families. y axis represents family size, which ranges from 2 to 7 (or more) persons, and x axis represents the number of infected persons within the household. Numbers within square represents the number of infected families; percentage numbers within the bracket and curve lines indicate the percentage of infected families in the same family size groups. Infected family: at least one person in the family was infected; non-infected family: all members in the family were not infected. Children: participant's age is less than 18 years for short, including children and adolescents.

Table 1 Demographic information of enrolled households and *Helicobacter pylori* infection risk factors

Categories	Total no. of household (10,735), n (%)	Infected household* (n=7636)	Uninfected household† (n=3099)	Household infection rate (%)‡	Crude OR (95% CI)	P value§	Adjusted OR (95% CI)	P value
Demographic and socioeconomic characteristics								
Geographical areas								
Southwest	2176 (20.27)	1392	784	63.97	Reference		Reference	
North	1739 (16.20)	1204	535	69.24	1.26 (1.10 to 1.45)	0.001	1.25 (1.08 to 1.43)	0.002¶
Central	748 (6.97)	535	213	71.52	1.39 (1.15 to 1.67)	<0.001	1.38 (1.14 to 1.66)	0.001¶
East	2791 (26.00)	2042	749	73.16	1.55 (1.37 to 1.76)	<0.001	1.45 (1.28 to 1.65)	<0.001¶
South	1025 (9.55)	766	259	74.73	1.67 (1.41 to 1.97)	<0.001	1.51 (1.27 to 1.79)	<0.001¶
Northeast	857 (7.89)	633	224	73.86	1.67 (1.40 to 2.00)	<0.001	1.50 (1.25 to 1.80)	<0.001¶
Northwest	1399 (13.03)	1064	335	76.05	1.86 (1.60 to 2.17)	<0.001	1.83 (1.57 to 2.13)	<0.001¶
Annual household income (thousand yuan)								
<100	6639 (61.84)	4691	1948	70.66	Reference			
100–300	3265 (30.41)	2352	913	72.04	1.03 (0.94 to 1.13)	0.547		
>300	831 (7.74)	593	238	71.36	0.97 (0.82 to 1.14)	0.668		
Resident location								
City	7961 (74.16)	5679	2282	71.34	Reference			
Rural	2774 (25.84)	1957	817	70.55	1.03 (0.93 to 1.13)	0.614		
Household living area (m^2)								
<60	1261 (11.75)	866	395	68.68	Reference		Reference	
60–120	6296 (58.65)	4462	1834	70.87	1.09 (0.96 to 1.25)	0.182	1.03 (0.90 to 1.18)	0.660
>120	3178 (29.60)	2308	870	72.62	1.18 (1.02 to 1.36)	0.028	1.07 (0.92 to 1.25)	0.359
Family size (n)								
2	5305 (49.42)	3339	1966	62.94	Reference		Reference	
3	2909 (27.10)	2195	714	75.46	1.84 (1.66 to 2.04)	<0.001	1.97 (1.76 to 2.21)	<0.001¶
4	1461 (13.61)	1162	299	79.53	2.39 (2.07 to 2.74)	<0.001	2.53 (2.17 to 2.95)	<0.001¶
5	680 (6.33)	588	92	86.47	3.96 (3.15 to 4.97)	<0.001	4.25 (3.32 to 5.43)	<0.001¶
6	257 (2.39)	233	24	90.66	6.25 (4.09 to 9.56)	<0.001	6.29 (4.07 to 9.71)	<0.001¶
Seven and above	123 (1.15)	119	4	96.75	18.83 (6.94 to 51.13)	<0.001	19.51 (7.15 to 53.20)	<0.001¶
Family size (n) (when adjusted for variables excluding 'generations in household' in multivariate logistic analysis)								
2	5305 (49.42)	3339	1966	62.94	Reference		Reference	
3	2909 (27.10)	2195	714	75.46	1.84 (1.66 to 2.04)	<0.001	1.80 (1.62-2.60)**	<0.001**
4	1461 (13.61)	1162	299	79.53	2.39 (2.07 to 2.74)	<0.001	2.26 (1.97-2.60)**	<0.001**
5	680 (6.33)	588	92	86.47	3.96 (3.15 to 4.97)	<0.001	3.75 (2.99-4.72)**	<0.001**
6	257 (2.39)	233	24	90.66	6.25 (4.09 to 9.56)	<0.001	5.60 (3.66-8.56)**	<0.001**
Seven and above	123 (1.15)	119	4	96.75	18.83 (6.94 to 51.13)	<0.001	17.31 (6.38-46.99)**	<0.001**
Generations in household								
1	3814 (35.53)	2556	1258	67.02	Reference		Reference	
2	4878 (45.44)	3477	1401	71.28	1.21 (1.10 to 1.33)	<0.001	0.82 (0.74 to 0.91)	<0.001¶
3	2043 (19.03)	1603	440	78.46	1.81 (1.59 to 2.05)	<0.001	0.79 (0.68 to 0.92)	<0.001¶
Generations in household (when adjusted for variables excluding 'family size' in multivariate logistic analysis)								
1	3814 (35.53)	2556	1258	67.02	Reference		Reference	
2	4878 (45.44)	3477	1401	71.28	1.21 (1.10 to 1.33)	<0.001	1.21 (1.10-1.32)††	<0.001††
3	2043 (19.03)	1603	440	78.46	1.81 (1.59 to 2.05)	<0.001	1.77 (1.56-2.01)††	<0.001††
Premeal factors								
Dishwashing								
Tap water	9022 (84.04)	6437	2585	71.35	Reference			
In a basin	1713 (15.96)	1199	514	69.99	0.95 (0.84 to 1.06)	0.341		
Tableware sterilisation								
No sterilisation	6999 (65.20)	4997	2002	71.40	Reference			
Disinfection cabinet	1791 (16.68)	1268	523	70.80	0.94 (0.84 to 1.06)	0.289		
Other disinfection methods	1945 (18.12)	1371	574	70.49	0.94 (0.84 to 1.05)	0.250		
Sources of drinking water								
Boiled water	8034 (74.84)	5730	2304	71.32	Reference			
Tap water	854 (7.96)	620	234	72.60	1.08 (0.92 to 1.26)	0.378		
Bottled water	1469 (13.68)	1027	442	69.91	0.94 (0.83 to 1.06)	0.302		

