APPENDIX

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Lee YC, Chiu HM, Chiang TH, *et al*. Accuracy of fecal occult-blood test and *Helicobacter pylori* stool antigen test for detection of upper gastrointestinal lesions

APPENDIX TABLES

Appendix Table 1. Base-case values, ranges, and distribution for sensitivity analyses

Variable	Base-case value*	Distribution for probabilistic sensitivity analysis†
Population characteristics		
Prevalence of important lesions in the upper gastrointestinal tract	0.16 (0–0.50)	Beta (523, 3171)
Prevalence of *H. pylori* infection in subjects with upper gastrointestinal lesions	0.53 (0.10–0.90)	Beta (277, 523)
Prevalence of latent *H. pylori* infection in subjects with no upper gastrointestinal lesions	0.19 (0–0.90)	Beta (511, 2648)
Stool test characteristics		
H. pylori stool antigen test		
True positive for *H. pylori*-related upper gastrointestinal lesions	0.88 (0.80–0.97)	Beta (51, 58)
False positive for *H. pylori*-unrelated upper gastrointestinal lesions	0.01 (0–0.14)	Beta (27, 2720)
True positive for *H. pylori* infection but no upper gastrointestinal lesions	0.88 (0.80–0.97)	Beta (51, 58)
False positive for no *H. pylori* infection and no upper gastrointestinal lesions	0.01 (0–0.14)	Beta (27, 2720)
Guaiac-based fecal occult-blood test (in the scenario of negative results on immunochemical test)		
True positive for *H. pylori*-related upper gastrointestinal lesions	0.19	Beta (49, 261)
True positive for *H. pylori*-unrelated upper gastrointestinal lesions	0.14	Beta (32, 236)
False positive for *H. pylori* infection but no upper gastrointestinal lesions	0.11	Beta (53, 493)
False positive for no *H. pylori* infection and no upper gastrointestinal lesions	0.10	Beta (199, 2049)

* Base-case values are derived from our hospital-based study. Data in parentheses are the range used in the one-way sensitivity analysis.

† Beta (*r*, *n*) = beta distribution with *r* positive cases from *n* subjects. The base-case values were applied with the nominator and denominator derived from our hospital-based study.

Appendix Table 2. One-way sensitivity analyses

Variable	***Helicobacter pylori* stool antigen test**		**Guaiac-based fecal occult-blood test**	
Prevalence of UGI lesions (%)	PPV (%)	NPV (%)	PPV (%)	NPV (%)
1	2.6	99.4	1.6	99.1
2	5.1	98.7	3.3	98.1
5 (threshold value)	12.2	96.7	8.0	95.3
10	22.7	93.3	15.5	90.6
16 (base-case value in our study)	34.3	88.7	24.5	84.5
30	53.1	78.4	41.4	71.5
50	72.6	60.8	62.2	51.8
Proportion of *H. pylori* related UGI lesions (%)	PPV (%)	NPV (%)	PPV (%)	NPV (%)
10	9.7	82.2	21.9	84.2
30 (threshold value)	23.1	85.1	23.2	84.3
53 (base-case value in our study)	34.3	88.7	24.5	84.5
70	40.7	91.6	25.5	84.6
90	46.8	95.3	26.7	84.8
Prevalence of latent *H. pylori* infection (%)	PPV (%)	NPV (%)	PPV (%)	NPV (%)

