



BMJ Open School-based Hygiene Intervention to Prevent *Helicobacter Pylori* infection among childrEn (SHIP HOPE): protocol for a cluster-randomised controlled trial

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ABSTRACT

Introduction *Helicobacter pylori* infection rates are high in China and worldwide, and maintaining good hygiene is effective in preventing *H. pylori* infection. Childhood is a critical stage for developing good hygiene practices. Therefore, in this study, we aimed to explore whether a comprehensive hygiene intervention can prevent *H. pylori* infection in primary schools in China.

Methods and analysis The School-based Hygiene Intervention to Prevent *Helicobacter Pylori* infection among childrEn study is a cluster-randomised controlled trial, which will include approximately 2400 children in grades 2–4 from 60 classes in 10 primary schools of Linqu County, Shandong Province. Schools will be randomly assigned (1:1) via a computer-generated list, to receive either comprehensive hygiene intervention (intervention) or the usual health education lessons (control), with stratification by area (urban or rural). The interventions will include the following: (1) Children's education: lessons and cartoon books designed to provide basic knowledge about hygiene, *H. pylori*, hand hygiene, diet and oral hygiene will be provided to children; (2) Caregiver's education: children will be empowered to share hygiene-related knowledge with their caregivers as homework; caregivers will be also invited to the school for hygiene lessons; (3) School hygiene promotion: suggestions will be provided for improving the hygienic environment. Children in control schools will receive usual health education lessons according to the arrangements of each school. The primary outcome is the prevalence and incidence of *H. pylori* infection among children at 1-year follow-up. The secondary outcomes are *H. pylori* and hygiene knowledge, family eating customs and hygiene practices among children and their caregivers, as well as school absences owing to diarrhoea. Additionally, growth in children is set as an exploratory outcome. General linear mixed models will be used to analyse differences between the intervention and control schools.

Ethics and dissemination Ethics approval has been obtained from the Institution Review Board of Tsinghua University (No: 20220020). Written informed consent will be obtained from each child and one of their caregivers. The findings of this study will be actively disseminated through scientific publications and conference presentations.

Trial registration number ChiCTR2200056191.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study will assess a comprehensive hygiene intervention to prevent *Helicobacter pylori* infection among children.
- ⇒ Outcomes include the prevention of *H. pylori* infection as well as an increase in *H. pylori* and hygiene knowledge and practices among children and caregivers, reduction in diarrhoea incidence in children, and improved children's growth.
- ⇒ To recognise the importance of the knock-on effects of health communication, children will be encouraged to impart hygiene-related knowledge to their caregivers in this study.
- ⇒ In comprehensive health interventions, it is difficult to distinguish the effect of each specific intervention.
- ⇒ The impact of COVID-19 restrictions and lockdowns could affect the progress and quality control of this project.

INTRODUCTION

Helicobacter pylori is a gram-negative bacterium that primarily colonises the human stomach and is transmitted by gastro-oral, oral-oral or faecal-oral routes.¹ It is estimated that more than 50% of the world's population is infected with *H. pylori*, with an infection rate as high as 70% in low-income and middle-income countries.^{2,3} *H. pylori* infection has harmful effects on several gastrointestinal diseases, such as duodenal or gastric ulcers, gastric cancer and gastric mucosa-associated lymphoid-tissue lymphoma.^{4,5} In recent years, increasing studies have revealed that *H. pylori* infection also has a wide range of impacts on health through extragastrintestinal effects, such as iron-deficiency anaemia, chronic immune thrombocytopenic purpura and growth in children.^{6,7} Therefore, solutions to reduce *H. pylori* infection are urgently needed.