Continued

Table 1 Continued

Categories	Total no. of household (10,735), n (%)	Infected household* (n=7636)	Uninfected household† (n=3099)	Household infection rate (%)‡	Crude OR (95% CI)	P value§	Adjusted OR (95% CI)	P value
Purified water	291 (2.71)	198	93	68.04	0.89 (0.69 to 1.14)	0.354		
Well water	87 (0.81)	61	26	70.11	0.92 (0.58 to 1.47)	0.732		
Mid-meal factors								
Individual dining								
No	9289 (86.53)	6633	2656	71.41	Reference			
Yes	1446 (13.47)	1003	443	69.36	0.91 (0.80 to 1.02)	0.111		
Dish sharing								
No	1704 (15.87)	1207	497	70.83	Reference			
Yes	9031 (84.13)	6429	2602	71.19	1.04 (0.93 to 1.17)	0.505		
Serving chopsticks and spoons								
No	8484 (79.03)	6070	2414	71.55	Reference		Reference	
Yes	2251 (20.97)	1566	685	69.57	0.89 (0.81 to 0.99)	0.034	0.92 (0.83 to 1.02)	0.129
Post-meal factors								
Water cup sharing								
No	8014 (74.65)	5687	2327	70.96	Reference			
Yes	2721 (25.35)	1949	772	71.63	1.06 (0.97 to 1.17)	0.210		
Dental mouthwash cup sharing								
No	9719 (90.54)	6931	2788	71.31	Reference			
Yes	1016 (9.46)	705	311	69.39	0.91 (0.79 to 1.05)	0.202		
Dental appliances sharing								
No	10 263 (95.60)	7294	2969	71.07	Reference			
Yes	472 (4.40)	342	130	72.46	1.06 (0.86 to 1.30)	0.600		
Others								
Family history of diseases								
None	9018 (84.01)	6386	2632	70.81	Reference		Reference	
Peptic ulcers	1447 (13.48)	1043	404	72.08	1.06 (0.94 to 1.20)	0.337	1.02 (0.90 to 1.16)	0.724
Gastric cancer	270 (2.52)	207	63	76.67	1.35 (1.02 to 1.80)	0.037	1.28 (0.96 to 1.71)	0.099
Pets in household								
No	9526 (88.74)	6775	2751	71.12	Reference			
Yes	1209 (11.26)	861	348	71.22	0.98 (0.86 to 1.12)	0.768		
Poultry in household								
No	10 359 (96.50)	7365	2994	71.10	Reference			
Yes	376 (3.50)	271	105	72.07	1.12 (0.89 to 1.41)	0.337		
Livestock in household								
No	10 525 (98.04)	7491	3034	71.17	Reference			
Yes	210 (1.96)	145	65	69.05	0.96 (0.71 to 1.29)	0.796		

*Infected household is defined as a household with at least one *H. pylori*-infected family member.
†Uninfected household is defined as a household without any *H. pylori*-infected family member.
‡Household infection rate is defined as percentage of infected household among all households.
§P value was calculated by univariate logistic regression, p<0.05 indicates that infection risk increase/decrease significantly compared with the reference groups.
¶These are independent risk/protective factors for household *H. pylori* infection compared with reference group. P value was calculated by multivariate logistic regression, and was adjusted with items of p<0.1 in univariate logistic regression.
**These were results when 'family size' was adjusted for variables excluding 'generations in household' in multivariate logistic analysis, all other variable adjustment did not change this result and conclusion.
††These were results when 'generations in household' was adjusted for variables excluding 'family size' in multivariate logistic analysis, all other variable adjustment did not change this result and conclusion.

family members. In the 3339 two-person families, 32.91% had both members infected (figure 2C).

An average of 1.66 persons were infected in the 7636 infected households, accounting for 54.53% of the total household members (online supplemental table 2). In addition, in order to understand the cluster level of the infected families, we mapped the family infection index of *H. pylori*-infected patients within the household in all 29 provinces analysed (online supplemental figure 1).

Of the enrolled families, 7961 (74.16%) were urban residents, and 2774 (25.84%) were from rural areas (table 1). Among many variables, household location or geographical area (eg, northwest China: OR 1.83, 95% CI 1.57 to 2.13), and family size (eg, family of three: OR: 1.97, 95% CI 1.76 to 2.21) were independent risk factors for increased infection risk (p<0.001), and more generations living in a household (eg, three generations: OR: 0.79, 95% CI 0.68 to 0.92) was an independent protective factor. However, the role of generations as a risk/

protective factor appeared to be biphasic and was closely related to the family size, it was a risk factor for household infection before multivariate logistic regression analysis, but a protective factor after adjustment, and became a risk factor again when it was adjusted excluding the family size (table 1), while all other variable adjustments did not change this conclusion.

Other factors did not affect infection risk ($p>0.05$), such as dishwashing; tableware sterilisation; drinking boiled water, tap water, bottled water, purified water or well water; family members sharing dishes, cups or dental appliances; and having pets, poultry or livestock in the household. However, using serving chopsticks or spoons reduced the infection risk ($p<0.05$), whereas a family history of gastric cancer increased the infection risk ($p<0.05$). Although the household infection rate did not differ among various income groups (table 1), stratified analysis showed that high-income groups had a lower average infection rate and lower all-member-infection rate, and vice versa ($p<0.05$, figure 3A,B).