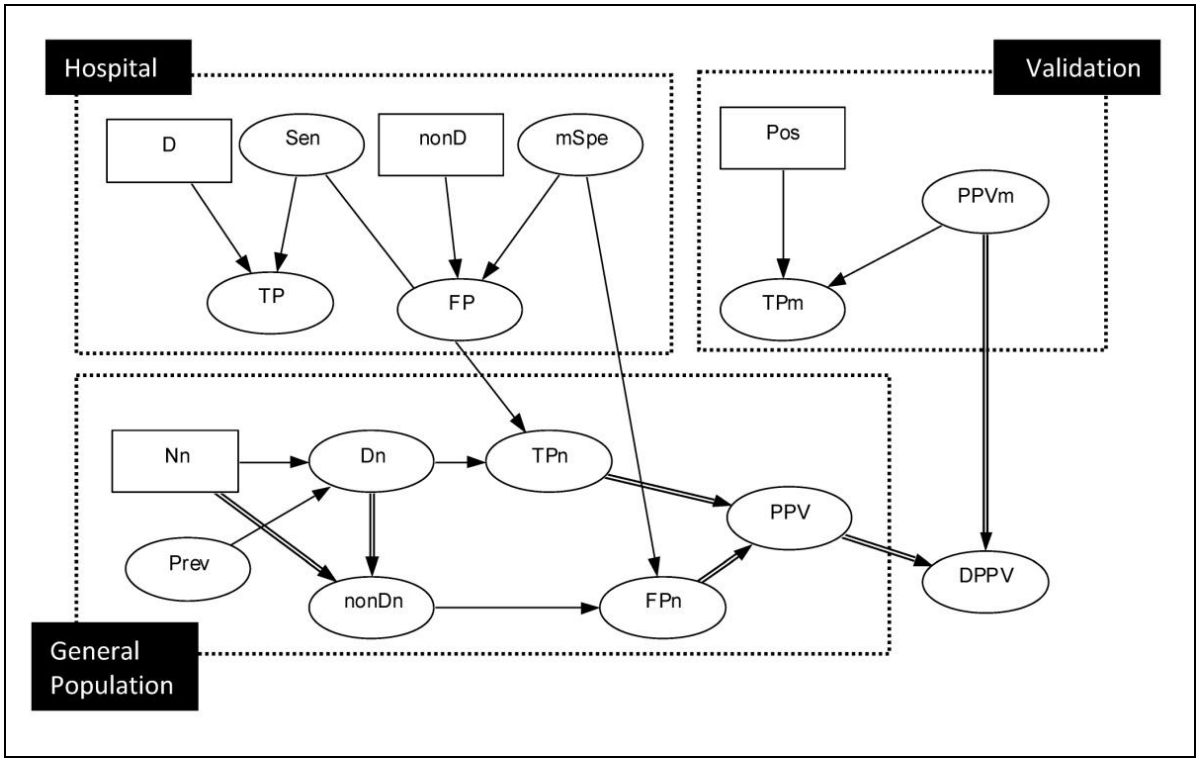
1	83.3	90.4	24.9	84.5
2	77.2	90.3	24.9	84.5
5	63.5	90.1	24.8	84.5
10	48.9	89.6	24.7	84.5
19 (base-case value in our study)	34.3	88.7	24.5	84.5
32 (threshold value)	24.4	87.2	24.3	84.5
50	17.3	84.2	24.0	84.5
90	10.5	66.5	23.2	84.4

Abbreviation: UGI=upper gastrointestinal; PPV=positive predictive value; NPV=negative predictive value

APPENDIX FIGURES

Appendix Figure 1. Estimation of the positive predictive value using the directed acyclic graph

In the hospital-based study, data on true positive (*TP*) and false positive (*FP*) follow two binomial distributions: Bin (*D*, *Sen*) and Bin (*nonD*, *mSpe*), where *D* and *nonD* are referred to number of subjects with upper gastrointestinal lesions and subjects with no upper gastrointestinal lesions, and *Sen* and *mSpe* are two non-informative priors, both following the Beta (1, 1) distribution for the sensitivity and one minus specificity. Such stochastic relationships between *TP*, *D*, and *Sen* and between *nonD*, *mSpe*, and *FP* are linked with a solid arrow. The *Sen* and *mSpe* are further linked with the community population to estimate the number of true positives (TPn~Bin (*Dn*, *Sen*)) and the number of false positives (FPn~Bin (*nonDn*, *mSpe*)), which can be used to calculate positive predictive value (*PPV*) for the *H. pylori* stool antigen test applied in the community population (the double-line arrow for logic link with symbolic formula). The positive predictive value for the validation (community) dataset (*PPVm*) can be also modeled as number of true positives (*TPm*), which is followed by the Bin (*Pos*, *PPVm*) distribution. Therefore, the point estimates and 95% credible intervals of *PPV*, *PPVm*, and *DPPV* (*i.e.*, the difference between *PPV* and *PPVm*) can be obtained.

