ORIGINAL ARTICLE



A Population-Based *Helicobacter pylori* Eradication Strategy Is More Cost-Effective than Endoscopic Screening

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Abstract

Background *Helicobacter pylori* (HP) eradication therapy is an efficient primary prevention method to reduce gastric cancer development. In Japan, biennial endoscopic screening for individuals aged 50 years and older is currently conducted as a national gastric cancer prevention program.

Aims We aimed to evaluate which strategy was the most optimal and cost-effective among HP eradication strategy, annual, biennial, and triennial endoscopic screening, and no screening as a national gastric cancer prevention program.

Methods We developed a state-transition model for HP eradication strategy, annual, biennial, and triennial endoscopic screening, and no screening using a healthcare payer perspective and a lifetime horizon. We targeted a hypothetical cohort of the Japanese population in their 20 s to 80 s. The main outcomes were costs, quality-adjusted life-years (QALYs), incremental cost-effectiveness ratios, gastric cancer cases, and deaths from gastric cancer. We performed one-way, two-way, and probabilistic sensitivity analyses.

Results HP eradication strategy was more cost-effective than endoscopic screening at any interval in all age groups. Costeffectiveness was sensitive to HP infection rate. Cost-effective acceptability curves by Monte Carlo simulations for 10,000 trials demonstrated that HP eradication strategy was 100% cost-effective at a willingness-to-pay threshold of US\$50,000 per QALY gained in all age groups. Over a lifetime, HP eradication strategy saves US\$28.07 billion, increases 37.16 million QALYs, prevents 4.47 million gastric cancer cases, and saves 319,870 lives from gastric cancer.

Conclusion A population-based HP eradication strategy is optimal and cost-effective for a national gastric cancer prevention program in Japan, replacing the current secondary prevention-focused biennial endoscopic screening.

Keywords *Helicobacter pylori* · Disease eradication · Endoscopy · Stomach neoplasms · Primary prevention · Health economics

Abbreviations

HP	Helicobacter pylori
QALY	Quality-adjusted life-year
ICER	Incremental cost-effectiveness ratio
WTP	Willingness-to-pay

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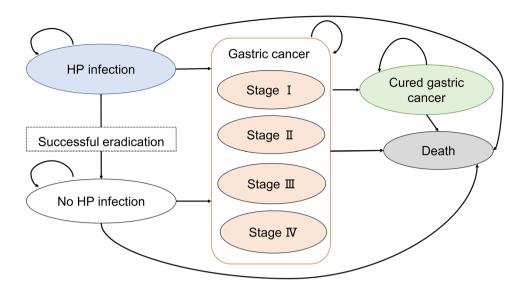
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Introduction

More than half of the world's population is infected with *Helicobacter pylori* (HP) [1]. HP infection is responsible for 810,000 new cancer cases worldwide in 2018, mainly non-cardia gastric adenocarcinoma [2]. East Asia accounts for 480,000 cases of cancer attributable to HP infection, mostly in China (340,000 cases), Japan (100,000 cases), and South Korea (30,000 cases) [2]. HP infection causes chronic gastritis and leads to gastric cancer development. Gastric cancer has the fifth highest incidence rate and is the fourth major cause of cancer-related deaths in the world [3]. HP eradication therapy reduces gastric cancer development by healing the intragastric mucosal inflammation and halting the histological progression in patients with chronic atrophic gastritis, a pre-cancerous condition of the stomach [4–7], and follow-up endoscopy

Fig. 1 Schematic depiction of a Markov cycle tree in a statetransition model. We show the health states in the model as ovals. In a yearly model cycle, transitions can occur between the health states and other health states, represented by the arrows. *HP Helicobacter pylori*



is necessary for early detection of gastric cancer after successful HP eradication therapy [8]. In 2014, an International Agency for Research on Cancer (IARC) working group recommended that countries should explore the possibility of implementing population-based HP screening and treatment programs, after careful consideration at the regional level of disease burden, other health priorities, cost-effectiveness analysis, scientifically valid assessment of program processes, feasibility, effectiveness, and possible adverse effects [9]. The Taipei global consensus guidelines for screening and eradication of HP for gastric cancer prevention recommend that mass screening and eradication of HP should be considered in populations at higher risk of gastric cancer and that eradication therapy should be offered to individuals infected with HP [10].

Japan has the second-highest age-standardized rate for gastric cancer, one of the high-incidence countries in the world [3]. HP infection is estimated to be responsible for 98% of gastric cancer patients in Japan [11-14]. In February 2013, HP eradication therapy for patients with HPassociated chronic gastritis became covered by the national health insurance in Japan. The 2014 edition of Japanese guidelines for gastric cancer screening recommends biennial endoscopic screening for people aged 50 years and older for the population-based secondary prevention of gastric cancer [15]. Guidelines for the management of HP infection by the Japanese Society for Helicobacter Research recommend HP eradication therapy for gastric cancer prevention for all patients with HP infection [16]. Although the number of deaths from gastric cancer is gradually decreasing, the number of gastric cancer patients in their 80 s and older has not yet declined in Japan [17].

In this study, we aimed to evaluate which strategy was the most optimal and cost-effective among HP eradication strategy, annual, biennial, and triennial endoscopic screening, and no screening as a national gastric cancer prevention program.

Methods

Study Design and Model Structure

We constructed a state-transition model with a Markov cycle tree for five strategies: HP eradication strategy, annual endoscopic screening, biennial endoscopic screening, triennial endoscopic screening, and no screening using a healthcare payer perspective and a lifetime horizon. In this study, HP eradication strategy is defined as a primary prevention strategy in which individuals in their 20 s to 40 s do not perform post-eradication endoscopy and individuals in their 50 s to 80 s perform annual post-eradication endoscopy to detect early-stage gastric cancer [18]. A cycle length of one year was chosen. The half-cycle correction was applied. In the model, decision branches led directly to one Markov node per intervention strategy, and the first event was modeled within the Markov cycle tree (Fig. 1). The current national gastric cancer prevention program in Japan is no screening for individuals in their 20 s to 40 s, and biennial endoscopic screening for individuals in their 50 s to 80 s.

We used TreeAge Pro 2022 (TreeAge Software Inc., Williamstown, Mass.) for the decision-analytical calculations. As this was a modeling study with all inputs and parameters derived from the published literature and Japanese statistics, ethics approval was not required.