The general family *H. pylori* infection rates in 29 of the 31 provinces ranged from 50.27% to 85.06%, and the average infection rate was 71.21% (table 2). Among the 29 provinces, 26 had household infection rates above 60%, and 20 provinces had

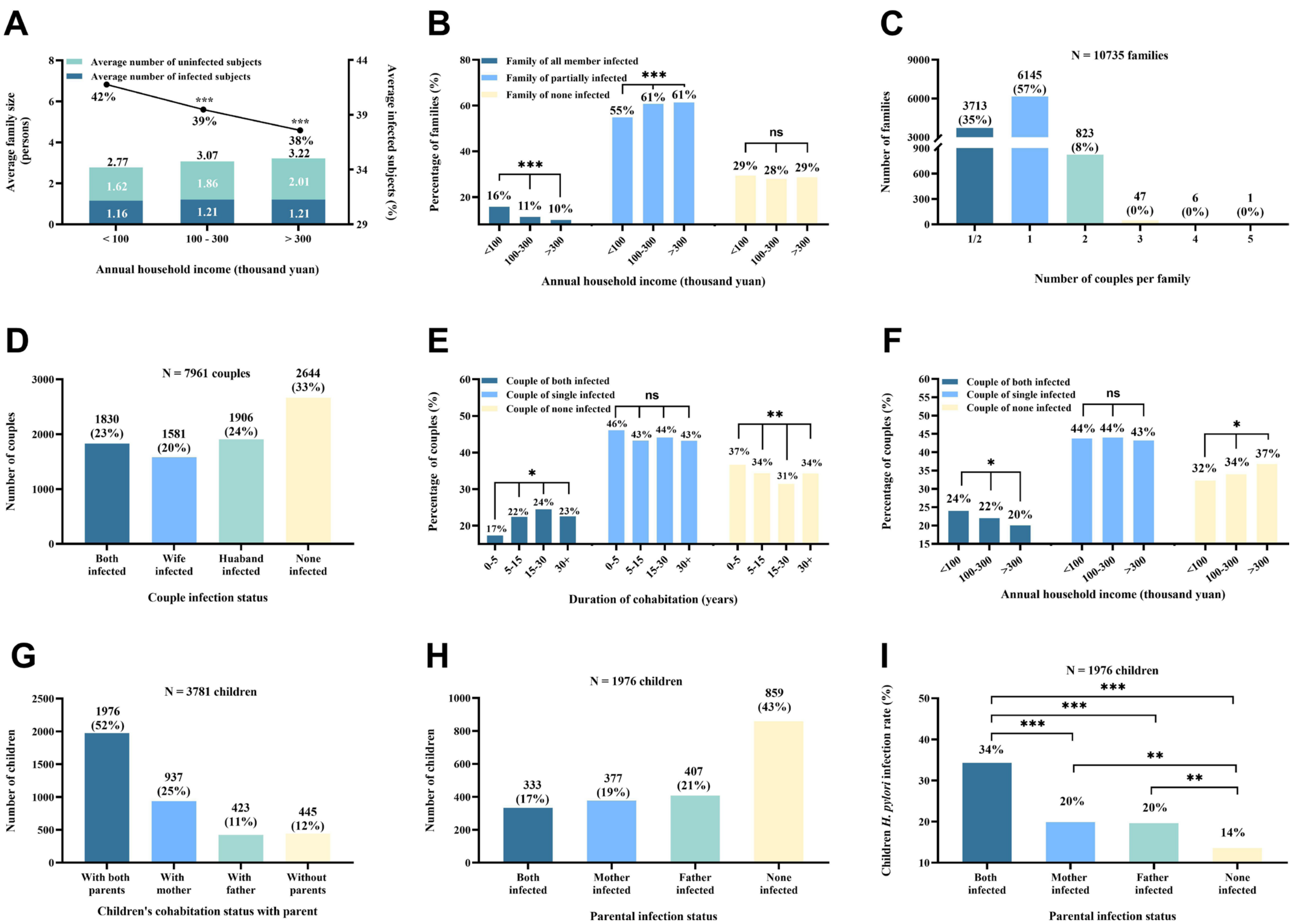

Figure 3 Stratified analysis of *Helicobacter pylori* infection in the enrolled families. (A) Correlation of annual household income, average family size and proportion of infected person in different household income groups. Left: y axis represents average family size, and right: y axis represents average percentage of infected participants, and x axis indicates annual household income. *p<0.05 when compared with household income < ¥100 000 group. (B) Correlation of stratified annual household income and infection rate in 10 735 families. The y axis represents percentage of families, and x axis indicates annual household income. ***p<0.001 when compared with household income < ¥100 000 group; NS, not significant when these groups were compared with each other, p>0.05. (C) Distribution of couples/generations number per household in 10 735 enrolled families; y axis represents the number of family, and x axis represents the number of couples/generations within the family. (D) Infection status of the total 7961 couples; y axis represents the number of couples, and x axis indicates the infection status of these couples. (E) Correlation of couple cohabitation time and *H. pylori* infection rate of 7961 couples. The y axis represents percentage of couples, and x axis indicates couple cohabitation time (years). *p<0.05 and **p<0.01, when compared with 0–5 years cohabitation group; NS, not significant when these groups were compared with each other, p>0.05. (F) Correlation of annual household income and couple infection status. The y axis represents percentage of couples, and x axis indicates annual household income. *p<0.05 when compared with household income <¥100 000 group; NS when these groups were compared with each other, p>0.05. (G) The total 3781 children's cohabitation status with their parents, y axis represents children number, and x axis indicates children's cohabitation status with their parents, the percentages inside the bracket are the percentages of the total children number. (H) Parental infection status of 1976 children who cohabitated with them, y axis represents children number, and x axis indicates *H. pylori* infection status of these parents. (I) Correlation of parental infection status and children infection rate, y axis represents the infection rate, x axis indicates *H. pylori* infection status of these parents. **p<0.01, ***p<0.001 when infection rates between the two groups were compared.