In 2015, the Kyoto global consensus report on *H. pylori* gastritis recommended that all *H. pylori*-infected individuals should be offered

eradication therapy unless there are competing considerations.⁸ This recommendation was subsequently adopted in other updated guidelines or expert consensus for the management of *H. pylori* infection.^{9–13} However, large-scale treatment of *H. pylori* in the general population is not feasible. First, more than half the global population is infected with *H. pylori*, making the cost for therapy immeasurable. Second, triple, or quadruple concomitant therapies for *H. pylori* eradication are very complicated,^{8 9 11} and there are problems with drug non-compliance and antibiotic resistance.^{14 15} Moreover, antibiotic treatment could alter the normal gastrointestinal flora in the body and cause multiple adverse effects on health.¹⁶

In addition to eradication therapy, another cost-effective and feasible way to reduce the prevalence of *H. pylori* among the general population is to take measures to prevent infection with *H. pylori*. Although the risk factors of *H. pylori* infection have been well-studied,^{17–19} there is little intervention research on how to prevent *H. pylori* infection in daily life. The known modifiable risk factors of *H. pylori* infection include inadequate sanitation, unhealthy hygiene practices, and infection among family members.²⁰ Therefore, it is possible to prevent *H. pylori* infection by changing behaviours and lifestyles and improving environmental hygiene through hygiene intervention for susceptible populations.

Hand hygiene is considered to be one of the most effective ways to reduce infectious diseases. A meta-analysis suggested that handwashing can significantly reduce the risk of diarrhoeal disease by 40%.²¹ Studies have found that improving hand hygiene could promote children's growth and reduce absence owing to illness among children in educational settings.^{22 23} Because the oral cavity is an extragastric reservoir of *H. pylori* and the bacterium is mainly spread via the mouth, it is very important to maintain good oral hygiene.^{24 25} A study from China reported that the positive rate of *H. pylori* infection decreased significantly owing to a special toothpaste treatment ($p < 0.01$).²⁶ Additionally, disinfecting toilets, using serving chopsticks, providing individually served meals and drinking boiled water are also important ways to prevent infectious gastrointestinal diseases.²⁷ Given that *H. pylori* infection is caused by multiple factors, it is necessary to develop comprehensive hygiene intervention to prevent *H. pylori* infection.

Studies have shown that the high incidence of adult *H. pylori* infection and gastrointestinal diseases is closely related to childhood *H. pylori* infection.^{28–30} Because childhood is an important stage of human growth and development as well as a critical period for the development of good hygiene practice, it is of great importance to establish comprehensive hygiene interventions to prevent *H. pylori* infection during childhood.

We, therefore, designed the School-based Hygiene Intervention to Prevent *Helicobacter Pylori* infection among children (SHIP HOPE) study with the aim to explore whether a comprehensive hygiene intervention

implemented in primary schools could reduce the incidence of *H. pylori* infection in children.

Methods and analysis

Study aims

The SHIP HOPE study was approved in July 2021, with the aim to implement a comprehensive hygiene intervention in primary school students to reduce *H. pylori* infection. Because children have a substantial influence on their family members in China, this intervention would also encourage the delivery by children to their caregivers of *H. pylori* and hygiene information; thus, knowledge and hygiene practice among caregivers would also be evaluated.

It is hypothesised that (1) school-based comprehensive hygiene interventions can increase hygiene knowledge and improve hygiene practice among children; (2) comprehensive hygiene interventions can help enhance hygiene knowledge and impact the hygiene practice of caregivers and (3) the incidence of *H. pylori* infection will be significantly lower in the intervention group than in the control group among children.

Study design

Because most hygiene interventions will be provided at the school and class levels, and it is difficult to evaluate the impact of intervention on the incidence of *H. pylori* in a self-controlled study. Therefore, the design of a cluster randomised controlled trial was adopted in this study, with primary schools as randomisation units.

Setting

This study will be conducted in Linqu County, an underdeveloped region in Shandong Province, China. The region has been identified to be one of the areas with the highest incidence of gastric cancer in China, with an age-adjusted rate of 55 per 100 000 for men and 19 per 100 000 for women in 1980–1982.³¹ A previous meta-analysis showed that the relative risk of gastric cancer was 0.66 with *H. pylori* eradication (95% CI 0.46 to 0.95),³² suggesting that reducing *H. pylori* infection is effective in preventing gastric cancer. Therefore, preventing *H. pylori* infection is of great public health importance in this area of China.

