Epidemiol. Infect. (2015), **143**, 2520–2531. © Cambridge University Press 2015
doi:10.1017/S0950268814003938

Environmental risk factors associated with Helicobacter pylori seroprevalence in the United States: a cross-sectional analysis of NHANES data

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Received 9 September 2014; Final revision 10 December 2014; Accepted 17 December 2014; first published online 16 January 2015

SUMMARY

Helicobacter pylori imparts a considerable burden to public health. Infections are mainly acquired in childhood and can lead to chronic diseases, including gastric ulcers and cancer. The bacterium subsists in water, but the environment's role in transmission remains poorly understood. The nationally representative National Health and Nutrition Examination Survey (NHANES) was examined for environmental risk factors associated with *H. pylori* seroprevalence. Data from 1999–2000 were examined and weighted to represent the US population. Multivariable logistic regression estimated adjusted odds ratios (aOR) and 95% confidence intervals (CI) for associations with seropositivity. Self-reported general health condition was inversely associated with seropositivity. Of participants aged <20 years, seropositivity was significantly associated with having a well as the source of home tap water (aOR 1·7, 95% CI 1·1–2·6) and living in a more crowded home (aOR 2·3, 95% CI 1·5–3·7). Of adults aged ⩾20 years, seropositivity was not associated with well water or crowded living conditions, but adults in soil-related occupations had significantly higher odds of seropositivity compared to those in non-soil-related occupations (aOR 1·9, 95% CI 1·2–2·9). Exposures to both well water and occupationally related soil increased the effect size of adults' odds of seropositivity compared to non-exposed adults (aOR 2·7, 95% CI 1·3-5·6). Environmental exposures (well-water usage and occupational contact with soil) play a role in *H. pylori* transmission. A disproportionate burden of infection is associated with poor health and crowded living conditions, but risks vary by age and race/ethnicity. These findings could help inform interventions to reduce the burden of infections in the United States.

Key words: Environmental exposure, *Helicobacter pylori*, nutrition surveys, seroepidemiological studies, seroprevalence.

INTRODUCTION

It is estimated that half of the world's population is infected with *Helicobacter pylori* [1]. While the majority of those infected will remain asymptomatic, up to 20% of *H. pylori* infections induce gastric inflammation that can lead to severe chronic disease outcomes, including chronic gastritis, peptic ulcer, gastric mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric cancer [2–5]. Epidemiological studies of *H. pylori* suggest the bacterium primarily spreads person-to-person via oral–oral and faecal–oral routes; however, conflicting results and knowledge gaps have precluded a clear

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understanding of pathogen transmission and the role of environmental factors [6]. Further insight into the pathogen's routes of transmission is essential to guide public health interventions aimed at controlling its spread and lessening its health burden [7].

Although prospective studies have not clearly identified causal aetiological associations between exposures and infection, observational studies have correlated key risk factors with *H. pylori* infections. Humans are most likely to acquire *H. pylori* in early childhood (before age 10 years) due to intrafamilial transmission [7, 8]. Studies have observed a higher prevalence in siblings (and parents) of infected children, and results have consistently supported infected siblings as a risk factor for *H. pylori* infection [6, 7, 9–11]. Acquisition rates during childhood are markedly higher in developing countries [12], and have been associated with living in impoverished regions with overcrowding and poor sanitation and hygiene [10, 13, 14]. Variable infection acquisition patterns have been observed between developed and developing countries, as well as within specific geographical areas by age, race, and socioeconomic groups, which may complicate public health risk assessments [12, 15–17].

Evidence suggests that *H. pylori* has an environmental pathogen reservoir, in which water has been implicated as the most likely medium conducive to pathogen survival, particularly in rural areas and developing countries [6]. When out of its natural environment, *H. pylori* morphologically adapts into a coccoid form that is viable and infective, but nonculturable [14, 18]. The bacterium forms biofilms as a protective niche in water [19–22] and can survive ozone and chlorination treatments [18, 23, 24]. *H. pylori* has been detected in shallow ground water [25], fresh and marine surface water [26–28], untreated well water [29], and untreated municipal wastewater [30, 31] in the United States and Europe. The bacterium has also been detected in treated municipal drinking water in Iraq, Iran, and Pakistan [32–35]. Although cross-sectional studies examining correlations between human infections and drinking-water source have produced inconsistent results, many suggest that contaminated drinking water is associated with a higher prevalence of *H. pylori* infections [6, 7, 9–11, 14, 36–43]. In addition, the US Environmental Protection Agency (EPA) considers *H. pylori* a Contaminate Candidate for possible regulation under the Safe Drinking Water Act (SDWA) [44–46].