Table 2 *Helicobacter pylori* infection status among different provinces

	Provinces	Household-based analysis			Individual-based analysis			Children-based analysis*		
		Subtotal household, n	Infected household†, n	Household infection rate (%)‡	Subtotal individual, n	Infected individual, n	Individual infection rate (%)	Subtotal children, n	Infected children, n	Children infection rate (%)
1	Qinghai	395	336	85.06	1129	673	59.61	93	51	54.84
2	Hainan	430	359	83.49	1454	744	51.17	237	59	24.89
3	Gansu	303	246	81.19	819	415	50.67	85	22	25.88
4	Jiangsu	535	430	80.37	1680	845	50.30	203	64	31.53
5	Liaoning	308	247	80.19	982	433	44.09	92	34	36.96
6	Shaanxi	153	119	77.78	527	234	44.40	45	8	17.78
7	Shandong	457	354	77.46	1412	611	43.27	199	52	26.13
8	Anhui	450	346	76.89	1395	568	40.72	200	35	17.50
9	Xinjiang	95	73	76.84	238	112	47.06	23	6	26.09
10	Fujian	229	175	76.42	558	276	49.46	46	14	30.43
11	Tianjin	311	230	73.95	911	360	39.52	165	27	16.36
12	Hebei	426	313	73.47	1340	526	39.25	292	62	21.23
13	Jiangxi	531	390	73.45	1654	635	38.39	334	67	20.06
14	Jilin	203	147	72.41	587	230	39.18	63	6	9.52
15	Shanxi	362	261	72.10	944	405	42.90	39	7	17.95
16	Hunan	352	253	71.88	992	386	38.91	124	23	18.55
17	Hubei	272	195	71.69	860	300	34.88	80	10	12.50
18	Sichuan	733	518	70.67	2052	832	40.55	207	44	21.26
19	Henan	124	87	70.16	319	137	42.95	33	7	21.21
20	Chongqing	522	366	70.11	1659	616	37.13	230	44	19.13
21	Heilongjiang	346	239	69.08	1007	414	41.11	93	22	23.66
22	Guangdong	595	407	68.40	1811	642	35.45	325	43	13.23
23	Ningxia	453	290	64.02	1184	431	36.40	132	20	15.15
24	Inner Mongolia	238	152	63.87	628	218	34.71	37	3	8.11
25	Zhejiang	372	230	61.83	886	327	36.91	90	12	13.33
26	Beijing	402	248	61.69	1152	394	34.20	104	13	12.50
27	Yunnan	734	414	56.40	1810	564	31.16	88	10	11.36
28	Shanghai	217	117	53.92	583	185	31.73	59	8	13.56
29	Guizhou	187	94	50.27	525	133	25.33	63	4	6.35
Total/average§		10 735	7636	71.21§	31 098	12 646	40.66§	3781	777	20.55§

*Children is defined as participants less than 18 years of age, including children and adolescents.
†Infected household is defined as a household with at least one *H. pylori*-infected family member
‡Household infection rate is defined as percentage of infected household among all households.
§Average infection rate (per column).

infection rates above 70%. In five provinces—Qinghai, Hainan, Gansu, Jiangsu and Liaoning—the infection rates were alarmingly above 80%. The average family infection rate (71.21%) was much higher than the individual average *H. pylori* infection rate (40.66%). Detailed *H. pylori* infection rate and its correlation with age in the 29 provinces by different geographical regions are presented in online supplemental figure 2 . We failed to correlate the infection rates with per capita gross domestic product (GDP) or general GDP levels in all 29 provinces (online supplemental figure 3), but found the infection rate correlated well with the gastric cancer incidence in most provinces in China (online supplemental figure 4).

Individual-based *H. pylori* infection status and risk factors

Individual-based infection status and risk factors are presented in table 3. A higher *H. pylori* infection risk was observed for individuals who were male, not living in southwest areas, married and living in rural areas, as well as those who reported more roadside restaurant dining, were exposed to infected family members, and previously tested *H. pylori*-positive ($p<0.05$). Individuals with higher education levels, reporting more cafeteria dining and previously tested negative had a lower infection risk ($p<0.05$).

In multivariate logistic analysis, individual infection was strongly associated with the presence of infected members (eg, five infected members per household group: OR 2.72, 95% CI 1.86 to 4.00). In addition, geographical area of residence (eg, northwest China: OR 1.64, 95% CI 1.48 to 1.82), male sex (OR 1.14, 95% CI 1.08 to 1.21), being married (OR 1.31, 95% CI 1.18 to 1.45) and previous positive *H. pylori* tests (OR: 6.28, 95% CI: 5.41 to 7.28) were independent infection risk factors. Younger age (OR 0.57, 95% CI 0.46 to 0.70), higher education level (OR 0.85, 95% CI 0.79 to 0.91) and previous negative *H. pylori* tests (OR 0.44, 95% CI 0.39 to 0.48) were independent protective factors (table 3).

The individual infection rate also varied greatly depending on different provinces (table 2). It was as high as 59.61% in Qinghai, northwest China, and as low as 25.33% in Guizhou, southwest China (table 2). These infection rates were in accordance with household infection rates (table 1). A summary of the overall risk and protective factors was presented in online supplemental figure 5.

H. pylori infection status and risk factors in couples

To further investigate the risk factors and the transmission pattern between couples, we analysed the infection status in this group of population. Among 10 735 families, 6145 (57.24%) contained one couple, and 877 (over 8%) contained more than two generations or couples (figure 3C); 3713 (34.59%) families only had either a wife or a husband (figure 3C). Of the total of 7961 couples (figure 3D), 1830 (22.99%) were both *H. pylori*-infected, 2644 (33.21%) were both not infected, and the rest had either the husband or wife infected. The infection rate increased with the duration of cohabitation ($p<0.05$, figure 3E); couples with a shorter cohabitation time (figure 3E) and higher income had lower infection rates, and *vice versa* (figure 3F, $p<0.05$).

H. pylori infection status and risk factors for children and adolescents

In order to explore the *H. pylori* infection risk factors, and their correlation with parental infection status in children and adolescent, we further analysed their infection status and the possible transmission routes within the household. A total of 3781 children and adolescents were enrolled in this cohort (figure 3G, table 4); 2310 (61.09%) were from a one-child family and had no siblings (table 4). The rest had 1–3 or more siblings (table 4). The overall *H. pylori* infection rate in the 3781 children and adolescents was 20.55% (table 2, figure 1), which varied hugely depending on geographical area. For example, in Qinghai, a developing province in northwest China, the infection rate was 54.84%, but in Beijing, Shanghai, and other well-developed regions or provinces, the infection rates were all below 15% (table 2).