HP Eradication Strategy

An individual receives an HP antibody test. If the HP antibody test is negative, the individual doesn't receive HP eradication therapy. If the HP antibody test is positive, the individual receives an endoscopy. If gastric cancer is detected by endoscopy, the individual receives the standard treatment for gastric cancer according to the Japanese guidelines for gastric cancer treatment: endoscopic mucosal resection (EMR), endoscopic submucosal dissection treatment (ESD), surgery, chemotherapy, and radiotherapy with palliative care according to cancer stage, stage I-IV [19]. If gastric cancer is not detected by endoscopy, the individual receives a first-line HP eradication therapy (Vonoprazan 40 mg/day, Clarithromycin 400 mg/day, and Amoxicillin 1500 mg/day for 7 days) and two stool antigen tests before and after eradication. If the first-line HP eradication therapy is unsuccessful, the individual receives a second-line HP eradication therapy (Vonoprazan 40 mg/day, Metronidazole 500 mg/day, and Amoxicillin 1500 mg/day for 7 days). Successful HP eradication therapy results in a change from the HP-positive state to the HP-negative state. The first-line and second-line HP eradication therapies are based on the guidelines for the management of HP infection by the Japanese Society for Helicobacter Research [16, 20]. The rationale for adding two stool antigen tests before and after eradication is based on the guidelines for the management of HP infection by the Japanese Society for Helicobacter Research [16], which requires one stool antigen test to confirm HP negativity before eradication if the HP antibody test is negative, and another stool antigen test for confirmation of HP negativity after eradication. Endoscopic surveillance is performed for the early detection of gastric cancer in individuals over 50 years of age after successful HP eradication therapy according to the guidelines for the management of HP infection by the Japanese Society for Helicobacter Research [16]. If both HP eradication therapies are unsuccessful, the HPpositive state remains until death.

Annual, Biennial, and Triennial Endoscopic Screening

An individual receives regular endoscopic screening once a year, once every two years, or once every three years. If gastric cancer is detected by endoscopy, the individual receives the standard treatment for gastric cancer according to the Japanese guidelines for gastric cancer treatment [19]. The compliance rate in gastric cancer screening (49.5%) was derived from Japanese cancer statistics and considered in the model [21].

No Screening

An individual has no opportunity to receive any gastric cancer screening.

Target Population

We targeted a hypothetical cohort of the Japanese population in their 20 s to 80 s. Children and adolescents (age < 20 y) were not included in the model. Age-specific HP infection rates were considered.

Epidemiologic Parameters and Clinical Probabilities

Epidemiologic parameters and clinical probabilities were collected using MEDLINE from 2000 to December 2022, the national census, and Japanese cancer statistics (Table 1) [6, 11–14, 22–29]. The age-dependent effects on gastric cancer incidence, HP infection rate, and mortality from other causes were taken into account in the model [22, 23, 29]. Relative risk rate of gastric cancer development after successful eradication, eradication success rates of HP eradication therapies, and compliance rates of HP eradication therapies were obtained from the literature [6, 24]. Stage-specific 5-year survival rates and stage-specific detection rates of gastric cancer were obtained from Japanese cancer statistics [22, 27]. The responsibility rate of HP infection for gastric cancer development was assumed to be 98% [11–14]. The sensitivity and specificity of endoscopy and HP antibody test were obtained from the literature [25, 28].

Costs

Costs were calculated based on the costs from the Japanese national fee schedule [30], and were adjusted to 2021 Japanese yen, using the medical care component of the Japanese consumer price index and were converted to US dollars, using the Organisation for Economic Co-operation and Development (OECD) purchasing power parity rate in 2021 (US\$1 = ¥96.76) (Table 1) [31]. The discount rate of costs was set at 3% per year [32, 33]. Incremental cost-effectiveness ratios (ICERs) were calculated and compared to a willingness-to-pay (WTP) level of US\$50,000 per quality-adjusted life-year (QALY) gained [34].

Health State Utilities

Health status was included to represent the possible eight clinical states: (i) no HP infection, (ii) HP infection, (iii) stage I gastric cancer; (iv) stage II gastric cancer; (v) stage III gastric cancer; (vi) stage IV gastric cancer, (vii) cured gastric cancer, and (viii) death (Fig. 1). Health state utilities were obtained from the literature and were calculated using utility weights (Table 1) [26]. The discount rate of utilities was set at 3% per year [32, 33].

The health outcomes were QALYs, ICERs, gastric cancer cases, and deaths from gastric cancer. We calculated age-specific cumulative lifetime health outcomes of HP

Incidence of gastric cancer 0.000003950 20-24 years 0.000003657 25-29 years 0.000013657 30-34 years 0.000013657 30-34 years 0.000013657 35-39 years 0.000013657 35-39 years 0.000013658 40-44 years 0.000013498 55-59 years 0.00013408 55-59 years 0.00013408 60-64 years 0.000111067 65-69 years 0.001211067 65-69 years 0.001211067 65-69 years 0.001211067 65-69 years 0.000332193 80-84 years 0.000321193 80-84 years 0.000321193 80-84 years 0.000321193 80-84 years 0.000321193 80-84 years 0.000322193 80-84 years 0.000322193 80-84 years 0.000332193 80-84 years 0.000332193 80-84 years 0.000332193 80-84 years 0.000332193 80-84 years 0.0001211067 80-84	of gastric cancer ears 0.0 ears 0.0	000003950 000013657 000029844 000028365 000168943 000168943 000168943 000168943 0001211067 00031805 00031805 001211067 0022348 00022348 00022348 00027345 002735 002735 002735 002735 002735 002735 002735 002735 002735 002735 002735 002735 002735 002735 002735 002735 002735 0020000000000000000000000000000000000								[22]
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30 13.8	20									[23]
8. 8.	5.2		30	40	50	60	70	80		
Stage-specific 5-year gastric cancer survival rate, % Stage I 96.0 Stage II 69.2 Stage II 41.9 Stage IV 6.3 Eradication success rate 0.901 of 1st-line HP eradication 0.901 therapy 0.901 fraction success rate 0.901 of 1st-line HP eradication 0.901 therapy 0.901 fractication success rate 0.901 of 2nd-line HP eradication 0.901 therapy 0.901 of 2nd-line HP eradication 0.901 therapy 0.901 development with HP 0.54		7	13.8	22.9	32.5	46.2	57.2	63.0	1–70	
ion tion	cific 5-year gastric cancer survive	ıl rate, %								[22]
ion tion ncer	96	0.							86-06	
ion tion		.2							60–75	
ion tion ncer		6.							35-45	
ion tion ncer									5-10	
tion	ion	106							0.6–1.0	[24]
c cancer HP	tion	106							0.6–1.0	[24]
eradication therapy	c cancer HP	54							0.46-0.95	[9]
Compliance rate of 1st-line 0.891 HP eradication therapy		391							0.6–1.0	[24]
Compliance rate of 2nd-line 0.901 HP eradication therapy		106							0.6–1.0	[24]