Because relatively few studies have considered environmental risk factors for *H. pylori* transmission in the United States, and because considerable research gaps prevent targeted interventions to mitigate public health risks, nationally representative population-based data was used to examine risk factors associated with *H. pylori* seroprevalence. The National Health and Nutrition Examination Survey (NHANES) [47], within the National Center for Health Statistics of the Centers for Disease Control and Prevention (CDC), has conducted large-scale surveys designed to assess changes over time in the health and nutritional status of adults and children in the United States. NHANES released *H. pylori* serology results in HANES III (1988–1991) and the Continuous NHANES (1999–2000). Analyses of HANES III revealed that demographic factors, including socioeconomic status and race/ethnicity were significantly associated with *H. pylori* seroprevalence in the United States [15, 48]. The Continuous NHANES (1999–2000) data has been used to identify correlations with *H. pylori* seroprevalence, including positive associations with smoking [49] and iron deficiency anaemia [50], an inverse association with childhood asthma [51], and mixed results for biomarkers of type 2 diabetes [52, 53].

Grad *et al*. compared trends in *H. pylori* seroprevalence between HANES III (1988–1991) and Continuous NHANES (1999–2000) in adults aged $\geqslant$20 years [54]. The authors reported disparities in prevalence by race/ethnicity, in which seroprevalence 'preferentially' declined for the non-Hispanic White population, yet remained constant for non-Hispanic Blacks and Mexican Americans. However, the authors noted that indicators of socioeconomic status, including income–poverty ratio, country of birth origin, and educational attainment, while significantly associated with seropositivity, did not fully explain the observed disparities by race/ethnicity. They hypothesized that other factors not considered in their analyses were probably playing a role in *H. pylori* incidence and prevalence in US populations.

In this paper, the Continuous NHANES (1999–2000) data was further analysed to examine whether environmental factors were associated with *H. pylori* seroprevalence in the population as a whole and across stratified demographic groups by age and race/ethnicity.

METHODS

A single 2-year cycle of Continuous NHANES (1999–2000) data [47] was examined using SAS v. 9.3 (SAS Institute Inc., USA). Data were collected using a complex survey design; therefore, seroprevalence estimates were weighted to represent the total US civilian non-institutionalized population, and CDC's recommended approaches for SAS survey analysis procedures were followed [47]. Available sera from eligible participants aged ⩾3 years were tested by the CDC for immunoglobulin G (IgG) antibodies against *H. pylori* by an enzyme-linked immunoassay (ELISA). A dichotomous seropositivity cut-off was provided by the CDC, in which an optical density (OD) ⩾1·1 = positive and OD <1·1 = negative [55]. The authors selected covariates of interest *a priori,* based on previous reports and biological plausibility, to examine associations with *H. pylori* seropositivity.

Adulthood was defined using CDC's previously established cut-point of 20 years [56]. The two NHANES race/ethnicity categories of 'Mexican American' and 'other Hispanic' were combined into a shared category of 'Hispanic', and the race/ethnicity group of 'other, including multi-racial' was excluded from the stratified analyses due to a limited sample size. An objective measurement for current smoking status was based on serum cotinine level (non-smoker ⩽15 ng/ml and smoker >15 ng/ml), as previously reported [49].

In the Housing Characteristics (HOQ) questionnaire, participants were asked: *'What is the source of tap water in this home? Is it a private or public water company, a private or public well, or something else?'* and *'Are any of the water treatment devices listed on this card used in your home?'* Listed treatment devices included Brita® or other pitcher water filter, ceramic or charcoal filter, water softener, aerator, and reverse osmosis. To evaluate crowded housing, a new variable was calculated as described previously [57], with the total number of people living in a household as the numerator and the number of rooms in the home (excluding bathrooms) as the denominator. As described previously [57], because the room count includes the kitchen, a value of 1 was subtracted from homes with more than one room, for a more accurate indicator of living spaces in a home.

Because soil could be tainted by *H. pylori*-contaminated surface and ground waters, occupational exposures to soil were assessed by examining occupation categories reported in the Occupation Questionnaire (OCQ). Participants aged ⩾16 years who reported working in the last week were asked in what occupation their current job was. Using CDC's Occupation Group Codes [58], the authors *a priori* selected occupations likely to involve soil exposures and created a three-tier categorical variable to classify unemployed participants, those with occupations not likely to involve soil exposures, and occupations with likely soil exposure, for adults aged ⩾20 years to include in the adult subgroup analysis. Soil-related occupations included farm operators, managers, and supervisors; farm and nursery workers; related agricultural, forestry, and fishing occupations; construction trades; extractive and precision production occupations (e.g. miners and oil-well drillers); construction labourers; and labourers not employed in construction.