This study has been registered in the Chinese Clinical Trial Registry (<http://www.chictr.org.cn/index.aspx>), with registration number ChiCTR2200056191.

Recruitment

Recruitment of schools

Like most areas of China, primary schools in Linqu have six grades in total, with children ranging in age from 7 to 12 years. Because children in the first grade have just started primary education and children in higher grades might have a higher rate of *H. pylori* infection at baseline, this study will be carried out among children in grades 2–4 (approximately ages 8–10 years). The eligibility criteria for schools are as follows: (1) the principal and teachers

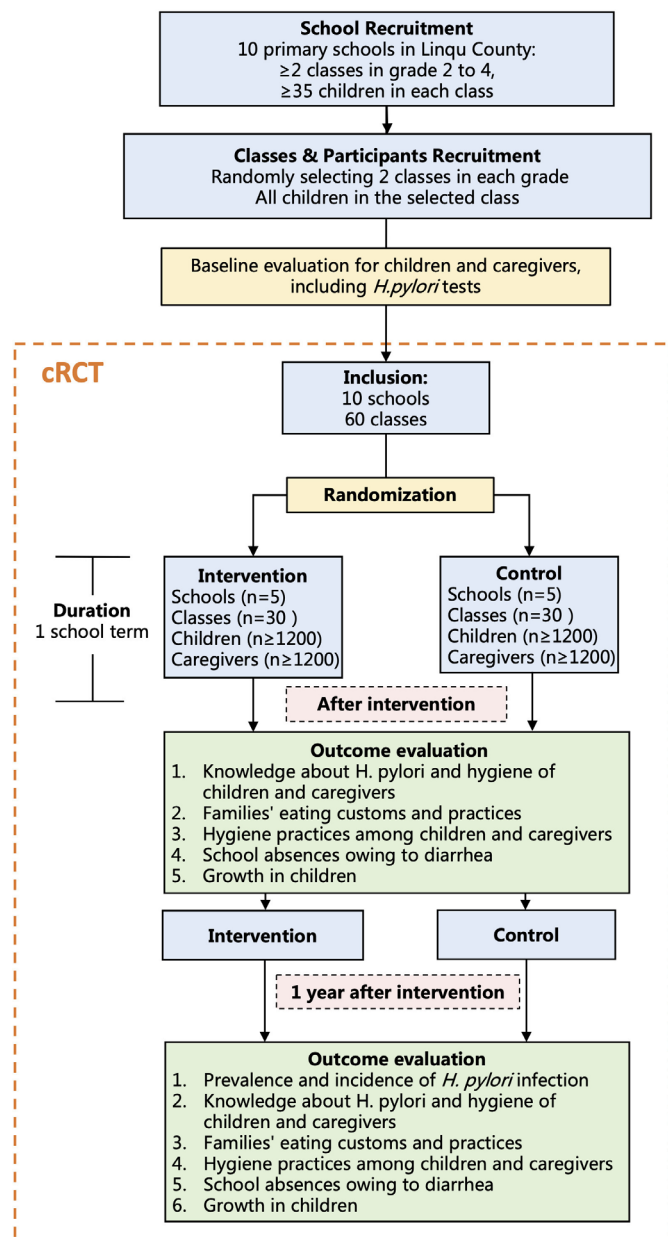


Figure 1 Flow diagram for the SHIP HOPE trial. SHIP HOPE: School-based Hygiene Intervention to Prevent *Helicobacter Pylori* infection among children. cRCT, cluster randomised controlled trial

in the school are willing to participate in the study and can adhere to the randomised results; (2) the number of classes in each school from grade 2 to grade 4 is ≥ 2 and (3) the number of students in each class is ≥ 35 (figure 1).

A total of three steps will be implemented to recruit participating schools. First, researchers will calculate the number of clusters required for school and class recruitment. Second, we will cooperate with the Linqu Center for Disease Prevention and Control and the Education and Sports Bureau of Linqu to contact and recruit eligible primary schools. Third, a final list of 10 eligible schools and classes will be provided to the principal investigator and schools will be invited to participate in the study.