 Table 1 Model inputs for selected variables

Muldle Bealler vale Seatility rue of H	Table 1 (continued)									
09-1.0 02-0.8 0.2-0.8 0.982-0.999 0.982-0.999 0.982-0.999 0.982-0.994 0.882-0.994 0.882-0.994 0.882-0.994 0.882-0.994 0.2 0.2 0.2 0.2 0.2 0.2 0.882-0.994 0.8 0.9 0.1 0.3 0.2 0.8 0.9 0.1 0.3 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.4 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5	Variable	Baseline value							Sensitivity analysis range	References
0.2-0.8 0.681-0.998 0.681-0.998 0.82-0.994 0.82-0.994 0.832-0.994 0.472-0.870 0.412-0.870 0.412-0.870 0.412-0.810 0.412-0.810 0.412-0.5337 0.372-3.8377 0.372-3.8377 0.372-3.83776 0.372-3.8377 0.372-3.83776 0.372-3.83776 0.372-3.8377 0.3726 0.372-3.336 0.372-3.336 0.372-3.337 0.3726 0.372-3.337 0.3726 0.372-3.337 0.3726 0.372-3.337 0.3726 0.372-3.337 0.3726 0.3726-3.337 0.3726 0.3726-3.337 0.3726 0.3726-3.337 0.3726 0.3726-3.337 0.3726 0.3726-3.337 0.3726 0.37	Responsibility rate of HP infection for gastric cancer development	86.0							0.9–1.0	[11–14]
40 50 60 70 80 57.7 63.1 63.7 65.9 61.3 53.3 19.1 18.8 17.4 19.8 53.3 19.1 18.8 17.4 19.8 63.1 63.7 65.9 61.3 30-70 9.2 9.4 9.8 9.0 9.6 7-15 9.2 9.4 9.8 9.0 9.6 7-15 9.3 19.1 18.8 17.4 19.8 15-50 63.4 5.5 9.4 9.6 7-15 9.4 9.8 9.0 9.6 7-15 9.4 9.8 17.4 19.8 15-50 8.4-147.3 8.4-147.3 8.4-147.3 9.38-32.56 2.325-3.8756	Compliance rate of endoscopic screening	0.495							0.2-0.8	[21]
0681-0.98 082-0.999 082-0.994 082-0.994 082-0.994 082-0.994 082-0.994 083-0.802 87-92 4-7 4-7 4-7 1-3 2-4 2-4 2-4 2-4 2-4 2-4 2-4 2-4	Accuracy, % HP antibody test									[28]
40 50 60 70 80 57.7 63.1 63.7 65.9 61.3 30-70 9.8 9.4 9.8 9.0 9.6 7-15 9.2 9.4 9.8 9.0 9.6 7-15 9.2 9.4 9.8 9.0 9.6 7-15 9.2 9.4 9.8 9.0 9.6 7-15 9.2 9.4 9.8 9.0 9.6 7-15 9.2 9.4 9.8 17.4 19.8 15-50 19.1 18.8 17.4 19.8 15-50 6.20-10.34 11.0-18.35 44.22-73.70 8.4-147.3 6.58-10.981 15.500 8.4-147.3 6.533-32.56 23.23-38.756 23.23-38.756 23.23-38.756 23.23-38.756	Sensitivity	0.933 0.995							0.681–0.998 0.982–0.998	
40 50 60 70 87-0.994 87-0.902 0.883-0.892 887-0.992 93 0.91 1-3 2-4 1-3 2-4 2-4 2-4 40 50 60 70 80 57.7 63.1 63.7 65.9 61.3 30-70 92 9.4 9.8 9.0 9.6 7-15 92 9.4 9.8 9.0 9.6 7-15 92 9.4 9.8 17.4 19.8 15-50 23.3 19.1 18.8 17.4 19.8 15-50 21.0 9.1 18.8 17.4 19.8 15-50 21.0 9.1 18.8 17.4 19.8 15-50 21.0 9.1 18.8 17.4 19.8 15-50 21.0 9.1 18.8 17.4 19.8 16.2-68.70 21.0 9.1 9.2 9.2.55.3837 19.378-32.296 21.55.39.3776 9.3.2.596 2.3.255.38377 19.378-32.296 <td>Endoscopy</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>[25]</td>	Endoscopy									[25]
40 50 60 70 80 57.7 63.1 63.7 65.9 61.3 57.7 63.1 63.7 55.9 61.3 9.8 9.4 9.8 9.0 9.6 7.15 9.2 9.4 9.8 9.0 9.6 7.15 9.2 9.4 9.8 9.0 9.6 7.15 9.2 9.4 9.8 9.0 9.6 7.15 9.2 9.4 9.8 17.4 19.8 15-50 9.1 18.8 17.4 19.8 15-50 9.1 1.8.8 17.4 19.8 15-50 9.4 9.8 19.4 19.35 41.22-68.70 8.4 - 147.3 6.50-10.34 11.01-18.35 41.22-68.70 8.4 - 147.3 6.538-10.981 15.502-25.8337 19.378-32.296 9.3.2556 23.253-38.756 23.255-38.756 23.255-38.756	Sensitivity	0.954							0.842 - 0.994	
47 47 40 50 60 70 80 57.7 63.1 63.7 65.9 61.3 30-70 9.8 9.4 9.8 9.0 9.6 715 9.2 9.4 9.8 9.0 9.6 715 9.2 9.4 9.8 9.0 9.6 715 9.2 9.4 9.8 9.0 9.6 715 9.2 9.4 9.8 17.4 19.8 15-50 23.3 19.1 18.8 17.4 19.8 15-50 8.4-147.3 6.20-10.34 1101-18.35 44.22-73.70 8.4-147.3 6.588-10.981 15.502-25.837 19.378-32.296 2.3.255-38.756 23.253-38.756 23.2536 23.2536	Specificity	0.888							0.883-0.892	
89.8 5.4 5.4 5.4 5.4 5.3 2.0 2.0 2.0 2.0 2.1 2.4 2.4 2.4 2.4 2.4 2.4 2.4 2.4	Stage-specific detection rate of gastric c	cancer with endo	scopic screening,	%						[27]
	Stage I	89.8							87–92	