Multivariable logistic regression was used to compare the seroprevalence of IgG antibodies against *H. pylori* with key demographic characteristics and potential risk factors. Wald χ^2 odds ratio (OR) estimates and 95% confidence intervals (CI) were ascertained for unadjusted and adjusted regression models. Covariates with P values <0·2 in a simple logistic model were considered for inclusion in multivariable models. Multivariable models were selected using stepwise backwards elimination of covariates with P values >0·05, with the highest corresponding P value removed each step. Three models were co-developed that included the NHANES population as a whole, as well as two stratified models by age group and race/ethnicity. Selected models included all covariates with P values <0·05, as well as *a priori* selected demographic characteristics known to be associated with the outcome and the exposure variables of interest. To allow for direct comparisons between the final models, covariates selected for inclusion in any of the final models were retained in all three models to provide direct comparisons across strata.

RESULTS

In one 2-year cycle of continuous survey data (1999–2000), NHANES released *H. pylori* serology results for 7493 participants aged ⩾3 years, of which 25·4% were seropositive (Table 1). Associations between demographic characteristics and seropositivity in all participants were similar to previously published descriptive reports that included all participants [50] and only adults [49, 53, 54]. Increasing age was significantly associated with *H. pylori* seropositivity, but there was no difference in seropositivity between men and women. Compared to non-Hispanic Whites, Hispanics [adjusted OR (aOR) 3·5, 95% CI 2·6-4·8] and non-Hispanic Blacks (aOR 4·1, 95% CI 3·3-5·2) had higher odds of seropositivity. In addition,

Table 1. *Risk factors associated with elevated IgG antibodies against Helicobacter pylori in participants aged ⩾3 years (NHANES 1999–2000)*

Variable	*N*	Positive[a] (%)[b]	Unadjusted OR[c] (95% CI)	Adjusted OR (95% CI)
Age				
Continuous (years)	7493	25·4	**1·03 (1·02–1·03)**[d]	**1·04 (1·03–1·04)**
Age group (years)				
3–13	1806	7·1	Ref.	–
14–24	1927	17·0	**2·7 (2·1–3·4)**	–
25–51	1873	27·4	**5·0 (4·0–6·2)**	–
⩾52	1887	38·5	**8·2 (6·6–10·2)**	–
Gender				
Female	3829	25·3	Ref.	Ref.
Male	3664	25·6	1·0 (0·9–1·1)	1·0 (0·9–1·1)
Race/ethnicity				
Non-Hispanic White	2545	17·4	Ref.	Ref.
Non-Hispanic Black	1700	42·3	**3·5 (2·9–4·2)**	**4·1 (3·3–5·2)**
Hispanic	2998	45·3	**3·9 (3·2–4·8)**	**3·5 (2·6–4·8)**
Other, including multiracial	250	33·7	**2·4 (1·9–3·0)**	**2·2 (1·8–2·7)**
Country of birth origin[e]				
United States	5901	20·5	Ref.	Ref.
Non-US born	1587	54·0	**4·6 (3·8–5·5)**	**2·7 (2·1–3·4)**
Family income[e]				
⩾$ 20 000	4315	21·0	Ref.	Ref.
<$ 20 000	2735	34·8	**2·0 (1·5–2·6)**	**1·4 (1·1–1·7)**
Crowded housing[e]				
⩽1 person per room	5259	23·4	Ref.	Ref.
>1 person per room	2139	36·5	**1·9 (1·5–2·4)**	**1·7 (1·3–2·2)**
Smoking status[e,f]				
Non-smoker	6054	23·2	Ref.	Ref.
Smoker	1230	32·9	**1·6 (1·3–2·0)**	**1·8 (1·5–2·2)**
General health condition[e]				
Excellent	1953	17·6	Ref.	Ref.
Very good	1919	21·2	**1·3 (1·1–1·5)**	1·0 (0·9–1·2)
Good	2328	29·9	**2·0 (1·7–2·4)**	**1·2 (1·02–1·5)**
Fair/poor	1285	41·4	**3·3 (2·6–4·1)**	**1·4 (1·1–1·8)**
Source of tap water[e]				
Public/private water company	6595	25·4	Ref.	Ref.
Well water	735	24·9	1·0 (0·7–1·5)	1·5 (0·96–2·4)
At-home water-treatment device used[e,g]				
Yes	1457	19·3	Ref.	Ref.
No	5927	27·6	**1·6 (1·2–2·1)**	1·1 (0·9–1·4)

OR, Odds ratio; CI, confidence interval.

