Cost-effectiveness of *Helicobacter pylori* screening and treatment for gastric cancer in Hong Kong: a decision analytic approach

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KEY MESSAGES

1. A state-transition Markov model was developed to evaluate the cost-effectiveness of *Helicobacter pylori* screening and treatment in Hong Kong Chinese people, and to evaluate the uncertainty surrounding choice of strategies and the value of further research on the decision to initiate a mass screening programme.

2. A decision analytic framework and a societal perspective were adopted. The least costly and non-dominated strategy was *H pylori* serologic testing, followed by treating those positive for *H pylori*, with no follow-up testing. Its incremental cost-effectiveness ratio was US$20 547 for men and HK$26 840 for women per life year saved or US$17 886 for men and HK$23 905 for women per quality-adjusted life year (QALY) saved, compared with no screening or treatment.

3. *H pylori* screening and treatment could be cost-effective based on the threshold of US$50 000 per QALY.

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Introduction

In Hong Kong, gastric cancer is the fourth leading cause of cancer-related death following lung, colorectum, and liver cancer. Eradication of *Helicobacter pylori* may reduce the incidence of gastric cancer.[1] This study estimated the cost-effectiveness of *H pylori* screening and treatment in Hong Kong Chinese people, and evaluated the uncertainty surrounding choice of strategies and the value of further research on the decision to initiate a mass screening programme.

Methods

Study instruments and cost-effectiveness analyses

This study was conducted from December 2009 to November 2011. A state-transition Markov model was developed to simulate *H pylori* screening and treatment as well as gastric cancer diagnosis and treatment in Hong Kong Chinese people aged 20 years for the next 60 years. Participants were followed up throughout their lifetime. Disease progression could vary by *H pylori* status, sex, and age.

According to a gastric carcinogenesis model,[2] the natural history of non-cardia intestinal-type gastric adenocarcinomas was characterised as a progression of yearly transitions among various health states (Fig), including normal gastric mucosa, gastritis, gastric atrophy, intestinal metaplasia, dysplasia, early gastric cancer, distant gastric cancer, death from gastric cancer, and death from other causes. A cohort of individuals were distributed to either *H pylori*–positive or *H pylori*–negative precancerous health states. They could remain in one state or transit to other states at rates according to local-specific data and/or consensus from the literature. A cohort of 100 000 cancer-free 20-year-old people over a 60-year span was modelled. It was assumed that gastric cancer deaths could only occur in those in the metastatic state.

It was assumed that the effectiveness of *H pylori* treatment depends on the absence of advanced precancerous lesions and that treatment reduces disease progression probabilities in those with gastritis and atrophy.[3-5] Our model was based on a randomised controlled trial in a Japanese population evaluating the effectiveness of *H pylori* treatment to prevent (metachronous) cancers among early gastric cancer patients after endoscopic mucosal resection.[1]

Three strategies were evaluated: (1) no screening or treatment, (2) *H pylori* serologic testing, followed by treating those positive for *H pylori*, with no follow-up testing, (3) *H pylori* serologic testing, followed by treating those positive for *H pylori*, and confirming *H pylori* eradication using a C-urea breath test, and retreating those who were positive.

Four major direct medical costs were considered: the cost of screening for *H pylori*, the cost of treatment for *H pylori*, the one-time cost of invasive
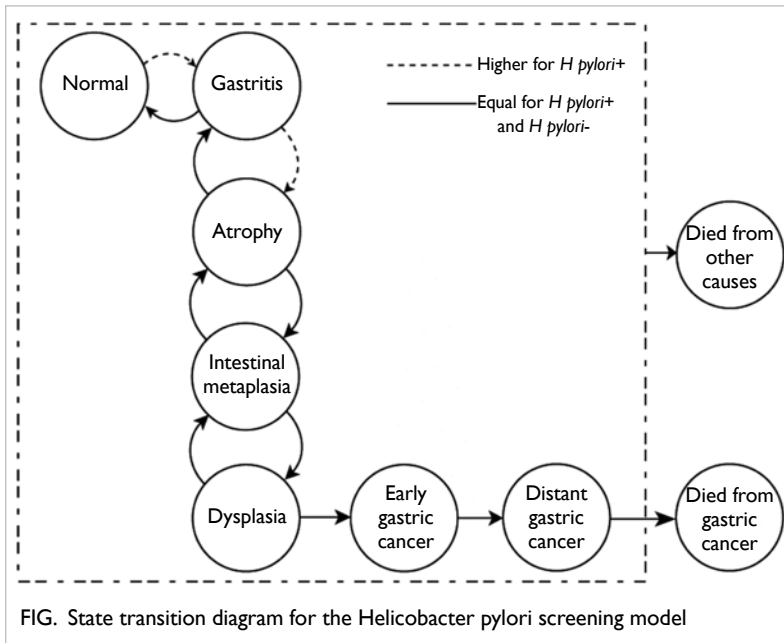
FIG. State transition diagram for the Helicobacter pylori screening model

Strategies that were less effective and more costly than a competing strategy were eliminated by simple dominance. Comparative performance of the remaining screening strategies was measured by the incremental cost-effectiveness ratio (ICER). Those that were less effective and had a higher ICER were ruled out by extended dominance and eliminated, and the ICERs of the remaining strategies were recalculated.