2.0 1.3 1.3 2.8 2.4 2.4 2.8 2.8 2.4 2.8 30 40 50 60 70 80 2.0 30 40 50 60 70 80 5-12 2.4 34.2 50 57.7 63.1 63.9 61.3 30-70 2.4 9.4 9.8 9.4 9.8 9.0 9.6 7-15 4.66 30.2 23.3 19.1 18.8 17.4 19.8 15-50 8.27 14.68 17.4 19.8 17.4 19.8 15-50 8.27 14.68 17.4 19.8 17.4 19.8 15-50 8.27 14.68 17.4 19.8 15-50 44.22-7370 8.296 11.3 18.8 17.4 19.8 44.22-7370 8.4.147.3 8.8.4.147.3 8.8.4.147.3 8.8.4.147.3 8.8.4.147.3 117.8 117.8 11.1 11.1 11.1.1 11.1.1 2.6.697 11.1	Stage II	5.4							4-7	
	Stage III	2.0							1–3	
Age 70 80 20 30 40 50 60 70 80 34.2 50 57.7 63.1 63.7 65.9 61.3 30-70 6.8 9.4 9.8 9.4 9.8 9.0 9.6 7-15 12.4 10.4 9.2 9.4 9.8 9.0 9.6 7-15 46.6 30.2 23.3 19.1 18.8 17.4 19.8 15-60 8.27 10.4 9.2 9.4 9.8 70 6.20-10.34 14.68 17.4 19.8 17.4 19.8 15-60 8.27 1.1.8 17.4 19.8 15-70 58.96 17.4 19.8 15-68.70 11.0 54.96 17.8 18.8 41.25.68.70 11.0 117.8 117.8 8.8.4.147.3 8.8.4.147.3 8.8.4.147.3 2669.7 10.4.5 10.5.52.5.837 19.378-32.296 20.004	Stage IV	2.8							2-4	
20 30 40 00 00 00 00 34.2 50 57.7 63.1 63.7 65.9 61.3 30-70 6.8 9.4 9.8 9.4 9.8 9.0 9.6 5-12 12.4 10.4 9.2 9.4 9.8 9.0 9.6 7-15 46.6 30.2 23.3 19.1 18.8 17.4 19.8 15-50 8.27 14.68 17.4 19.8 17.4 19.8 15-50 8.27 58.96 58.96 4.12-73.70 41.22-73.70 54.96 54.96 54.96 41.22-68.70 41.22-68.70 117.8 54.96 54.96 58.4-147.3 58.4-147.3 54.96 54.96 55.837 11.01-18.35 41.22-68.70 117.8 54.96 56.97 58.4-147.3 55.62-25.837 20.669.7 52.837.1 52.55-38.75 53.256 53.253-38.756 31.004.5 51.004.5 53.255-38.756 53.255-38.756 53.255-38.756	Stage-specific detection rate of gastric cancer with no screening %	Age	00	07	02	07		00		[27]
5.12 5.0 5.12 5.12 12.4 10.4 9.2 9.4 9.8 9.0 9.6 7.15 12.4 10.4 9.2 9.4 9.8 9.0 9.6 7.15 46.6 30.2 23.3 19.1 18.8 17.4 19.8 15.50 8.27 5.30 23.3 19.1 18.8 17.4 19.8 15.50 8.27 5.8.96 5.4.96 5.4.96 5.4.96 41.22-68.70 117.8 5.4.96 5.4.96 5.5.937 5.36-10.34 117.8 5.4.96 5.5.837 5.58-10.981 117.8 5.38.96 5.38.36 5.38.37 5.38.37 5.4.96 5.4.96 5.5.837 5.32-25.837 5.4.96 5.5.837 5.38.10.981 15.502-25.837 5.4.96 5.337.1 5.32-35.837 19.378-32.296 3.1,004.5 5.3.253-38.756 5.3.253-38.756	Starra I	24.7 24.7	00	57 7	00 63 1	00 63 7	0/	61 3	30-70	
12.4 10.4 9.2 9.4 9.8 9.0 9.6 7-15 46.6 30.2 23.3 19.1 18.8 17.4 19.8 15-50 8.27 6.20-10.34 11.01-18.35 6.20-10.34 11.01-18.35 14.68 1.4.68 1.4.6 6.20-10.34 11.01-18.35 58.96 58.96 1.1 1.8 1.22-68.70 54.96 1.17.8 8.84-147.3 6.588-10.981 117.8 8.784.6 6.588-10.981 15.502-25.837 20,669.7 21,04.5 23,2296 23,296 31,004.5 23,004.5 23,239 23,296	Stage II	6.8	9.4	8.6	9.4	9.8	0.0	9.6	5-12	
46.6 30.2 23.3 19.1 18.8 17.4 19.8 15-50 8.27 6.20-10.34 11.01-18.35 6.20-10.34 11.01-18.35 14.68 58.96 7 44.22-73.70 44.22-73.70 54.96 54.96 7 44.22-73.70 44.22-73.70 17.8 54.96 8.84-147.3 8.84-147.3 8.784.6 5.706.97 8.58-10.981 15.502-25.837 20.669.7 20.669.7 15.502-25.837 19.378-32.296 31.004.5 31.004.5 23.253-38.756 13.3756	Stage III	12.4	10.4	9.2	9.4	9.8	9.0	9.6	7–15	
8.27 $6.20-10.34$ 14.68 $6.20-10.34$ 14.68 $11.01-18.35$ 58.96 $44.22-73.70$ 54.96 $41.22-68.70$ 54.96 $81.2-68.70$ 117.8 $88.4-147.3$ $8.784.6$ $6.588-10.981$ $5.837.1$ $25,837.1$ $25,837.1$ $23,232-38,756$ $31,004.5$ $23,232-38,756$	Stage IV	46.6	30.2	23.3	19.1	18.8	17.4	19.8	15-50	
8.27 14.68 58.96 54.96 117.8 8,784.6 20,669.7 25,837.1 31,004.5	Cost, US\$									[30]
14.68 58.96 54.96 117.8 8,784.6 20,669.7 25,837.1 31,004.5	HP antibody test	8.27							6.20-10.34	
58.96 54.96 117.8 8,784.6 20,669.7 25,837.1 31,004.5	Stool antigen test	14.68							11.01-18.35	
54.96 117.8 8,784.6 20,669.7 25,837.1 31,004.5	1st-line HP eradication therapy	58.96							44.22-73.70	
117.8 8,784.6 20,669.7 25,837.1 31,004.5	2nd-line HP eradication	54 96							41 22-68 70	
117.8 8,784.6 20,669.7 25,837.1 31,004.5	therapy									
8,784.6 20,669.7 25,837.1 31,004.5	Endoscopy	117.8							88.4-147.3	
8,784.6 20,669.7 25,837.1 31,004.5	Treatment of gastric cancer									
20,669.7 25,837.1 31,004.5	Stage I	8,784.6							6,588 - 10,981	
25,837.1 31,004.5	Stage II	20,669.7							15,502-25,837	
31,004.5	Stage III	25,837.1							19,378–32,296	
	Stage IV	31,004.5							23,253–38,756	