Recruitment of participants

According to our estimation, at least 2400 children from 10 schools will be recruited in the study. Additionally, we will recruit one caregiver (parent or grandparent) from each child's family to participate in this study (figure 1). Before conducting the baseline assessment, written informed consent will be obtained from all students and their caregivers (parents or grandparents). If children or their caregivers refuse to participate in the survey, they will be excluded. For children or caregivers who refuse to participate, children can decide whether to receive the intervention courses or the related educational materials.

Baseline evaluation

The infection status of *H. pylori* will be detected using *H. pylori* stool antigen (HpSA) assay. All tests will be performed by the clinical lab of Weifang People's Hospital using a commercial double-antibody sandwich ELISA (InTec PRODUCT, Xiamen, China), which is proven to have a sensitivity of 96.34% and a specificity of 96.81%. Stool samples will be destroyed immediately after *H. pylori* testing.

A structured questionnaire for children at baseline includes items on demographic variables, medical history (especially gastrointestinal disease history), hygiene practices and knowledge about *H. pylori* and hygiene. The baseline questionnaire for caregivers includes demographic variables, education level, occupation, family information, medical history (especially gastrointestinal disease history), family cancer history, eating customs and practices, hygiene facilities at home, hygiene practices and knowledge about *H. pylori* and hygiene. Anthropometric indicators of all children will be measured at baseline, including height, sitting height, weight, chest circumference, waist circumference, hip circumference and blood pressure. Additionally, the hygiene environment of each school and the status of health education courses will also be investigated at baseline.

Randomisation

Participating schools will be randomly divided into the comprehensive intervention group and the control group at a ratio of 1:1, stratified by area (urban or rural) at school level. Randomisation will be carried out using a computer-generated random number system by a researcher who is not involved in the study and is blinded to the identity of the schools.

Blinding

Owing to the nature of the intervention, all children, caregivers and teachers who provide lessons will not be blinded to the assignments. Investigators who will conduct the baseline and follow-up surveys and tests will be blinded. All investigators will be recruited from Weifang Medical College, Shandong, China.

Interventions

Comprehensive hygiene intervention ('Good Hygiene Practice Package') will be implemented in this study,

Table 1 Hygiene education courses for children and their caregivers

Hygiene education activity	Class theme	Contents
Knowledge course	Basic knowledge about hygiene	<ol style="list-style-type: none"> 1. What is hygiene 2. Why we need hygiene and the harmful impact of unhygienic 3. How to keep hygiene to prevent diseases
Knowledge course	Basic knowledge about <i>H. pylori</i>	<ol style="list-style-type: none"> 1. What is <i>Helicobacter pylori</i> 2. The harmful effects of <i>H. pylori</i> infection 3. The infection route of <i>H. pylori</i> 4. How to prevent <i>H. pylori</i> infection
Knowledge and practice course	Hand hygiene	<ol style="list-style-type: none"> 1. The 'good friends' and 'bad friends' on the hands 2. The harmful effects of 'bad friends' 3. How to combat with 'bad friends'—hand hygiene 4. How to wash hands (seven steps for performance of hand hygiene) + practice 5. When to wash hands
Knowledge and practice course	Diet and oral hygiene	<ol style="list-style-type: none"> 1. The harmful effects of unhygienic diet 2. How to keep dietetic hygiene 3. Oral hygiene and health 4. How to brush teeth (Modified Bass Technique)+practice
Practice course	Making posters to deliver the knowledge of <i>H. pylori</i> and sharing	<ol style="list-style-type: none"> 1. Designing a cartoon character for <i>H. pylori</i> 2. Selecting a topic for the poster, for example: harmful effects of <i>H. pylori</i>, transmission routes of <i>H. pylori</i>, how to prevent <i>H. pylori</i> in daily life 3. Introduction to poster style
Meeting with caregivers	Sharing children's works; teaching caregivers how to prevent <i>H. pylori</i> in their daily life	<ol style="list-style-type: none"> 1. What is <i>H. pylori</i> 2. The harmful effects of <i>H. pylori</i> infection 3. The infection route of <i>H. pylori</i> 4. How to prevent <i>H. pylori</i> infection
Theme class meeting		Children sharing experiences and challenges in daily life
Final summary		Summary of knowledge about hygiene and <i>H. pylori</i> and vacation homework assignment