[a] IgG ELISA optical density (OD) ⩾1·1=positive; OD <1·1=negative. [b] All prevalence estimates were weighted. [c] Wald χ^2 logistic regression used. [d] Bold values denote statistically significant data (P<0·05). [e] Covariate has some missing data. [f] Based on serum cotinine level (non-smoker ⩽15 ng/ml, smoker >15 ng/ml). [g] Types of at-home water-treatment devices included: Brita® or other pitcher water filter, ceramic or charcoal filter, water softener, aerator, reverse osmosis.

participants born outside the United States were significantly more likely to be seropositive compared to those born in the United States (aOR 2·7, 95% CI 2·1-3·4). Members of families earning <$ 20 000 a year were more likely to be seropositive compared to families earning ⩾$20 000 (aOR 1·4, 95% CI 1·1-1·7). Similar to a report that analysed smoking in adults only [49], smoking was significantly associated with seropositivity when considering all participants (aOR 1·8, 95% CI 1·5-2·2).

An inverse association was observed with participants' self-reported general health condition: the worse the perceived health condition, the higher odds of seropositivity, with those reporting fair or poor health having higher odds of seropositivity compared to participants reporting being in excellent

https://doi.org/10.1017/S0950268814003938 Published online by Cambridge University Press

health (aOR 1·4, 95% CI 1·1-1·8) (Table 1). Participants living in a more crowded home with >1 person per room, were significantly more likely to be seropositive compared to participants with less crowded living conditions (aOR 1·7, 95% CI 1·3-2·2). Having a well as the source of home tap water compared to tap water provided by a private or public water company, was positively associated with seropositivity but did not reach the threshold for statistical significance (aOR 1·5, 95% CI 0·96-2·4). Similarly, participants who did not use at-home water-treatment devices had higher odds of seropositivity, but this association was not significant in the multivariable model.

Age group

Because the existing literature suggests that *H. pylori* infections are more often acquired in childhood, two multivariable models stratified by age group (3–19 and $\geqslant$20 years) were examined (Table 2). For the younger age group, in addition to demographic characteristics including age, race/ethnicity, birth origin, and family income, *H. pylori* seropositivity was significantly associated with living in a more crowded home (aOR 2·3, 95% CI 1·5-3·7) and having a well as the source of home tap water (aOR 1·7, 95% CI 1·1-2·6).

Conversely, in adult participants aged $\geqslant$20 years, *H. pylori* infections were not associated with family income, crowded living conditions, or well-water use (Table 2). In addition to age, race/ethnicity, birth origin, smoking, and educational attainment, occupational exposure to soil was significantly associated with seropositivity. Compared to participants with occupations not likely to involve soil exposure, workers in soil-related occupations had significantly higher odds of seropositivity (aOR 1·9, 95% CI 1·2-2·9), as did unemployed participants (aOR 1·4, 95% CI 1·1-1·7). Because exposures to both well water and soil might increase an individual's cumulative risk of infection [59], we repeated the regression model for adults and examined this combined exposure. Compared to all other NHANES participants (29·9% seropositive), 43·1% of 58 adult participants with both well water and occupational soil exposure were seropositive (aOR 2·7, 95% CI 1·3-5·6).

Race/ethnicity

Because *H. pylori* prevalence is also known to vary by race/ethnicity [7, 54], the odds of seropositivity were examined after stratification by the three major groups (Hispanic, non-Hispanic White, non-Hispanic Black) (Table 3). Well-water use had a positive association with *H. pylori* prevalence across all race/ethnicity groups, but was only statistically significant in non-Hispanic Blacks (aOR 2·1, 95% CI 1·02-4·4). Furthermore, not using any at-home water-treatment devices was also significantly associated with seropositivity in non-Hispanic Blacks (aOR 1·7, 95% CI 1·02-2·9), while home water treatment had no association with seropositivity for the other two groups.

Conversely, crowded housing had larger and significant associations with seropositivity in non-Hispanic Whites and Hispanics (aOR 1·9, 95% CI 1·2-3·2 and aOR 1·7, 95% CI 1·1-2·7, respectively), while in non-Hispanic Blacks, crowded housing was positively associated but not statistically significant (aOR 1·4, 95% CI 0·8-2·3).