lable 1 (continued)		
Variable	Baseline value	Sensitivity References analysis range
Utility [26]		
No HP infection	1.0	N/A
HP infection	0.9	0.8–0.95
Gastric cancer		
Stage I	0.82	0.7–0.9
Stage II	0.79	0.7–0.9
Stage III	0.68	0.6–0.8
Stage IV	0.5	0.4–0.6
Cured gastric cancer	0.95	0.92-0.97
Death	1.0	N/A

eradication strategy compared to no screening for individuals aged 20 to 49 years and biennial endoscopic screening for individuals aged 50 to 89 years.

Sensitivity Analyses

We performed a one-way sensitivity analysis to determine which strategy was more cost-effective when we tested a single variable over a wide range of possible values while holding all other variables constant and a two-way sensitivity analysis to assess the robustness of the overall results when the values of the two variables are varied simultaneously. A probabilistic sensitivity analysis using a secondorder Monte-Carlo simulation for 10,000 trials was also performed to assess the impact of the uncertainty in the model on the base case estimates at a WTP threshold of US\$50,000 per QALY gained [34]. The uncertainty had a beta distribution for clinical probabilities and accuracies, and a gamma distribution for costs.

Markov Cohort Analysis

In the Markov cohort analysis, we determined the cumulative lifetime probability of gastric cancer cases and gastric cancer deaths prevented by HP eradication strategy for individuals aged 20 to 49 years compared with no screening, and for individuals aged 50 to 89 years compared with biennial endoscopic screening. We calculated the number of cumulative lifetime gastric cancer cases and gastric cancer deaths prevented by HP eradication strategy for individuals aged 20 to 49 years compared with no screening and for individuals aged 50 to 89 years compared with biennial endoscopic screening, by multiplying the cumulative lifetime probability of gastric cancer cases and gastric cancer deaths prevented by the number of the Japanese population in 2022. The Japanese population in 2022 was obtained from Japanese population statistics; 12.58 million in their 20 s, 13.75 million in their 30 s, 17.59 million in their 40 s, 17.27 million in their 50 s, 15.06 million in their 60 s, 16.36 million in their 70 s, and 9.63 million in their 80 s [35].

Results

Base-Case Analysis

HP eradication strategy was the most cost-effective in all age groups (Table 2). The ICER of HP eradication strategy compared with no screening in the 20 s was US\$24.4 per QALY gained. HP eradication strategy provided greater health benefits with significant cost savings than no screening in the 30 s and 40 s and biennial endoscopic screening in the 50 s to 80 s.

Sensitivity Analysis

The ICER tornado diagrams for HP eradication strategy versus no screening in 20-year-old individuals and for HP eradication strategy versus biennial endoscopic screening in 50-year-old individuals showed that the ICERs always remained below the WTP threshold of US\$ 50,000 per QALY gained and that cost-effectiveness was not sensitive to the selected variables (Fig. 2a and b). Two-way sensitivity analyses for age baseline versus HP infection rate showed that HP eradication strategy was more cost-effective than no screening when HP infection rate was 0.032 or more in the 20 s, 0.043 or more in the 30 s, 0.059 or more in the 40 s, 0.079 or more in the 50 s, 0.105 or more in the 60 s, 0.143 or more in the 70 s, and 0.194 or more in the 80 s (Fig. 2c and d). Probabilistic sensitivity analyses using Monte-Carlo simulations for 10,000 trials demonstrated that HP eradication strategy was cost-effective 100% of the time at a WTP threshold of US\$50,000 per QALY gained in all age groups (Fig. 2e).

Cumulative Lifetime Economic and Health Impacts

Over a lifetime, for the Japanese population in their 20 s to 80 s in 2022, HP eradication strategy could save US\$28.07 billion, increase 37.16 million QALYs, prevent 4.47 million gastric cancer cases, and save 319,870 lives from gastric cancer prevention program (no screening for individuals aged 20 to 49 and biennial endoscopic screening for individuals aged 50 to 89) (Table 3).

Discussion

This study demonstrated that HP eradication strategy is more cost-effective with greater health benefits than no screening and endoscopic screening at any interval to prevent gastric cancer in Japan. The superiority of HP eradication strategy is mainly due to the high HP infection rates in the Japanese population, the evidence that HP eradication therapy for HP-positive patients reduces the incidence of gastric cancer by 46%, and the low cost of HP testing and eradication therapy compared to the cost of gastric cancer treatment. We previously showed that HP eradication strategy is more cost-effective than no screening [36, 37], upper gastrointestinal series [38], and endoscopic screening [38] for gastric cancer screening and that HP eradication strategy is more cost-effective than the proton pump inhibitors therapy strategy [39] for the management of peptic ulcers in high-risk populations. This study further demonstrated the definite cost-effectiveness advantage of HP eradication strategy over endoscopic screening, even when considering various intervals or the cost of follow-up endoscopy after successful HP eradication therapy at age 50 years or older.

To the best of our knowledge, this is the first study in the world to evaluate cumulative lifetime economic and health effects of HP eradication strategy compared to endoscopic screening with various intervals.