which includes three sections: children's education, caregiver's education and school hygiene promotion. Details of these three sections are as follows.

Children's education

Children in the intervention group will be provided information that includes basic knowledge of hygiene, *H. pylori*, hand hygiene, diet and oral hygiene. Eight hygiene education lessons (table 1) and cartoon books that include seven stories (table 2 and figure 2) have been designed to incorporate this hygiene information. While learning this content, children will be encouraged to make posters or draw illustrations to share their knowledge and experiences with each other. The contents of the lessons are designed and produced by teachers from the Vanke School of Public Health (VSPH), Tsinghua University and are polished by teachers from the Institute for Culture Creativity, Tsinghua University. Then, researchers from the VSPH will provide course training to the teachers from schools receiving the intervention. At least two outstanding teachers will be recommended for this training from each school in the intervention group. All teachers are required to be assessed and will be given

pre-lectures prior to giving formal lessons. In addition to teachers who provide the lessons, class teachers and the vice principal in charge of health will also be invited to participate in the project, to coordinate all events.

Caregiver's education

Children will be empowered to share their hygiene-related knowledge with their caregivers as homework. Caregivers will be invited to the school to learn how to prevent *H. pylori* infection in daily life, such as via hand hygiene, using serving chopsticks, providing individually served meals, disinfecting the toilet and drinking boiled water.

School hygiene promotion

Suggestions will be provided to schools for improving the hygiene environment according to the results of evaluation at baseline.

Controls

Children in the control schools will receive the usual health education lessons according to the arrangements of each school.

Table 2 Cartoon books designed for children

Chapter	Hygiene-related knowledge
Expeditions in microbe-themed food castle	<ol style="list-style-type: none"> 1. What are microbes 2. The role of microbes: the good and the bad 3. Transmission routes of pathogenic micro-organisms 4. What are microbes 'afraid of'
A big battle to protect A'hao and Xiaokan (A'hao and Xiaokan are the names of the characters)	<ol style="list-style-type: none"> 1. What is <i>Helicobacter pylori</i> and how can it harm the digestive tract (including an introduction to stomach and gastric acid) 2. Transmission routes of <i>H. pylori</i> 3. How to prevent <i>H. pylori</i> infection: hand hygiene, oral hygiene, diet hygiene and toilet hygiene 4. The story of Warren and Marshall
Who is the 'murderer'?	<ol style="list-style-type: none"> 1. The story of 'Typhoid Mary' 2. Emphasising the importance of hand hygiene 3. The 'good friends' and 'bad friends' on the hands 4. How to wash hands: 7 steps for performance of hand hygiene
Taking care of three "teeth baby"	<ol style="list-style-type: none"> 1. The relationship between oral hygiene and health 2. <i>H. pylori</i> in mouth 3. How to brush teeth and keep oral hygiene
Welcome to our restaurant	<ol style="list-style-type: none"> 1. Harmful effects of unhygienic food 2. Story of 'Hepatitis A epidemic in Shanghai: Caused by Eating Clams'
Fun digestive tract Amusement park	<ol style="list-style-type: none"> 1. The functions and characteristics of different digestive organs 2. Brief introduction of heart, lung and brain
Small hands holding big hands	Review knowledge about microbes, <i>H. pylori</i> and the digestive tract through games, and encourage children to deliver hygiene-related knowledge to their caregivers