The risk factors for *H. pylori* infection in children and adolescents were similar to those in adults (table 4). For example, frequent dining at roadside restaurants (OR=1.38) increased the infection risk ($p<0.05$), whereas washing hands before meals and after defecation, and avoiding drinking tap water reduced the infection risk ($p<0.05$). The number of siblings and birth order were not associated with the childhood infection risk ($p>0.05$) (online supplemental figure 3, table 4). Notably, an *H. pylori*-infected mother, father, grandmother or siblings was associated with increased infection risk ($p<0.001$), but only infected mothers (OR=1.70) and fathers (OR=1.68) were independent risk factors for infection ($p<0.05$; table 4).

To evaluate the impact of parental infection status on childhood infection rate, a stratified analysis was performed on subgroups. A total of 1976 children and adolescents cohabitated with parents (figure 3G), their parental infection status is shown in figure 3H. We noted that their infection rate increased along with parental infection ($p<0.001$), from 13.57% in the group with no parent infected to 34.32% in the group with both parents infected ($p<0.001$; figure 3I).

DISCUSSION

This work investigated family-based *H. pylori* infection together with individual-based infection pattern in mainland China. The results reveal that the family-based *H. pylori* infection rate was much higher than the individual-based infection rates, and a large portion of Chinese families were infected. In several provinces, the infection rates were alarmingly above 80%, which is a serious condition that has not been recognised previously. In addition, we noted that the infection is concentrated in certain groups of families, instead of being evenly distributed in the population.

These results provide evidences to support the novel concept of 'whole family-based *H. pylori* infection control and management'[16 17] for related disease prevention, and the sister consensus publication of this investigation: the 'Chinese consensus report on family-based *H. pylori* infection control and management (2021 edition)'.[6] Together, they can be considered landmark events to transform *H. pylori* treatment from individual-based care to family-based infection control in clinical practice. Because this approach is more effective and convenient, it facilitates *H. pylori* management through better engagement of family members, higher eradication rates, lower reinfection rates[16 17] and cost-effectiveness.[27] Despite previous reports have demonstrated *H. pylori* family-cluster infection,[9–15 18 28] large scale, detailed analysis the relationship of family member infection status, risk factor and pattern of infection has not been reported, this work provide novel insights on family-based *H. pylori* infection status at the national level.

Previously scattered small studies have investigated the relationship between household member *H. pylori* infection and various lifestyle risks.[8 29–31] To assess *H. pylori* intrafamilial transmission in the general population and the role of the family's

Table 3 Demographic information of enrolled individuals and *Helicobacter pylori* infection risk factors

Categories	Total no. of individual (31098), n (%)	H. pylori-infected, n	H. pylori uninfected, n	Infection rate (%)	Crude OR (95% CI)	P value*	Adjusted OR (95% CI)	P value
Demographic information								
Geographical areas								
Southwest	6046 (19.44)	2145	3901	35.48	Reference		Reference	
North	4975 (16.00)	1903	3072	38.25	1.13 (1.04 to 1.23)	0.003	1.17 (1.06 to 1.29)	<0.001†
Central	2171 (6.98)	823	1348	37.91	1.08 (0.97 to 1.20)	0.154	1.13 (1.00 to 1.28)	0.057
East	8168 (26.27)	3447	4721	42.20	1.37 (1.27 to 1.47)	<0.001	1.29 (1.19 to 1.42)	<0.001†
South	3265 (10.50)	1386	1879	42.45	1.34 (1.22 to 1.47)	<0.001	1.37 (1.23 to 1.53)	<0.001†
Northeast	2576 (8.28)	1077	1499	41.81	1.42 (1.29 to 1.57)	<0.001	1.26 (1.12 to 1.41)	<0.001†
Northwest	3897 (12.53)	1865	2032	47.86	1.76 (1.61 to 1.91)	<0.001	1.64 (1.48 to 1.82)	<0.001†
Gender								
Female	17620 (56.66)	6983	10637	39.63	Reference		Reference	
Male	13478 (43.34)	5663	7815	42.02	1.11 (1.06 to 1.16)	<0.001	1.14 (1.08 to 1.21)	<0.001†
Age								
Adult (≥18 years)	27317 (87.84)	11869	15448	43.45	Reference		Reference	
Children and adolescents (<18 years)	3781 (12.16)	777	3004	20.55	0.39 (0.35 to 0.42)	<0.001	0.57 (0.46 to 0.70)	<0.001†
Marital status								
Single	6350 (20.42)	1702	4648	26.80	Reference		Reference	
Married	24092 (77.47)	10678	13414	44.32	1.98 (1.86 to 2.11)	<0.001	1.31 (1.18 to 1.45)	<0.001 †
Other	656 (2.11)	266	390	40.55	1.76 (1.48 to 2.09)	<0.001	1.34 (1.07 to 1.69)	0.010 †
Resident location								
City	23203 (74.61)	9326	13877	40.19	Reference		Reference	
Rural	7895 (25.39)	3320	4575	42.05	1.16 (1.10 to 1.23)	<0.001	1.06 (0.98 to 1.14)	0.133
Education level								
Middle/high school	9861 (40.45)	4287	5574	43.47	Reference	<0.001	Reference	
College and above	14518 (59.55)	6131	8387	42.23	0.90 (0.85 to 0.95)	<0.001	0.85 (0.79 to 0.91)	<0.001 †
Occupation								
Farmer	3723 (11.97)	1579	2144	42.41	Reference		Reference	
Worker	3763 (12.10)	1702	2061	45.23	1.05 (0.95 to 1.15)	0.365	1.11 (0.97 to 1.27)	0.127
Teacher	1341 (4.31)	593	748	44.22	0.94 (0.83 to 1.08)	0.396	1.05 (0.89 to 1.25)	0.551
Investigator	2423 (7.79)	1040	1383	42.92	0.88 (0.79 to 0.98)	0.025	1.04 (0.89 to 1.22)	0.592
Doctor	4090 (13.15)	1729	2361	42.27	0.90 (0.82 to 0.99)	0.022	1.09 (0.95 to 1.26)	0.225
Soldier	91 (0.29)	44	47	48.35	1.21 (0.79 to 1.87)	0.377	1.37 (0.84 to 2.24)	0.213
Merchant	1778 (5.72)	796	982	44.77	1.04 (0.93 to 1.17)	0.488	1.07 (0.91 to 1.24)	0.422
Others	9752 (31.36)	4224	5528	43.31	0.95 (0.88 to 1.03)	0.229	1.10 (0.97 to 1.25)	0.131
Student	4137 (13.30)	939	3198	22.70	0.41 (0.37 to 0.46)	0.000	0.85 (0.69 to 1.05)	0.132
Lifestyle-related factors								
Drinking tap water								
No	28900 (92.93)	11759	17141	40.69	Reference			
Yes	2198 (7.07)	887	1311	40.35	1.02 (0.93 to 1.12)	0.698		
Washing hands before meal and after defecation								
No	2430 (7.81)	970	1460	39.92	Reference			
Yes	28668 (92.19)	11676	16992	40.73	0.97 (0.89 to 1.05)	0.421		
Cafeteria dining								
Rare	27700 (89.07)	11316	16384	40.85	Reference		Reference	
Frequent	3398 (10.93)	1330	2068	39.14	0.90 (0.83 to 0.97)	0.006	0.93 (0.85 to 1.02)	0.143
Dining at road side restaurant								
Rare	26318 (84.63)	10539	15779	40.04	Reference		Reference	
Frequent	4780 (15.37)	2107	2673	44.08	1.15 (1.08 to 1.23)	<0.001	0.99 (0.91 to 1.07)	0.789
Dining at hotel restaurant								
Rare	28578 (91.90)	11534	17044	40.36	Reference		Reference	
Frequent	2520 (8.10)	1112	1408	44.13	1.12 (1.02 to 1.22)	0.013	1.09 (0.98 to 1.21)	0.124
No. of infected family members exposed‡								
0	13804 (44.39)	4849	8955	35.13	Reference		Reference	
1	11358 (36.52)	4947	6411	43.56	1.56 (1.48 to 1.65)	<0.001	1.52 (1.43 to 1.62)	<0.001†
2	4121 (13.25)	1882	2239	45.67	1.67 (1.56 to 1.80)	<0.001	1.69 (1.55 to 1.85)	<0.001†