There are several cost-effectiveness studies of endoscopic screening compared to no screening for gastric cancer screening. Shah et al. demonstrated that one-time endoscopic screening for gastric cancer with ongoing surveillance of gastric preneoplasia is cost-effective for Japanese Americans ages 50 years or older in the USA and that biennial endoscopy is less effective and costlier [40]. Our study also showed that biennial endoscopic screening is not cost-effective for asymptomatic Japanese population aged 50 years. Ascherman et al. showed that biennial endoscopic screening is not cost-effective, while 5-year and 10-year endoscopic screening is cost-effective compared to no screening in the general Japanese population aged 40 years through 35 successive 1-year cycles of the model until age 75 [41]. Our study also demonstrated that endoscopic screening at the 1-year, 2-year, and 3-year intervals is not cost-effective in the Japanese population aged 40 years. Huang et al. found that the endoscopic screening program in Japan would be cost-effective when implemented between 50 and 75 years of age, with the screening repeated every 3 years, using a WTP threshold of US\$50,000 per QALY gained [42]. We found that triennial endoscopic screening is more cost effective than no screening for individuals aged 55 to 81 years. Our results are consistent with those of previous studies. In addition, we have shown for the first time that HP eradication strategy is definitely more cost-effective than endoscopic screening at any interval for all age groups.

This study has several limitations. First, we did not consider reinfection or recurrence of HP infection in our model. The reinfection rate after HP eradication is very low. HP infection occurs mainly in childhood, and recurrence of HP infection after successful eradication is rare in adults [43]. Second, this study does not include non-medical indirect costs such as productivity losses. Third, the complications of endoscopy such as perforation and hemorrhage were not considered in our models. Endoscopy should be carefully performed by well-trained, competent, and thoughtful endoscopists, ensuring not only patient safety but also a high level of quality control. Fourth, the target population for HP eradication strategy did not include children. Fifth, the difference of gastric mucosal atrophy after successful HP eradication was not considered in the model. Biennial endoscopy

Table 2 Results of the base-case analysis

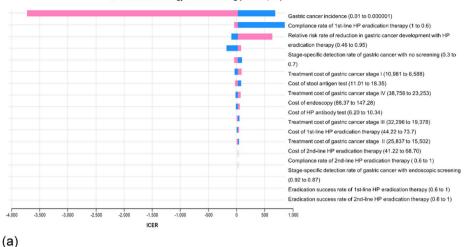
Age group, years	Strategy	Cost, US\$	Incremental cost, US\$	Effectiveness, QALYs	Incremental effec- tiveness, QALYs	ICER, US\$/ QALY gained
20	No screening	140.0	_	27.753056	_	_
	HP eradication strategy	141.4	1.4	27.810878	0.057822	24.4
	Triennial endoscopic screening	617.4	476.0	27.753728	- 0.057150	Dominated
	Biennial endoscopic screening	1070.8	929.4	27.754060	- 0.056818	Dominated
	Annual endoscopic screening	3526.0	3384.6	27.755058	-0.055820	Dominated
30	HP eradication strategy	300.5	-	25.866516	-	_
	No screening	366.8	66.2	25.657326	- 0.209190	Dominated
	Triennial endoscopic screening	809.7	509.1	25.659032	- 0.207484	Dominated
	Biennial endoscopic screening	1226.8	926.2	25.659867	- 0.206649	Dominated
	Annual endoscopic screening	3497.0	3196.5	25.662376	- 0.204140	Dominated
40	HP eradication strategy	544.3	_	23.337221	-	_
	No screening	723.9	179.6	22.992204	- 0.345017	Dominated
	Triennial endoscopic screening	1119.4	575.1	22.995320	- 0.341901	Dominated
	Biennial endoscopic screening	1487.9	943.6	22.996838	- 0.340383	Dominated
	Annual endoscopic screening	3511.9	2967.6	23.001389	- 0.335832	Dominated
50	No screening	1227.5	_	19.734550	-	_
	HP eradication strategy	1453.6	226.1	20.192466	0.457916	493.7
	Triennial endoscopic screening	1560.5	106.9	19.739590	- 0.452876	Dominated
	Biennial endoscopic screening	1866.6	413.0	19.742016	- 0.450450	Dominated
	Annual endoscopic screening	3577.0	2123.4	19.749310	- 0.443156	Dominated
60	No screening	1897.3	_	15.876433	_	_
	HP eradication strategy	1920.4	23.0	16.435276	0.558843	41.2
	Triennial endoscopic screening	2151.9	231.5	15.883442	- 0.551834	Dominated
	Biennial endoscopic screening	2382.4	462.0	15.886671	- 0.548605	Dominated
	Annual endoscopic screening	3715.6	1795.3	15.896370	- 0.538906	Dominated
70	HP eradication strategy	1930.6	_	12.098286	-	_
	No screening	2040.4	109.7	11.586851	- 0.511435	Dominated
	Triennial endoscopic screening	2227.9	297.3	11.593134	- 0.505152	Dominated
	Biennial endoscopic screening	2384.7	454.1	11.595861	- 0.502424	Dominated
	Annual endoscopic screening	3327.5	1396.9	11.604044	- 0.494241	Dominated
80	HP eradication strategy	1370.8	_	7.672079	_	_
	No screening	1381.1	10.3	7.332737	- 0.339342	Dominated
	Triennial endoscopic screening	1531.5	160.7	7.336227	- 0.335852	Dominated
	Biennial endoscopic screening	1630.1	259.3	7.337524	- 0.334555	Dominated
	Annual endoscopic screening	2227.4	856.6	7.341456	- 0.330623	Dominated

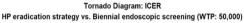
HP Helicobacter pylori, ICER incremental cost-effectiveness ratio, QALY quality-adjusted life-year; dominated, less effective and more costly than others

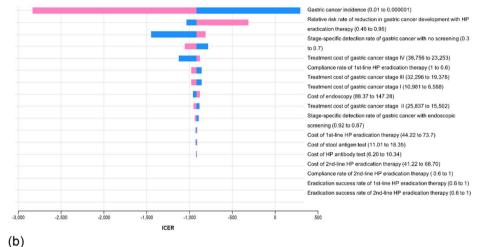
for patients with mild-to-moderate gastric mucosal atrophy and annual endoscopy for patients with severe gastric mucosal atrophy appear to be cost-effective after successful HP eradication [8]. Further epidemiologic studies on gastric mucosal atrophy after successful HP eradication therapy are needed. Finally, there are differences in costs, HP infection rates, epidemiological parameters, and healthcare systems among countries. Further cost-effectiveness studies based on country-specific variations are needed. In conclusion, HP eradication strategy provides greater health benefits with more significant cost savings than endoscopic screening at any interval and is absolutely recommended as a national gastric cancer screening program in Japan. The findings positively support the introduction of a population-based HP eradication strategy for primary prevention of gastric cancer instead of the current secondary prevention-oriented gastric cancer screening by endoscopy in high-incidence countries. Policy makers, physicians, and