Associations with occupational soil exposures were also considered in a race/ethnicity stratified multivariable model for adults after also controlling for educational attainment (Table 3). Working in a job likely to involve exposure to soil was only significantly associated with elevated odds of *H. pylori* seropositivity in non-Hispanic Whites (aOR 2·6, 95% CI 1·6-4·1). For both non-Hispanic Blacks and Hispanics, the statistically insignificant aOR was estimated at 1·2. Of non-Hispanic Whites, unemployment was also significantly associated with increased odds of seropositivity (aOR 1·5, 95% CI 1·2-2·0) compared to workers in non-soil related occupations.

Birth origin

To examine whether there were differences in odds of seroprevalence by country of birth origin, multivariable models were also stratified by country of birth origin (US-born and foreign-born) (data not shown). Overall seroprevalence in foreign-born participants was over twice that of those born in the United States (54·0% *vs.* 20·5%); however, adjusted odds for potential risk factors were comparable across the groups.

DISCUSSION

Given the high burden of *H. pylori*, it is important to understand environmental correlates of infection. This examination of 2 years of NHANES data augmented the existing literature by using a nationally representative sample. Well water was positively associated with

Table 2. *Risk factors associated with elevated IgG antibodies against Helicobacter pylori stratified by age group (NHANES 1999–2000)*

	3–19 years			⩾20 years		
Variable	*N*	Positive[a] (%)[b]	aOR[c] (95% CI)	*N*	Positive (%)	aOR (95% CI)
Age						
Continuous (years)	3348	21·0	**1·1 (1·1–1·2)**[d]	4145	30·1	**1·0 (1·02–1·03)**
Gender						
Female	1624	9·4	Ref.	2205	29·7	Ref.
Male	1724	10·9	1·3 (0·9–2·1)	1940	30·5	0·9 (0·8–1·1)
Race/ethnicity						
Non-Hispanic White	685	3·8	Ref.	1860	20·8	Ref.
Non-Hispanic Black	939	24·3	**6·4 (3·1–13·1)**	761	50·2	**3·6 (2·9–4·4)**
Hispanic	1600	18·0	**2·9 (1·4–5·9)**	1398	56·7	**3·5 (2·6–4·7)**
Other, including multiracial	124	11·9	1·7 (0·8–3·7)	126	44·6	**2·3 (1·6–3·2)**
Country of birth origin[e]						
United States	2890	8·3	Ref.	3011	24·7	Ref.
Non-US born	457	32·2	**4·0 (2·2–7·1)**	1130	57·0	**2·3 (1·7–3·0)**
Family income[e]						
⩾$ 20 000	1823	6·1	Ref.	2493	25·2	Ref.
<$ 20 000	1329	17·5	**2·1 (1·5–3·0)**	1406	41·3	1·1 (0·9–1·5)
Crowded housing[e]						
⩽1 person per room	1914	6·6	Ref.	3345	27·7	Ref.
>1 person per room	1395	19·5	**2·3 (1·5–3·7)**	744	48·7	1·3 (0·9–1·9)
Smoking status[e,f]						
Non-smoker	2976	9·8	Ref.	3078	28·4	Ref.
Smoker	269	14·3	1·0 (0·5–1·9)	961	34·9	**1·6 (1·2–2·0)**
General health condition[e]						
Excellent/very good	2040	8·2	Ref.	1832	23·9	Ref.
Good	1011	14·0	1·4 (0·9–2·1)	1317	34·0	1·1 (0·9–1·4)
Fair/poor	295	18·6	1·1 (0·7–1·9)	990	43·6	1·2 (0·9–1·6)
Source of tap water[e]						
Public/private water company	3004	10·3	Ref.	3591	30·2	Ref.
Well water	264	8·2	**1·7 (1·1–2·6)**	471	29·0	1·4 (0·9–2·4)
At-home water-treatment device used[e,g]						
Yes	548	4·3	Ref.	909	23·2	Ref.
No	2753	11·8	1·7 (0·7–4·1)	3174	32·8	1·1 (0·8–1·4)
Educational attainment[e]						
At least high school diploma/GED	–	–	–	2540	23·4	Ref.
Less than high school	–	–	–	1592	51·8	**1·7 (1·4–2·0)**
Soil-related occupation[e,h]						
No	–	–	–	1930	23·2	Ref.
Unemployed/not working	–	–	–	1878	39·0	**1·4 (1·1–1·7)**
Yes	–	–	–	337	42·4	**1·9 (1·2–2·9)**