Outcome evaluation

The primary outcomes are the prevalence and incidence of *H. pylori* infection among children at 1 year after the intervention. The prevalence of *H. pylori* infection at 1 year after intervention will be evaluated in the whole study population. The incidence of *H. pylori* will be evaluated among baseline *H. pylori* negative children. The secondary outcomes are *H. pylori* and hygiene knowledge, families' eating customs and practices, and hygiene practices among children and caregivers at the end of intervention and 1 year after intervention. Because the hygiene

intervention could also have an impact on the transmission of other enteric pathogens that cause diarrhoea, school absences owing to diarrhoea are considered as a secondary outcome in this study. Additionally, because studies have reported that *H. pylori* infection can affect children's growth, indicators of growth, such as height and weight, are also included as exploratory outcomes.

The infection status of *H. pylori* will be measured by the same HpSA assay used at baseline. Hand hygiene practices will be assessed according to the frequency of hand-washing and frequency of using hand sanitiser based on the questionnaire. The questionnaire will also be used to evaluate families' eating customs and practices as well as knowledge about *H. pylori* and hygiene among children and caregivers. School absence owing to diarrhoea will be recorded by teachers on the event record cards and via children's self-report. Anthropometric measurements will be collected by trained investigators during the on-site surveys.

Retention

To promote participant retention and complete follow-up, there are two main considerations. For school levels, we will cooperate with the Education and Sports Bureau of Linqu, which oversees schools, to improve compliance. School officials and teachers will be regularly informed of the status of the study and plans for the next phase. The benefits and public health implications of the study will also be presented to them in detail, to obtain their full support. For children and caregivers, the



Figure 2 Depiction of the designed cartoon books (A) Book cover. (B) *Helicobacter pylori* cartoon character in the book. These two pictures were drawn by Jiajing Wang, from the Institute for Culture Creativity, Tsinghua University (permission granted for publication).

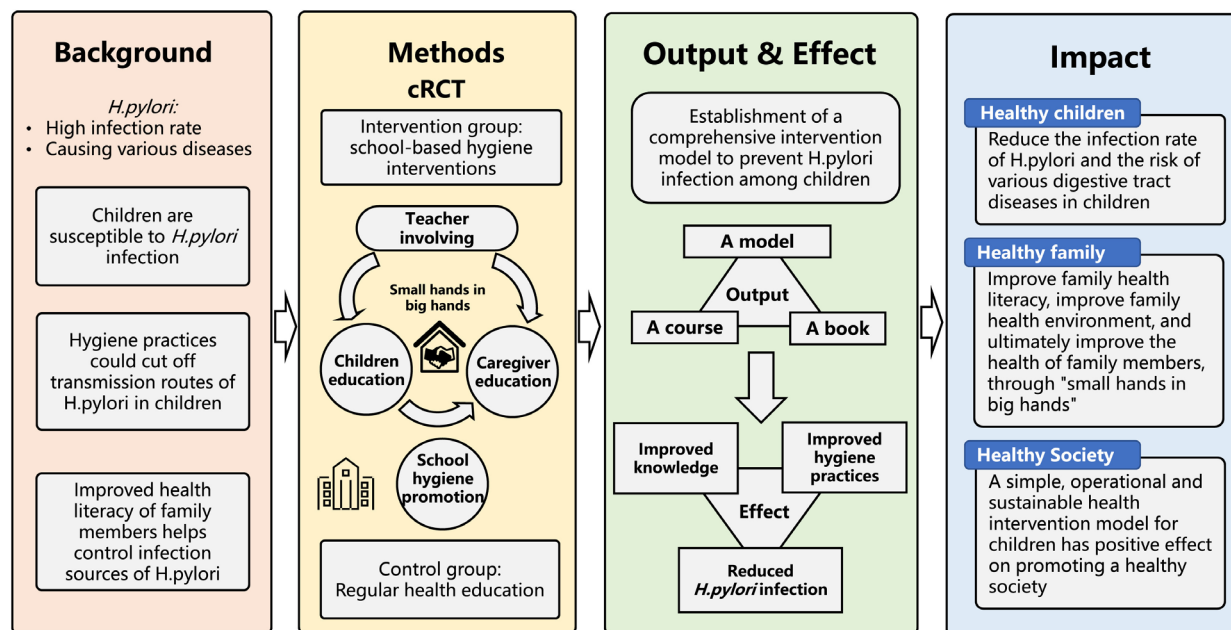


Figure 3 Study profile. cRCT, cluster randomised controlled trial.