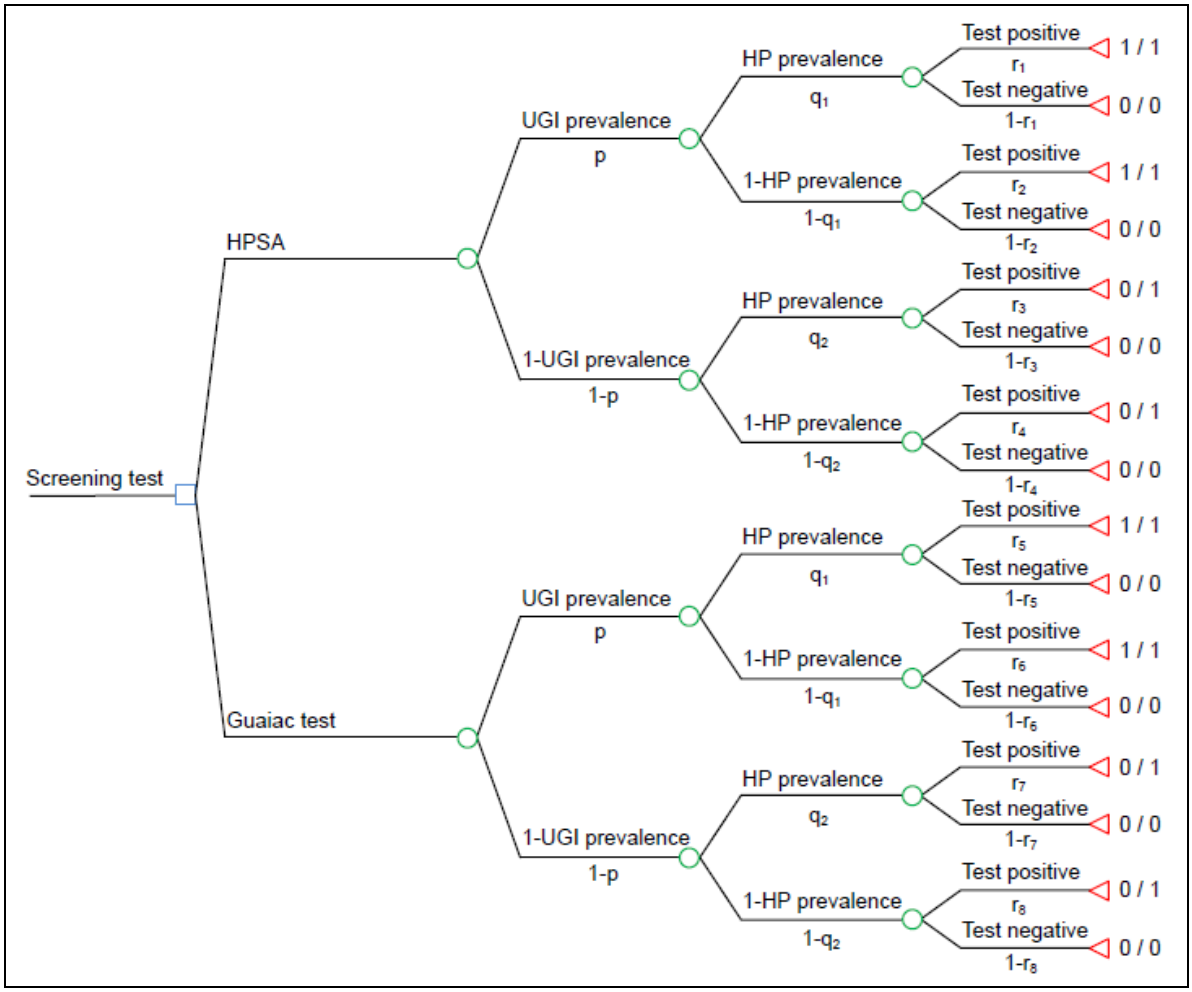


Appendix Figure 2. The framework of the decision model

Following the decision node, there are two choices of stool tests, including the *H. pylori* stool antigen test and the guaiac-based fecal occult-blood test. For each screening test, we created the first chance node to denote whether the subject has an important lesion in the upper gastrointestinal tract or not by setting a probability of p. The probability for a subject who has no upper gastrointestinal lesions was therefore equal to 1-p. Following this chance node, we created a second chance node to specify whether the upper gastrointestinal lesions are associated with the *H. pylori* infection or not. The probabilities of subjects who are positive for both upper gastrointestinal lesions and *H. pylori* infection and subjects who are negative for upper gastrointestinal lesions but positive for *H. pylori* infection are specified as q_1 and q_2, respectively; hence, the probabilities of subjects who are positive for upper gastrointestinal lesions but negative for *H. pylori* infection and subjects who are negative for both upper gastrointestinal lesions and *H. pylori* infection are equal to 1-q_1 and 1-q_2, respectively. The tree ends up with the terminal nodes, where we can express the positive predictive value based on the general form of Bayes' rule as follows:

$$P_{dis|test} = \frac{P_{dis} \times P_{test|dis}}{\sum_{i=1}^{n} P_{dis\,i} \times P_{test|dis\,i}}$$