aOR, Adjusted odds ratio; CI, confidence interval; GED, General education diploma.
[a] IgG ELISA optical density (OD) ⩾1.1=positive; OD <1.1=negative. [b] All prevalence estimates were weighted. [c] Wald χ^2 logistic regression used. [d] Bold values denote statistically significant data (P<0.05). [e] Covariate has some missing data. [f] Based on serum cotinine level (non-smoker ⩽15 ng/ml, smoker >15 ng/ml). [g] Types of at-home water-treatment devices included: Brita® or other pitcher water filter, ceramic or charcoal filter, water softener, aerator, reverse osmosis. [h] Soil-related occupations included: farm operators, managers, and supervisors; farm and nursery workers; related agricultural, forestry, and fishing occupations; construction trades; extractive and precision production occupations; construction labourers; labourers, except construction.

H. pylori seropositivity in all subjects, but was stronger and statistically significant in younger respondents aged 3–19 years. In addition to demographic characteristics associated with a lower socioeconomic status, living in a crowded home also increased these younger participants' odds of being seropositive. These results support the growing evidence for intrafamilial transmission in children in impoverished and crowded

https://doi.org/10.1017/S0950268814003938 Published online by Cambridge University Press

Table 3. *Risk factors associated with elevated IgG antibodies against Helicobacter pylori stratified by race/ethnicity*[a] *(NHANES 1999–2000)*

	Non-Hispanic White			Non-Hispanic Black			Hispanic		
Variable	*N*	Positive[b] (%)[c]	aOR[d] (95% CI)	*N*	Positive (%)	aOR (95% CI)	*N*	Positive (%)	aOR (95% CI)
Age									
Continuous (years)	2545	17·4	**1·0 (1·03–1·04)**[e]	1700	42·3	**1·0 (1·03–1·04)**	2998	45·3	**1·0 (1·04–1·06)**
Gender									
Female	1288	18·2	Ref.	869	40·1	Ref.	1537	42·2	Ref.
Male	1257	16·5	0·9 (0·7–1·1)	831	44·9	1·3 (0·9–1·7)	1461	48·6	1·4 (1·0–1·9)
Country of birth origin[f]									
United States	2411	16·3	Ref.	1559	39·9	Ref.	1749	26·7	Ref.
Non-US born	132	37·9	**3·6 (2·0–6·5)**	140	63·1	**2·4 (1·6–3·6)**	1248	61·4	**2·5 (2·0–3·1)**
Family income[f]									
⩾$ 20 000	1865	14·7	Ref.	848	38·7	Ref.	1457	42·3	Ref.
<$ 20 000	602	26·3	**1·6 (1·2–2·2)**	705	44·1	1·2 (0·9–1·6)	1333	49·1	1·0 (0·8–1·3)
Crowded housing[f]									
⩽1 person per room	2322	17·2	Ref.	1243	42·5	Ref.	1498	43·1	Ref.
>1 person per room	194	9·5	**1·9 (1·2–3·2)**	433	41·8	1·4 (0·8–2·3)	1463	48·5	**1·7 (1·1–2·7)**
Smoking status[f]									
Non-smoker	1930	14·7	Ref.	1316	37·1	Ref.	2610	45·5	Ref.
Smoker	561	25·7	**2·1 (1·5–2·8)**	327	56·2	**1·7 (1·3–2·2)**	299	49·7	0·9 (0·7–1·2)
General health condition[f]									
Excellent/very good	1573	13·6	Ref.	863	37·2	Ref.	1299	37·5	Ref.
Good	669	19·9	1·2 (0·9–1·6)	573	44·2	1·1 (0·8–1·4)	1012	50·0	**1·4 (1·04–1·7)**
Fair/poor	300	32·0	**1·5 (1·1–2·1)**	264	53·3	1·3 (1·0–1·7)	684	56·4	1·1 (0·6–1·8)
Source of tap water[f]									
Public/private water company	2072	16·4	Ref.	1605	41·7	Ref.	2696	45·4	Ref.
Well water	440	22·1	1·6 (1·0–2·6)	59	56·7	**2·1 (1·02–4·4)**	214	48·7	1·6 (0·8–3·2)
At-home water-treatment device used[f,g]									
Yes	792	14·8	Ref.	152	33·4	Ref.	458	44·9	Ref.
No	1722	18·6	1·1 (0·8–1·5)	1529	43·3	**1·7 (1·02–2·9)**	2486	45·5	1·0 (0·7–1·5)
	Adults ⩾20 years old only[h]								
Soil-related occupation[f,i]									
No	894	13·1	Ref.	387	45·5	Ref.	594	53·4	Ref.
Unemployed/not working	843	31·5	**1·5 (1·2–2·0)**	330	56·3	1·0 (0·7–1·6)	642	58·8	0·9 (0·6–1·5)
Yes	123	32·7	**2·6 (1·6–4·1)**	44	62·0	1·2 (0·7–2·3)	162	66·5	1·2 (0·6–2·4)

aOR, Adjusted odds ratio; CI, confidence interval.