Continued

Table 3 Continued

Categories	Total no. of individual (31098), n (%)	H. pylori-infected, n	H. pylori uninfected, n	Infection rate (%)	Crude OR (95% CI)	P value*	Adjusted OR (95% CI)	P value
3	1260 (4.05)	637	623	50.56	2.12 (1.88 to 2.38)	<0.001	2.12 (1.84 to 2.45)	<0.001†
4	382 (1.23)	225	157	58.90	3.02 (2.45 to 3.73)	<0.001	2.86 (2.22 to 3.68)	<0.001†
Five and above	173 (0.56)	106	67	61.27	3.34 (2.44 to 4.56)	<0.001	2.72 (1.86 to 4.00)	<0.001†
Medical history								
Gastrointestinal symptoms within last 1 year								
No	22 519 (72.41)	8863	13 656	39.36	Reference			
Yes	8579 (27.59)	3783	4796	44.10	1.01 (0.96 to 1.07)	0.609		
Previous *H. pylori* diagnosis								
Did not test *H. pylori*	24 742 (79.56)	9261	15 481	37.43	Reference		Reference	
Tested as negative	3398 (10.93)	687	2711	20.22	0.42 (0.38 to 0.46)	<0.001	0.44 (0.39 to 0.48)	<0.001†
Tested as positive	2958 (9.51)	2698	260	91.21	6.56 (5.71 to 7.54)	<0.001	6.28 (5.41 to 7.28)	<0.001†
History of gastroduodenal surgery								
No	30 782 (98.98)	12 496	18 286	40.60	Reference			
Yes	316 (1.02)	150	166	47.47	1.10 (0.86 to 1.40)	0.453		

*P value was calculated by univariate logistic regression, p<0.05 indicates that infection risk increase/decrease significantly compared with the reference groups.
†These are independent risk (protective) factors for *H. pylori* infection compared with the reference group. P value was calculated by multivariate logistic regression and was adjusted with items of p<0.1 in univariate logistic regression.
‡Number of infected family members exposed is defined as the number of *H. pylori*-infected persons in a household that the participant is exposed.

social background, for example, one study in northern Italy in 1999 examined 416 families (3289 residents). The results indicated that family social status was independently related to infection in children, with blue-collar or farming families showing an increased infection risk compared with children of white-collar workers.[29] Another study conducted on 2752 household members in northern California in 2006 found that exposure to an *H. pylori*-infected person with gastroenteritis, particularly vomiting, markedly increased the risk for new infection.[8]

A community-based study in 2017 in Vietnam on 219 households (918 individuals) also showed that high monthly income, not regularly being fed chewed food, and being breastfed were protective factors against *H. pylori* infection. Risk factors for infection in children were not regularly handwashing after defecation, an *H. pylori*-infected mother and grandfather, the father's occupation, mother's education, and household size.[30] One 2022 family-based *H. pylori* infection survey on 282 families (772 individuals) also reported that the household infection rate was 87.23% in central China.[31] The current work is in line with these studies and provides important evidence indicating that the clustering of infections within the same family was due to increased infection, not simply by chance. It also highlights the importance of implementing family-based *H. pylori* infection control and management in clinical practice.

This survey enrolled families of largely urban residence (74.61%) and a small portion of rural residents (25.39%), which differs from a previous investigation in 1992.[32] However, it reflects the current social structure in Chinese society, because decades-long urbanisation and industrialisation have profoundly changed its population structure. The latest national census in 2021[23] revealed that the proportion of urban residents in 2021 (urban 64.72%, rural 35.28%) was much higher than that in 1990 (urban 26.41%, rural 73.59%), and the average family size has shrunk to 2.62 persons in 2021 from 4.05 persons in 1990. The present enrolments thus are consistent with the latest national demographic trends.[23]

Earlier small studies have provided clues on the correlation of marriage time and infection risk,[12 33 34] and the result supported a spouse-to-spouse transmission, although the infection between couples were thought to be infrequent and dependent on the social economic status. The current work with 7961 couples have demonstrated that there are indeed increased infection rate from 17% to 22%–24% when their cohabitation time increase from 5 to 30 years (figure 3E). However, it is not clear if the increased infection rate is because of the transmission between couple themselves or from outside the family, or both. As *H. pylori* infection rate increase with age (figure 2A), future studies using the DNA fingerprinting technology are required to clarify the infection pattern between couples.