results regarding children's *H. pylori* infection status will be fed back to school officials and caregivers will be free to decide whether to receive these results. Students and caregivers will be informed of upcoming data collection and the intervention in advance. A small gift will be given to children at the baseline survey.

Data management

The collected data will be checked every day during the investigation, and missing data will be requested from children and caregivers by telephone. The information obtained from the questionnaire and the infection status of *H. pylori* will be double-recorded by trained staff using EpiData V.3.1 (EpiData Association, Odense, Denmark); inconsistent records will be checked against the original data for confirmation. In total, 5% of participants' records will be randomly selected and checked against the original data to confirm the accuracy of the information. Finally, all collected data will be entered into an electronic database containing deidentified information. This database will be accessed by designated staff using a password.

Sample size

First, we calculated the sample size using incidence as the outcome indicator. According to a meta-analysis, the annual incidence of *H. pylori* infection is estimated to be 4% among children aged 6–14 years.³³ Considering the high prevalence of *H. pylori* in the general population of Linqu, we assumed that the annual incidence of *H. pylori* infection is 5% in the control group and 2% in the intervention group, the number of children without *H. pylori* infection is 30 in each class, the intragroup correlation coefficient is 0.01, the alpha level is 0.05 and statistical power is 0.80. Thus, at least 26 classes in the intervention

group and 26 classes in the control group are needed to detect differences.

Additionally, we calculated the sample size using prevalence as the outcome indicator. A meta-analysis reported that the prevalence of *H. pylori* infection is 33.9% in children aged 7–12 years.³⁴ Therefore, we assumed that the prevalence of *H. pylori* infection is 34% in the control group and 27% in the intervention group, the number of children is 40 in each class, the intra-group correlation coefficient is 0.01, the alpha level is 0.05 and statistical power is 0.80. Thus, at least 24 classes in the intervention group and 24 classes in the control group are needed to detect differences.

After comprehensive consideration, two classes will be selected from each of three grades (grades 2–4) from 10 schools. In this study, 30 classes from 5 schools receiving comprehensive hygiene intervention and 30 classes for another 5 schools as the control group will be recruited.

Statistical analyses

Descriptive data will be presented as mean±SD, median (IQR), or number (percentage). General linear mixed models will be used to analyse differences between the intervention and control schools, with the covariance structure appropriately adjusted for variability both between clusters (schools and classes) and within a cluster (students within the same classes). For binary outcomes, we will report preintervention/postintervention percentages for the intervention and control groups and adjusted ORs and 95% CIs between groups. For continuous outcomes, we will report preintervention/postintervention means for the intervention and control groups and model-adjusted mean differences between groups.

Subgroup analysis will also be conducted based on children's grade, school area (urban/rural), frequency of

handwashing, frequency of using hand sanitiser and level of hygiene knowledge, etc.

Statistical analyses will be performed using SAS V.9.4 (SAS Institute). All statistical tests will be two sided at the 5% level of significance. For variables with missing data, we will impute the missing values using the sequential regression multiple imputation method if the percentage of missing data exceeds 5%.

Trial status

The initial proposed start date of this study was March 2022. However, the COVID-19 epidemic and local control policies led to postponement of this study. We are well prepared to conduct this study and plan to start the study in early November 2022 and complete data collection in December 2023.

Patient and public involvement

None.

Ethics and dissemination

Ethics approval was obtained from the Institution Review Board of Tsinghua University (No: 20220020). Written informed consent will be obtained from each child and one of their caregivers (online supplemental material). Because all children included in this study are under 16 years old, the consent form for children will be signed under the supervision of their caregivers and signed consent will be obtained from both children and caregivers. The results from the trial will be disseminated through manuscript publications and conference presentations. Once proven effective, our intervention strategy can be generalised to other primary schools in China, and the designed cartoon books will be published and made available to the public.