[a] Race/ethnicity category of 'Other, including multiracial' was excluded due to small sample size. [b] IgG ELISA optical density (OD) ⩾1·1=positive; OD <1·1=negative. [c] All prevalence estimates were weighted. [d] Wald χ^2 logistic regression used for adjusted odds ratios. [e] Bold values denote statistically significant data ($P < 0{\cdot}05$). [f] Covariate has some missing data. [g] Types of at-home water-treatment devices included: Brita® or other pitcher water filter, ceramic or charcoal filter, water softener, aerator, reverse osmosis. [h] Multivariable model for adults only also included educational attainment. [i] Soil-related occupations included: farm operators, managers, and supervisors; farm and nursery workers; related agricultural, forestry, and fishing occupations; construction trades; extractive and precision production occupations; construction labourers; labourers, except construction.

areas with the potential for accompanying poor hygienic conditions. The attenuated associations between tap-water source, crowded housing, and *H. pylori* seropositivity in the older NHANES population suggests that *H. pylori* infections associated with these exposures may be important when pathogen acquisition occurs during childhood.

By contrast, in NHANES participants aged ⩾20 years who were asked about occupational exposures, occupational exposures to soil were significantly associated with seropositivity. Exposures to both well water and occupationally related soil increased the effect size of adults' odds of seropositivity, which suggests a cumulative risk associated with exposure to both contaminated water and soil.

Using occupation codes to determine soil exposure limited interpretations because of the age restriction and requirement for employment in the prior week. The elevated odds of seropositivity observed in those not working in the week prior to the interview may be attributable to underlying differences in socioeconomic status or involvement in soil-related temporary or intermittent jobs not recorded by the OCQ. Nonetheless, the increased odds of seropositivity observed in those working in soil-related occupations suggests that transmission routes other than those associated with living conditions play a role in pathogen acquisition, including exposures to soil tainted by *H. pylori*-contaminated surface and ground waters.

Due to the health implications associated with *H. pylori* in public water systems, the US EPA has included *H. pylori* in all three of its Contaminate Candidate Lists, released in 1998, 2005, and 2009, for possible future regulation under the SDWA [44–46]. Recently, Ryan *et al.* evaluated potential drinking-water guidelines at the point of ingestion for *H. pylori* [60]. They performed a quantitative microbial risk assessment (QMRA) to identify effective guidelines that would protect human health to an acceptable level of risk while also considering sources of uncertainty. Their analyses concluded that current levels of *H. pylori* in drinking water might pose a potential public health risk.

This analysis only suggested an association with not using at-home water-treatment devices and odds of *H. pylori* seropositivity in non-Hispanic Blacks. Due to the broad NHANES question that did not distinguish which specific treatments were used, it is difficult to evaluate the impact of specific home treatments on infection risk. Water softeners would be ineffective, and most water filters are designed to reduce taste, odours, or concentrations of chemicals such as lead and chlorine. The *H. pylori* bacterium is 3 μm long with a diameter of ~0·5 μm. Standard Brita® filters, including the tap (0·5 μm) and pitcher (1 μm) filters, may not effectively remove the bacterium, and other filters solely designed for taste and odour improvement would be ineffective. Moreover, the effectiveness of home treatments relies on proper maintenance and upkeep.

Two published studies detected *H. pylori*-specific DNA in soil collected from residential areas of Japan [61] and from public playgrounds in Spain [62], but the bacterium's viability was not assessed. Another study conducted in Japan found no evidence of *H. pylori*-specific DNA in soil collected from public parks [63]. Although evidence for *H. pylori* occurring in soil has been scarce, it was worth consideration in this analysis, since the bacterium can form biofilms and has been found in ground and surface water [25–28].