In addition, the role of generation in household infection appears biphasic and only closely related to family size in current study, since it showed opposite effects before and after multivariate logistic adjustment (table 1). The generation was a risk factor for household infection before multivariable logistic adjustment, but a protective factor after adjustment, and became a risk factor again when it was not adjusted by the family size, furthermore, testing on all other variable adjustments did not change this conclusion. This result is not expected, and was not reported before, previously studies have clearly demonstrated that large family size, crowded condition, more sibling, poor household hygiene are risk factors for *H. pylori* infection,[8 28–30] and more generation in a household tend to have larger family size, but no study have focused on the role of generation on household infection prior to this work. These results unexpectedly revealed its role in household infection and indicated a complex pattern of *H. pylori* intrafamilial spread. The explanation for these subtle discrepancies could be due to the fact that at a given family size, more generations in a family means fewer members in each generation, and possibly higher income, lower infection risk; while at a given number of generations, larger family size is a risk factor for infection, which is in line with the current concept and observations. However, future studies may be required to clarify the role of generation in the household infection in more detail.

The general *H. pylori* infection status at national level has not been evaluated in China. *H. pylori* infection rate has been declining both globally and in China,[35] but existing infected individuals still pose a great health threat to the uninfected population. One meta-analysis[24] in 2020 in China which included

Table 4 Demographic information and risk factors for *Helicobacter pylori* infection in children and adolescents

Category	Total no. of children/ adolescents (3781), n (%)	*H. pylori* infected, n	*H. pylori* uninfected, n	*H. pylori* infection rate (%)	Crude OR (95% CI)	P value*	Adjusted OR (95% CI)	P value
Demographic information								
Gender								
Female	1771 (46.84)	351	1420	19.82	Reference			
Male	2010 (53.16)	426	1584	21.19	1.10 (0.93 to 1.29)	0.265		
Age (year)								
1–6	966 (25.55)	170	796	17.60	Reference		Reference	
7–11	1522 (40.25)	309	1213	20.30	1.18 (0.96 to 1.45)	0.124	1.32 (0.79 to 2.22)	0.287
12–17	1293 (34.20)	298	995	23.05	1.35 (1.09 to 1.67)	0.005	1.34 (0.76 to 2.36)	0.309
No. of siblings								
0	2310 (61.09)	473	1837	20.48	Reference			
1	1290 (34.12)	269	1021	20.85	1.02 (0.86 to 1.21)	0.821		
2	147 (3.89)	30	117	20.41	1.02 (0.67 to 1.54)	0.943		
Three and more	34 (0.90)	5	29	14.71	0.68 (0.26 to 1.77)	0.433		
Birth order								
First	3012 (79.66)	640	2372	21.25	Reference			
Second	702 (18.57)	129	573	18.38	0.85 (0.69 to 1.05)	0.121		
Third	57 (1.51)	7	50	12.28	0.53 (0.24 to 1.18)	0.530		
Fourth and more	10 (0.26)	1	9	10.00	0.42 (0.05 to 3.33)	0.412		
Living habits								
Drinking tap water								
No	3502 (92.62)	705	2797	20.13	Reference		Reference	
Yes	279 (7.38)	72	207	25.81	1.39 (1.05 to 1.84)	0.023	1.64 (0.74 to 3.64)	0.227
Washing hands before meal and after defecation								
No	328 (8.67)	81	247	24.70	Reference		Reference	
Yes	3453 (91.33)	696	2757	20.16	0.76 (0.59 to 1.00)	0.047	0.87 (0.39 to 1.91)	0.723
Cafeteria dining								
Rare	3203 (84.71)	657	2546	20.51	Reference			
Frequent	578 (15.29)	120	458	20.76	1.02 (0.82 to 1.27)	0.870		
Dining at road side restaurant								
Rare	3514 (92.94)	709	2805	20.18	Reference		Reference	
Frequent	267 (7.06)	68	199	25.47	1.38 (1.04 to 1.84)	0.028	2.06 (0.99 to 4.28)	0.052
Dining at hotel restaurant								
Rare	3623 (95.82)	743	2880	20.51	Reference			
Frequent	158 (4.18)	34	124	21.52	1.05 (0.71 to 1.56)	0.802		
Parental mouth-to-mouth feeding								
No	3781 (100.00)	777	3004	20.55				
Yes	0 (0.00)	0	0	NA	NA			
Habit of holding toys in mouth								
No	3605 (95.35)	739	2866	20.50	Reference			
Yes	176 (4.65)	38	138	21.59	1.07 (0.74 to 1.54)	0.726		
Parents kissing their children mouth-to-mouth								
No	3515 (92.96)	721	2794	20.51	Reference			
Yes	266 (7.04)	56	210	21.05	1.03 (0.76 to 1.40)	0.833		
Family member infection status								
Father infected†								
No	1266 (52.77)	203	1063	16.03	Reference		Reference	
Yes	1133 (47.23)	305	828	26.92	1.91 (1.57 to 2.34)	<0.001	1.68 (1.08 to 2.61)	0.020‡
Mother infected§								
No	1661 (57.02)	248	1413	14.93	Reference		Reference	
Yes	1252 (42.98)	339	913	27.08	2.06 (1.71 to 2.48)	<0.001	1.70 (1.10 to 2.63)	0.017‡
Grandfather infected¶								
No	474 (52.20)	85	389	17.93	Reference			
Yes	434 (47.80)	93	341	21.43	1.24 (0.89 to 1.72)	0.209		
Grandmother infected**								
No	728 (58.24)	109	619	14.97	Reference		Reference	

Continued

Table 4 Continued

Category	Total no. of children/ adolescents (3781), n (%)	*H. pylori* infected, n	*H. pylori* uninfected, n	*H. pylori* infection rate (%)	Crude OR (95% CI)	P value*	Adjusted OR (95% CI)	P value
Yes	522 (41.76)	121	401	23.18	1.72 (1.29 to 2.29)	<0.001	1.32 (0.85 to 2.03)	0.214
Sibling infected								
All negative or no sibling	3449 (91.22)	638	2811	18.50	Reference		Reference	
At least one positive	332 (8.78)	139	193	41.87	3.19 (2.52 to 4.04)	<0.001	0.44 (0.17 to 1.10)	0.080

*P value was calculated by univariate logistic regression, p<0.05 indicates that infection risk increase/decrease significantly compared with the reference group.
†Only children who cohabitated with their father were included.
‡Independent risk factors for *H. pylori* infection compared with the reference group. P value was calculated by multivariate logistic regression and was adjusted with items of p<0.1 in univariate logistic regression.
§Only children who cohabitated with their mother were included.
¶Only children who cohabitated with their grandfather were included.
**Only children who cohabitated with their grandmother were included.