DISCUSSION

The harmful effects of *H. pylori* infection have been well recognised since it was isolated and reported in 1983 by Barry Marshall and Robin Warren. Based on evidence regarding the role of *H. pylori* in gastric cancer, the International Agency for Research on Cancer classified *H. pylori* as a class I carcinogen in 1994.³⁵ In December 2021, *H. pylori* infection was first listed as a carcinogen in the 15th Report on Carcinogens of the US Department of Health and Human Services. It is estimated that *H. pylori* infection contributes to 780 000 new cancer cases each year, approximately 6.2% of all cancer cases worldwide.³⁶ Consequently, a growing number of guidelines recommend a 'test and treat' strategy, which requires eradication therapy once *H. pylori* infection is confirmed, unless there are competing considerations. However, large-scale treatment of *H. pylori* in the general population is not feasible. Therefore, finding new solutions is warranted for this global public health problem.

To our knowledge, the SHIP HOPE study is the first to propose a comprehensive hygiene intervention for the

prevention of *H. pylori* infection among children. We will use the social ecological model to identify intervention elements in this study.³⁷ We not only target risk factors at individual level but also at family and school environment levels, with the aim to improve knowledge, attitudes and behaviours among children, family members and teachers to promote a healthy society (figure 3). This study also has several other special and distinguishing features. (1) We have selected Linqu County, which is an underdeveloped area in China with a high rate of *H. pylori* infection and a high risk of gastric cancer, to implement this study. Therefore, the study can be generalised to other underdeveloped regions that have higher rates of *H. pylori* infection to obtain greater benefits of hygiene intervention. (2) Although the reduction of *H. pylori* infection is our main goal, the benefits of hygiene interventions are extensive and varied. (3) The components of the intervention are diverse but easy to implement. Once proven effective, a wider range of promotion can be carried out. (4) Children in different grades will be considered in this study; thus, we can explore the best time to provide the intervention.

There are also some limitations and challenges in the implementation of this study. First, according to the study design, it is difficult to distinguish the effect of each specific intervention in this study. Second, the COVID-19 epidemic is ongoing around the world. Although the epidemic in China has been well controlled, sporadic cases and local epidemics may still affect on-site investigations in schools. Some response strategies and alternatives in the investigation have been prepared in advance. Our on-site investigation work will be adjusted according to the COVID-19 epidemic situation and epidemic prevention policies in Shandong Province. We will try our best to avoid teaching online, considering the teaching effect and interaction. During the time of intervention, if schools are closed because of the epidemic, our intervention will be terminated until the schools reopen. Because the normal quarantine time is 14 days, a short pause in our intervention will have a minimal influence on the effect of the intervention. However, if the schools cannot resume normal classes for more than 1 month, we will adopt online teaching. We will select a time when the epidemic is completely under control in Shandong to conduct on-site investigation and intervention to reduce the probability of the above-mentioned situation. Additionally, the enhanced hygiene education provided during the COVID-19 epidemic may weaken the effect of the intervention.

In conclusion, this SHIP HOPE study will determine whether a comprehensive hygiene intervention to prevent *H. pylori* infection among children is effective. If effective, the intervention might not only reduce the incidence rate of *H. pylori* infection but could also reduce the risk of other gastrointestinal diseases, improve the health literacy of children and caregivers, and improve household hygiene, which in turn will improve the health level of the whole population.

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Contributors FC contributed to the conception and design of the study, gave final approval for publication, and is accountable for all aspects of the work. MZ and YZ contributed to the conception and design of the study, literature search, drafting and critical revision of the manuscript, development of intervention materials, and implementation of this study. YX, SL, JQ, GZ, YS and YG contributed to the literature search, designing the study, revision of the manuscript, and implementation of this study. All authors read and approved the final manuscript.

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