Fig. 2 One-way, two-way and probabilistic sensitivity analyses. a The ICER tornado diagram for HP eradication strategy versus no screening in 20-year-old individuals. b The ICER tornado diagram for HP eradication strategy versus biennial endoscopic screening in 50-year-old individuals. c Two-way sensitivity analysis plot for age baseline versus HP infection rate in the 20 s to 40 s age groups. Colors represent the different strategies for the combination of the 2 parameters at a WTP threshold of US\$50,000 per QALY gained based on the net monetary benefit. d Two-way sensitivity analysis plot for age baseline versus HP infection rate in the 50 s to 80 s age groups. e Cost-effectiveness acceptability curve. ICER incremental cost-effectiveness ratio, HP Helicobacter pylori, QALY quality-adjusted life-year, WTP willingness-to-pay

Tornado Diagram: ICER HP eradication strategy vs. No screening (WTP: 50,000)







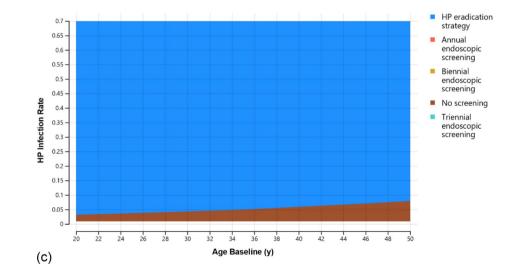


Fig. 2 (continued)

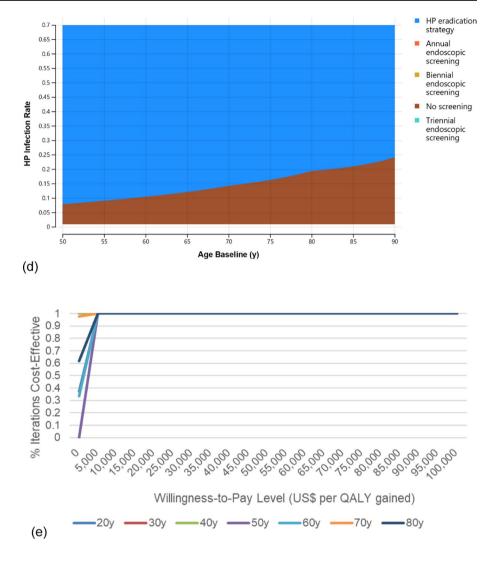


Table 3 Cumulative lifetime economic and health impacts of HP eradication strategy compared with the current gastric cancer screening program

Age group, years	Population	Cost savings, US\$	QALY gain, QALYs	Gastric cancer cases prevented	Gastric cancer-associ- ated deaths prevented
20	12,580,000	- 17,754,916	727,395	136,266	6,221
30	13,750,000	910,377,099	2,876,368	354,081	16,077
40	17,590,000	3,159,596,766	6,068,843	735,676	33,219
50	17,270,000	7,133,337,630	7,779,266	919,014	72,887
60	15,060,000	6,957,723,353	8,261,994	1,015,711	81,451
70	16,360,000	7,428,998,931	8,219,659	991,409	81,772
80	9,630,000	2,497,330,429	3,221,765	322,089	28,243
Total	102,240,000	28,069,609,293	37,155,290	4,474,246	319,870

We calculated age-specific cumulative lifetime economic and health impacts of HP eradication strategy compared to no screening for individuals aged 20 to 49 years and biennial endoscopic screening for individuals aged 50 to 89 years. *HP Helicobacter pylori*, *QALY* quality-adjusted life-year

their respective governments should promote populationbased HP eradication strategies as national gastric cancer policies to reduce gastric cancer morbidity and mortality in high-incidence countries.

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Declarations

Conflict of interest The author has no conflicts of interest to declare.

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References

- Hooi JKY, Lai WY, Ng WK et al. Global prevalence of *Helicobacter pylori* infection: systematic review and meta-analysis. *Gastroenterology* 2017;153:420–429.
- de Martel C, Georges D, Bray F, Ferlay J, Clifford GM. Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. *Lancet Glob Health*. 2020;8:e180–e190.
- World Cancer Research Fund International. Stomach cancer statistics. https://www.wcrf.org/cancer-trends/stomach-cancer-stati stics/. Accessed 5 December, 2022.
- Fukase K, Kato M, Kikuchi S et al. Effect of eradication of *Heli-cobacter pylori* on incidence of metachronous gastric carcinoma after endoscopic resection of early gastric cancer: an open-label, randomised controlled trial. *Lancet* 2008;372:392–397.
- Choi IJ, Kook MC, Kim YI et al. *Helicobacter pylori* therapy for the prevention of metachronous gastric cancer. *N Engl J Med.* 2018;378:1085–1095.
- 6. Ford AC, Yuan Y, Moayyedi P. *Helicobacter pylori* eradication therapy to prevent gastric cancer: systematic review and meta-analysis. *Gut.* 2020;69:2113–2121.
- Asaka M, Kato M, Sakamoto N. Roadmap to eliminate gastric cancer with *Helicobacter pylori* eradication and consecutive surveillance in Japan. *J Gastroenterol*. 2014;49:1–8.
- Kowada A. Endoscopy Is Cost-Effective for Gastric Cancer Screening After Successful *Helicobacter pylori* Eradication. *Dig Dis Sci.* 2021;66:4220–4226.
- IARC Helicobacter pylori Working Group. *Helicobacter pylori* eradication as a strategy for preventing gastric cancer. Lyon, France: International Agency for Research on Cancer (IARC Working Group Reports, No. 8). https://publications.iarc.fr/Book-And-Report-Series/Iarc-Working-Group-Reports/-Em-Helicobact er-Pylori-Em-Eradication-As-A-Strategy-For-Preventing-Gastric-Cancer-2014 Accessed 5 December, 2022.