670572 participants found that the infection rates during 1983–1994, 1995–2005 and 2006–2018 were 63.8%, 57.5% and 46.7% respectively, with an annual decline rate of 0.9%. The current overall infection rate of 40.66% is thus in line with such trend. This could be attributed to the continued education, improved economic and sanitary conditions, better water quality and interventions over the past decades. However, we also noted that only 13.44% (1,699/12,646) of *H. pylori*-infected patients had received treatment. Although this number may not be exactly proportional to the national eradication level, it indicates a critical challenge that has yet to be met for population-wide infection control.

Geographical location is important for diverse *H. pylori* infection status due to various lifestyle among different countries, in accordance with the already known risk factors from previous studies,[29–32 36] this survey reveals risk factors that have not been well recognised, and some are unique to China or Asian countries. One of them is that using serving chopsticks and spoons was associated with a lower infection rate. Sharing food with the same utensils or dishes is a traditional habit preserved in China and many Asian countries for centuries. This was considered a risk factor for *H. pylori* infection because the saliva culture of *H. pylori*-infected patients has confirmed the existence of oral *H. pylori*,[37] and *H. pylori* DNA can be detected on chopsticks.[38] Another family habit is chewing food before feeding it to children, a practice that was very common previously but is now rare in childcare. This is also supported by a population-based study in China[36] in 2015, which showed that individually served meals represented an independent protective factor for *H. pylori* infection.

H. pylori infection rates vary greatly depending on different geographical locations in China, the north and northwest regions are high prevalence regions for both *H. pylori* infection and gastric cancer incidence, and are also economically developing areas historically, this correlated well with the social economic status, living conditions and lifestyle habits.[24 39 40] For example, in Qinghai and Gansu, the two developing pasturing northwest region, has the higher *H. pylori* infection rate and gastric cancer incidence (online supplemental figure 4). In addition, a previous positive *H. pylori* test was shown as a risk factor in the current work. According to the questionnaire, this was partially due to a small proportion of enrolled participants who were either unable or unwilling to receive treatment, and thus had persistent infections.

Contaminated water has been recognised as a source of *H. pylori* spread,[41] however, whether or not it is still an important factor for current *H. pylori* spread in China remains to be evaluated. In this work, we noted drinking various types of water was not an independent risk factor for infection. This is probably because tap water and sewer systems are routinely available in all urban areas and most rural villages in China, and acquiring *H. pylori* infection from this route appears rare now.

H. pylori plays an important role in the increased prevalence of precancerous changes in relatives of gastric cancer patients, however, compared with healthy controls, relatives of patients with gastric cancer had a higher prevalence of hypochlorhydria but a similar prevalence of *H. pylori* infection.[18] A study in Germany showed that the prevalence of *H. pylori* infection was much higher among participants with a parental history of stomach cancer than among other participants.[42] Another study in San Marino indicated that *H. pylori* seropositivity was significantly associated with peptic ulcer in patients and their close relatives, in siblings and gastric cancer in fathers. In contrast, *H. pylori* seropositivity was not significantly associated with gastroduodenal diseases in partners.[43] In the current work, a familial history of gastric cancer was a risk factor for *H. pylori* infection, but a family history of either gastric cancer or peptic ulcer was not an independent factor for *H. pylori* infection. These results are partially in line with the described observations and indicate a complex pattern of *H. pylori* spread among family members, which deserves further delineation.

In the current study, the risk factors for childhood infection were infected family members, older age and unhygienic living habits, and the most vulnerable time for infection is at preschool and school ages. This is in line with previous small studies[36 44] and a 2022 meta-analysis report[45] that included 152650 children. The result of the latter indicated that paediatric *H. pylori* infection was significantly associated with lower economic status, having an infected mother or infected sibling, and older age. However, due to the previous national 'one-child-per-family' policy between 1982 and 2016, most Chinese families only have one child and two generations. These children usually have no or few siblings, so transmission among siblings may not be the major route in the Chinese setting. This is also indicated in the current study data that 61.09% of children had no siblings.

This study has limitations. First, the survey adopted a convenience sampling method instead of randomised sampling, which might have biased the selection of the population. However, due to the large sample size, the impact might be minor and does not affect the conclusions. Second, *H. pylori* infection was evaluated using ^{13}C-UBT test, and not combined with serum antibody or stool antigen tests. This only indicates the current infection status, therefore, it was not a complete landscape of *H. pylori* infection, and probably underestimated the real infection rate. Third, this is a cross-sectional study without data from endoscopy, thus missing more in-depth information on related diseases. Fourth, the work was performed in the Chinese setting, and the results may not apply to other areas. Fifth, the *H. pylori* genotype in infected families was not evaluated due to the lack of bacteria strain culture and DNA fingerprinting data; future in-depth studies are warranted. However, even with these limitations, the study has provided important evidence and novel points about family-based *H. pylori* infection.

CONCLUSIONS

The current work provides insights on family-based *H. pylori* infection in Chinese society, and important sources for its spread. These evidences support shifting from current individual-based care to family-based *H. pylori* infection management in clinical practice. Therefore, the test/treat strategies in family setting have important clinical and public health implications for infection control and related disease prevention, and are also valuable to other communities that have high infection rates and gastric cancer burdens.

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