A societal perspective was adopted. Recommendations of the Panel on Cost-Effectiveness in Health and Medicine were used in performing cost-effectiveness calculations.

Sensitivity analysis

A probabilistic sensitivity analysis was conducted to examine uncertainty surrounding choice of strategies. Clinical and cost parameters were specified with appropriate probabilistic distributions, and cost-effectiveness results associated with selecting values at random from the distributions were used in a Monte Carlo simulation of the model with 1000 runs. Based on the simulated cost-effectiveness results, a cost-effectiveness acceptability curve was constructed to present the uncertainty of the ICER across different values of the ceiling ratios (ie acceptability willingness-to-pay thresholds).

The uncertainty that potentially existed in decision and the model parameters in value of information analyses were assessed. That is, the uncertainty surrounding choice of strategies and whether further research could add value to the decision of initiating a population-wide screening programme were evaluated, as was the expected value of perfect information (EVPI) for the entire cost-effectiveness model.[6]

cancer treatment, and the cost of terminal care during the final 6 months before death. The cancer treatment cost included diagnosis (eg endoscopy), major surgical procedure (eg gastrectomy), hospitalisation after surgery, chemotherapy, and staff costs. The first-line treatment for *H pylori* (a 14-day course of proton pump inhibitor, clarithromycin, and amoxicillin) was used. The costs of treatment were estimated based on per unit/month drug price and fees and charges in a public hospital. The terminal costs were calibrated according to the trajectory of US cancer costs. Other major non-health care costs were also considered, including transportation and time costs. All costs were adjusted to the 2012 level.

TABLE. *Helicobacter pylori* screening and treatment strategies for a cohort of 100 000 Hong Kong Chinese people aged 20 years for the next 60 years*

Strategy*	Projected total mortality in the next 60 years	Projected gastric cancer-related mortality in the next 60 years	Lifetime costs (million US$)	Life years	Incremental cost-effectiveness ratio†	
					Cost per life year saved	Cost per quality-adjusted life year saved
Men						
No screening or treatment	95 100	814	23.73	5 970 700		
Screening and treatment	95 091	773	35.03	5 971 250	20 547	17 886
Screening, treatment, and rescreening	95 088	759	54.03	5 971 432	104 463	90 712
Women						
No screening or treatment	86 962	520	14.99	6 546 824		
Screening and treatment	86 955	494	26.29	6 547 245	26 840	23 905
Screening, treatment, and rescreening	86 953	486	45.29	6 547 375	146 341	130 239

* Assuming health-related utilities of 0.9 and 0.3 for early and advanced invasive cancer for the remaining time spent in the same state
† Relative to the less costly, non-dominated strategy above

Results

Cost-effectiveness and associated uncertainty

Compared with no screening or treatment, screening and treatment for *H pylori* resulted in a gain in life expectancy of 1.2 to 2 days at an incremental cost of US$113 to US$303 per person (Table). The most cost-effective (non-dominated) strategy was *H pylori* serologic testing, followed by treating those positive for *H pylori*, with no follow-up testing. Its ICER was US$20547 for men and HK$26840 for women per life year saved or US$17886 for men and HK$23905 for women per quality-adjusted life year (QALY) saved, compared with no screening or treatment. In probabilistic sensitivity analyses, the probability of the ICER being below a threshold of US$50000 per life year saved was 51.9% for men and 50.7% for women.

Expected value of perfect information

The results of the model were subject to limited uncertainty (cost per man/woman=US$825/US$790). The EVPI for the patient populations was estimated to be US$13.4 million over 40 years if a willingness-to-pay threshold was US$50000 per life year saved.

Discussion

The most cost-effective strategy was *H pylori* serology testing, followed by antibiotic treatment for those positive, with no follow-up testing. The probability sensitivity analyses and the EVPI analyses showed the robustness of the results by considering several dimensions of uncertainty. The state-transition model captured the natural history of non-cardia intestinal-type gastric adenocarcinoma, and reflected the role of *H pylori* infection in the pathogenesis of gastric cancer.

A potential limitation of this study was that we did not have aggregate local stage-specific treatment costs for invasive gastric cancer, and instead relied on individual itemised cost data. In addition, we did not evaluate the full spectrum of screening strategies for *H pylori* (eg screening at different ages).

This mathematical decision analytic model could provide insight about the long-term outcomes and the cost-effectiveness of *H pylori* screening and treatment strategies.

Acknowledgement

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