- 1745
- Liou JM, Malfertheiner P, Lee YC et al. Screening and eradication of *Helicobacter pylori* for gastric cancer prevention: the Taipei global consensus. *Gut.* 2020;69:2093–2112.
- 11. Matsuo T, Ito M, Takata S et al. Low prevalence of *Helicobacter pylori*-negative gastric cancer among Japanese. *Helicobacter*. 2011;16:415–419.
- Sato C, Hirasawa K, Tateishi Y et al. Clinicopathological features of early gastric cancers arising in *Helicobacter pylori* uninfected patients. *World J Gastroenterol*. 2020;26:2618–2631.
- Yamada A, Kaise M, Inoshita N et al. Characterization of *Helicobacter pylori*-Naïve early gastric cancers. *Digestion*. 2018;98:127–134.
- Mizutani T, Araki H, Saigo C et al. Endoscopic and pathological characteristics of *Helicobacter pylori* infection-negative early gastric cancer. *Dig Dis.* 2020;38:474–483.
- Hamashima C; Systematic Review Group and Guideline Development Group for Gastric Cancer Screening Guidelines. Update version of the Japanese Guidelines for Gastric Cancer Screening. *Jpn J Clin Oncol.* 2018; 48:673–683.
- Kato M, Ota H, Okuda M, et al. Guidelines for the management of *Helicobacter pylori* infection in Japan: 2016 Revised Edition. *Helicobacter*. 2019; 24:e12597.
- Asaka M, Kobayashi M, Kudo T et al. Gastric cancer deaths by age group in Japan: outlook on preventive measures for elderly adults. *Cancer Sci.* 2020;111:3845–3853.
- Asaka M. A new approach for elimination of gastric cancer deaths in Japan. *Int J Cancer*. 2013;132:1272–1276.
- Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4). *Gastric Cancer*. 2017; 20:1–19.
- Yuan Y, Ford AC, Khan KJ et al. Optimum duration of regimens for Helicobacter pylori eradication. *Cochrane Database Syst Rev.* 2013;12:8337.
- Ministry of Health, Labour, and Welfare. Pref Cancer Screening Rate 2019. National Life Foundation Survey. https://www.mhlw. go.jp/toukei/saikin/hw/k-tyosa/k-tyosa19/dl/04.pdf. Accessed 5 December, 2022. [Japanese]
- Cancer Information Service, National Cancer Center, Japan. Cancer Registry and Statistics. https://ganjoho.jp/reg_stat/statistics/ stat/summary.html Accessed 5 December, 2022. [Japanese]
- 23. Wang C, Nishiyama T, Kikuchi S et al. Changing trends in the prevalence of H pylori infection in Japan (1908–2003): a systematic review and meta-regression analysis of 170,752 individuals. *Sci. Rep.* 2017;7:15491.
- 24. Mori H, Suzuki H, Omata F et al. Current status of first- and second-line *Helicobacter pylori* eradication therapy in the metropolitan area: a multicenter study with a large number of patients. *Ther Adv Gastroenterol.* 2019;12:1756284819858511.
- Hamashima C, Okamoto M, Shabana M et al. Sensitivity of endoscopic screening for gastric cancer by the incidence method. *Int J Cancer*. 2013;133:653–659.
- Lee HJ, Ock M, Kim KP et al. Estimation of population-based utility weights for gastric cancer-related health states. *Patient Prefer Adherence*. 2018;12:909–918.
- Kyushu University Hospital Gastric Cancer Registration Information. https://www.gan.med.kyushu-u.ac.jp/result/gastric_cancer/ index9. Accessed 5 December, 2022. [Japanese]
- Kusano C, Gotoda T, Ikehara H et al. The accuracy of the serum antibody test for *Helicobacter pylori* infection among junior high school students. *Digestion*. 2021;102:155–160.
- Ministry of Health, Labour and Welfare. Vital Statistics. https:// www.mhlw.go.jp/toukei/list/81-1a.html Accessed 5 December, 2022. [Japanese]
- Igakutsushin-sya. National fee schedule and Medical insurance reimbursement table in Japan. Tokyo: *Igakutsushin-sya*, Japan, 2020. [Japanese]

- PPPs (Purchasing Power Parities) and exchange rates [Organisation for Economic Co-operation and Development (OECD)Web site]. https://data.oecd.org/conversion/purchasing-power-paritiesppp.htm. Accessed 25 July 2022.
- 32. Sanders GD, Neumann PJ, Basu A et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. *JAMA* 2016;316:1093–1103.
- 33. World Health Organization, Baltussen, Rob M. P. M, Adam, Taghreed, Tan-Torres Edejer, Tessa, Hutubessy, Raymond C. W. et al. (2003). Making choices in health: WHO guide to cost-effectiveness analysis. https://apps.who.int/iris/handle/10665/42699. Accessed 5 December, 2022.
- 34. Ministry of Health, Labor and Welfare. Establishment of reference values for cost-effectiveness evaluation. 2018. https://www.mhlw.go.jp/file/05-Shingikai-12404000-Hokenkyoku-Iryouka/0000211609.pdf (Japanese) Accessed 5 December, 2022.
- Statistics Bureau of Japan. Population Estimates Monthly Report. May 1, 2022 (Provisional estimates). https://www.stat.go.jp/engli sh/data/jinsui/2.html. Accessed 5 December 2022.
- Kowada A. Cost-effectiveness of *Helicobacter pylori* screening followed by eradication treatment for employees in Japan. *Epidemiol Infect.* 2018;146:1834–1840.
- Kowada A, Asaka M. Economic and health impacts of introducing *Helicobacter pylori* eradication strategy into national gastric cancer policy in Japan: a cost-effectiveness analysis. *Helicobacter*. 2021;26:e12837.

- 38. Kowada A. Cost-effectiveness of *Helicobacter pylori* test and eradication versus upper gastrointestinal series versus endoscopy for gastric cancer mortality and outcomes in high prevalence countries. *Scand J Gastroenterol.* 2019;54:685–689.
- Kowada A, Asaka M. Economic and health impacts of *Helicobacter pylori* eradication strategy for the treatment of peptic ulcer disease: a cost-effectiveness analysis. *Helicobacter*. 2022;27:e12886.
- Shah SC, Canakis A, Peek RM Jr, Saumoy M. Endoscopy for gastric cancer screening is cost effective for Asian Americans in the United States. *Clin Gastroenterol Hepatol.* 2020;18:3026–3039.
- Ascherman B, Oh A, Hur C. International cost-effectiveness analysis evaluating endoscopic screening for gastric cancer for populations with low and high risk. *Gastric Cancer*. 2021;24:878–887.
- 42. Huang HL, Leung CY, Saito E et al. Effect and cost-effectiveness of national gastric cancer screening in Japan: a microsimulation modeling study. *BMC Med.* 2020;18:257.
- 43. Xie Y, Song C, Cheng H et al. Long-term follow-up of *Helicobac*ter pylori reinfection and its risk factors after initial eradication: a large-scale multicentre, prospective open cohort, observational study. *Emerg Microb Infect.* 2020;9:548–557.

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