We set two payoff values for each terminal node, including 1/1 for a true positive result, 0/1 for a false positive result, and 0/0 for a negative result. In our study, the performance of stool tests has been evaluated under different clinical scenarios and the positive rates (r_1–r_4) of each test are known. By adding up the probabilities along a specific decision tree and multiplying the payoff values in the terminal node, the positive predictive value of each stool test can be expressed by the sum in the nominator (true positive) divided by the sum in the denominator (test positive). By changing of payoff values, the same approach can be applied to the estimation of the negative predictive values.


Screening test
HPSA
Guaiac test
UGI prevalence
p
1-UGI prevalence
1-p
HP prevalence
q_1
1-HP prevalence
$1-q_1$
HP prevalence
q_2
1-HP prevalence
$1-q_2$
Test positive
r_1
Test negative
$1-r_1$
Test positive
r_2
Test negative
$1-r_2$
Test positive
r_3
Test negative
$1-r_3$
Test positive
r_4
Test negative
$1-r_4$
Test positive
r_5
Test negative
$1-r_5$
Test positive
r_6
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$1-r_6$
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r_7
Test negative
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Test positive
r_8
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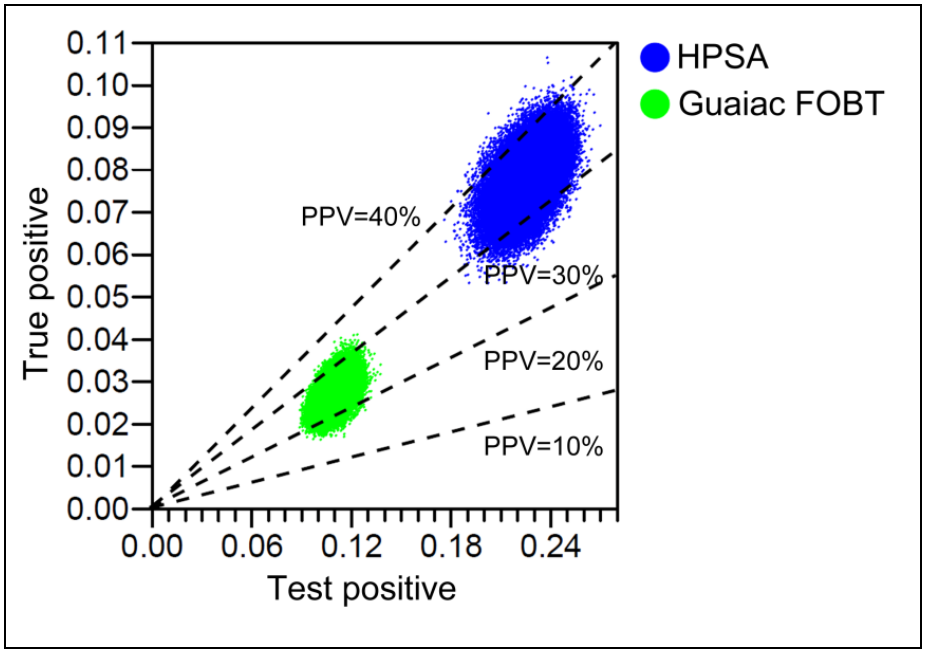
Appendix Figure 3. Probabilistic sensitivity analyses using the Monte Carlo simulation

The distribution of randomly sampled 100,000 individuals is shown in the scatter plot. Given the probabilities of test positive and true positive, the slope of each point is equal to the positive predictive value. The uncertainty of positive predictive values for the *H. pylori* stool antigen test and the guaiac-based fecal occult-blood test are shown across different levels.



Appendix Figure 4. Two-way sensitivity analyses

To predict the upper gastrointestinal lesions, the slash-line area represents the area where the positive predictive value of the *H. pylori* stool antigen test is higher than 10% while the blank area is less than 10%. The vertical dash line indicates the threshold value at which the *H. pylori* stool antigen test and the guaiac-based fecal occult-blood test may have the same level of the positive predictive values. In this two-way sensitivity analysis, we set the proportion of *H. pylori* infection in subjects with upper gastrointestinal lesions at 53% (*i.e.*, the base-case value of our study) as this proportion was similarly observed in both eastern and western countries.