

Project title: Two-stage gastric cancer service screening model

A Two-Stage Gastric Cancer Prevention Model in Taiwan

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Background and aim: The incidence, mortality, and case-fatality of gastric cancer remain high in Taiwan. *Helicobacter pylori* infection is the most important cause of gastric cancer. We aim to develop an applicable approach by *H. pylori* eradication in order to eliminate the thread of gastric cancer in Taiwan, which can be tailored to the needs of different subpopulations. **Methods:** (1) For the high-risk populations, the model may consist of the initial screening test of C13 urea-breath test for subjects aged 30 years or more; for those who test positive, they will receive the second-stage of eradication therapy with or without endoscopy. (2) For the intermediate-risk populations, the model may consist of the initial screening test with *H. pylori* stool antigen test (SAT) for subjects aged 50-69 years, which is integrated with colorectal cancer screening with fecal immunochemical testing (FIT); subjects who test positive for *H. pylori* infection will be referred to receive the second-stage antibiotic treatment and/or endoscopy.

Results: (1) For the high-risk populations, starting 2004, the mass eradication program has been implemented on Matsu Island, with about a 5-fold higher incidence of gastric cancer than that of general Taiwanese population. Five years after the intervention, the prevalence of atrophic gastritis declined from 59.9% to 13.7%, yielding a significant reduction of 77.2%. The 5-year average incidence of gastric cancer went from 40.3 to 30.4 per 100,000 person-years, with a 24.7% reduction of gastric cancer. Up to now, there have been 5 rounds of mass screening and the *H. pylori* prevalence rate declined from 70% to less than 10%. Another program will be carried out in Taitung County, in the eastern part of Taiwan, where the gastric cancer incidence is about two-fold higher than the average rate for the Taiwanese population. Also, in this area, there is a high prevalence of oral cancer, especially in the aboriginal population, because alcohol, betel nut, and cigarette consumption is very common. Therefore, the integration of two screening programs (one to prevent gastric cancer by mass eradication of *H. pylori* infection and one to prevent oral cancer by oral inspection and health-behavior education, especially targeting the younger population) is highly desirable. (2) For the intermediate-risk population, starting 2014, a randomized trial has been launched in Chang-Hua County (a gastric-cancer incidence rate of about 17 per 100,000 person-years). Based on the population list, we have generated the invitation list for both the case and control groups (1:1); we used this information to potential participants to participate in this trial. The case group would receive both *H. pylori* SAT and FIT

while control group only received the FIT. For those who were tested positive for *H. pylori*, they would receive sequential antibiotic treatment and/or endoscopic screening. For those who tested positive for FIT, they would receive colonoscopy. From 2014 to 2017, we have successfully reached the goal for enrolling 30,000 subjects for both the case and control groups. The positivity rate of HPSA was 36.8% and the adding of SAT can substantially increase the attendance to screening. The intra-gastric pathology in this population was highly prevalent regarding the peptic ulcer disease. The long-term benefit of using this approach has been estimated by a systematic review and meta-analysis, which found that after adjustment for baseline gastric cancer incidence, individuals with eradication of *H. pylori* infection had a lower incidence of gastric cancer than those who did not receive eradication therapy (pooled incidence rate ratio: 0.53; 95% confidence interval: 0.44-0.64; a 47% risk reduction). According to the trial data, a health economic model has been established and showed that this two-in-one strategy is a cost-saving strategy (the estimates of ICER are -1237.14 USD/LYS compared to no screening strategy); combination of the SAT and FIT would further increase the cost-effectiveness. We also applied this model to Chia-Yi City, where the delivery method was based on the hospital-based inreach approach, which was different from that used in the Chung-Hua County Trial that was based on the community-based outreach approach. To standardize the management of *H. pylori* infection (such as the optimal antibiotic regimen) and gastric cancer prevention in Taiwan, we have invited experts from different geographic locations in Taiwan and the consensus statements have been accomplished by using the modified Delphi method. **Conclusion:** We have successfully developed a two-stage model for gastric cancer prevention using *H. pylori* eradication in Taiwan; this model can be utilized by the heterogeneous populations with different baseline risk of gastric cancer in Taiwan.