While differences in risk factor associations across the race/ethnic groups were observed, it is difficult to conclude how socioeconomic status and the built environment are disproportionately affecting these groups because the diminished sample sizes across the strata probably limited the statistical power necessary to detect significant associations. Although there were sample size limitations, our additional stratified analyses for all NHANES participants suggests that variance patterns may be attributable to disparities in socioeconomic status and living conditions, including overcrowding and drinking well water. In addition, the survey's general health marker, which had not been considered in previous publications, had an inverse correlation with seroprevalence. Poorer perceived health was associated with higher odds of seropositivity. Still, little is known regarding the variability in *H. pylori* transmission and lifetime seropositivity rates in different demographic groups in the United States.

NHANES collects a variety of health and nutritional information from a nationally representative sample of the United States population, which makes it a valuable tool for hypothesis generation and exploring correlations between exposures and health outcomes; however, this analysis has some limitations. The cross-sectional design prevents us from inferring causality. In addition, the risk factor analyses is limited to what was asked of participants during the 1999–2000 NHANES. Several questionnaires were administered only to subgroups (e.g. adults aged ⩾20 years), including the occupational questions. Moreover, the survey did not collect data regarding participants' behavioural health risk factors, a crucial component when studying *H. pylori* transmission. Because the bacterium often spreads via faecal–oral transmission, this analysis would have benefited from consideration for participants' hygienic behaviours, including hand hygiene habits and food preparation practices. Infrequent hand-washing has been associated with *H. pylori* infections, [64] and raw food contaminated by *H. pylori*-infected human faeces or cleaned with *H. pylori*-contaminated water may be a source of faecal–oral or environmental transmission of *H. pylori* [65]. An inherent limitation in serological tests is their inability to distinguish between current and prior infections. If an *H. pylori* infection is cleared, circulating anti-*H. pylori* IgG antibodies also decline, but complete seroreversion can take decades [66]. While positive IgG serology results acceptably correlate with an active *H. pylori* infection [67], an undetermined proportion of the seroprevalence may be attributed to previously cleared *H. pylori* infections. Using NHANES data also limited us from considering genetic and virulence factors that play a role in pathogen transmission and acquisition. The virulence factor CagA enhances *H. pylori*'s ability to evade apoptosis and cause persistent infections [68–70]. In addition, studies have suggested that distinct immune mechanisms according to age may also be involved in *H. pylori* pathogenesis, because immunophenotypes have been shown to differ between *H. pylori*-positive children and adults with duodenal ulcers [71].

Despite these limitations, this study provides risk factor data that can inform future environmental assessments and prospective human studies to better link environmental exposures to *H. pylori* infections. The results of our analyses using this nationally representative population further support the hypothesis that exposure to well water, particularly during childhood, may be a possible source of *H. pylori* infection in the United States [38, 43, 72, 73]. Having well water may also be an indicator of other environmental exposures related to rural residence and associated with *H. pylori* infections that were not evaluated in this analysis. As suggested by Ryan *et al*., future research is warranted to examine pathogen occurrence in source and finished water, treatment removal rates, and infection risks for other water sources to validate their maximum contaminant level (MCL) model [60].

CONCLUSIONS

Even though a casual association cannot be demonstrated with the cross-sectional design of NHANES, a better understanding of risk factors associated with *H. pylori* acquisition will help identify infection prevention strategies that can target populations with increased risk and reduce the burden of disease associated with chronic infections. Our analyses indicate that associations with environmental risk factors (well-water usage and occupational exposures to soil) and *H. pylori* seropositivity differ by demographic characteristics such as race/ethnicity and age. Moreover, this analysis of a nationally representative dataset indicates a disproportionate burden of infection associated with poor health and residential crowding, which may be related to unhygienic living conditions. Before effective interventions can be targeted at the necessary demographic groups, transmission and acquisition pattern dynamics must be addressed. Based on the association with well water and soil, and because of the bacterium's multiple niches in the natural world, differences in *H. pylori* occurrence by urban/rural residence deserve further evaluation. In addition, further investigations are warranted to examine how drinking water may be contaminated with *H. pylori*, and what role drinking-water systems may play in maintaining and spreading the bacterium.

ACKNOWLEDGEMENTS

We thank Sarah Collier at the US Centers for Disease Control and Prevention (CDC) for her review and comments. The manuscript has been subjected to the U.S. EPA's peer review and has been approved for publication.

This project was supported in part by an appointment to the Internship/Research Participation Program at the Office of Research and Development, U.S. Environmental Protection Agency, administered by the Oak Ridge Institute for Science and Education through an inter-agency agreement between the U.S. Department of Energy and EPA.

The views expressed in this paper are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

DECLARATION OF INTEREST

None.

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