

1 **Supplementary tables:**

2 **Table S1. Definitions of medication and diagnostic test costs for *Helicobacter pylori* eradication therapy.**

<b>Cost</b>	<b>Definition</b>
<b>First-line eradication therapy</b>	
Medication costs	Costs for acid-inhibitory medicines (P-CAB [vonoprazan] or PPI [esomeprazole, lansoprazole, omeprazole, or rabeprazole]) with two antibiotics (AMPC + CAM) for 7 consecutive days, or triple-drug blister packaged products for <i>H. pylori</i> first-line eradication therapy
Diagnostic test costs	Costs for evaluating <i>H. pylori</i> infection, whichever is closer to completion of first-line medication: the month after a prescription for first-line eradication therapy and the month starting a prescription for second-line eradication therapy, or within 6 months of a prescription for first-line eradication therapy
<b>Second-line eradication therapy</b>	
Medication costs	Costs for acid-inhibitory medicines with AMPC and MNZ for 7 consecutive days, or triple-drug blister packaged products for <i>H. pylori</i> second-line eradication therapy prescribed in the months after first-line eradication therapy
Diagnostic test costs	Costs for evaluating <i>H. pylori</i> infection within 6 months of starting a prescription for second-line eradication therapy
<b>Medical fees</b>	
Subsequent visit fees	Uniformly added JPY 720 for subsequent visit fees across all patients in accordance with visits to medical institutes as defined below. The fees were not derived from the claims data (a 3rd subsequent visit fee was only added to patients who failed first-line eradication therapy) <ul style="list-style-type: none"> <li>• First-line eradication therapy</li> <li>• Diagnostic tests after first-line eradication therapy and starting second-line eradication therapy</li> <li>• Diagnostic tests after second-line eradication therapy</li> </ul>

3 **Abbreviations:** AMPC, amoxicillin; CAM, clarithromycin; JPY, Japanese yen; MNZ, metronidazole; P-CAB, potassium-competitive acid blocker; PPI, proton  
4 pump inhibitor.

5 **Table S2. Definition of medications for *Helicobacter pylori* eradication therapy.**

Classification		Definition	Health insurance codes <sup>a</sup> and/or name
<b>First-line eradication therapy</b>	Triple-drug blister packaged products	Having one of the medical action codes listed on the right	610462048 (LANSAP <sup>®</sup> 400)
			610462049 (LANSAP <sup>®</sup> 800)
			622289101 (Rabecure <sup>®</sup> pack 400)
			622289201 (Rabecure <sup>®</sup> pack 800)
			622485401 (VONOSAP <sup>®</sup> pack 400)
			622485501 (VONOSAP <sup>®</sup> pack 800)
	P-CAB/PPI, amoxicillin, and clarithromycin prescribed in one medical practitioner's receipt for a health insurance claim per patient	P-CAB	622404401 (Takecab <sup>®</sup> 10 mg tablet)
			622404501 (Takecab <sup>®</sup> 20 mg tablet)
		PPI	ATC codes: A2B2 (PPIs) <sup>b</sup>
		Amoxicillin (generic name)	Amoxicillin hydrate Amoxicillin hydrate/potassium clavulanate
Clarithromycin (generic name)	Clarithromycin		
<b>Second-line eradication therapy</b>	Triple-drug blister packaged products	Having one of the medical action codes listed on the right	622029101 (LAMPION <sup>®</sup> pack)
			622289301 (Rabefine <sup>®</sup> pack)
			622485601 (VONOPION <sup>®</sup> pack)
	P-CAB/PPI, amoxicillin, metronidazole prescribed in 1 medical practitioner's receipt for a health insurance claim per patient	Metronidazole (generic name)	Metronidazole

6 **Note:** <sup>a</sup>Referred to by the Medical Fee Information Service (<http://www.iryohoken.go.jp/shinryohoshu/>), LANSAP<sup>®</sup> interview form  
7 ([http://www.info.pmda.go.jp/go/pack/6199100X1025\\_1\\_29/](http://www.info.pmda.go.jp/go/pack/6199100X1025_1_29/)) and LAMPION<sup>®</sup> Pack interview form ([http://www.info.pmda.go.jp/go/pack/6199101X1020\\_1\\_16/](http://www.info.pmda.go.jp/go/pack/6199101X1020_1_16/)).

8 <sup>b</sup>Referred to by the European Pharmaceutical Market Research Association (<https://www.ephmra.org/classification/anatomical-classification/>).

9 **Abbreviations:** ATC, anatomical therapeutic chemical system; P-CAB, potassium-competitive acid blocker; PPI, proton pump inhibitor.

11 Table S3. Definition of diagnostic tests for *Helicobacter pylori* eradication therapy.

Diagnostic test name	Definition of cost calculation		Code of medical service fee <sup>a</sup>	Health insurance code <sup>a</sup>
	Definition of diagnostic test	Related-tests in a prescription		
Rapid urease test	Rapid urease test (qualitative)		D012	160172750
		Gastroduodenal endoscopy	D308	160093810
		Endoscopic biopsy	D414	160098210
		Immunological test diagnostic fee	D026	160062110
Direct microscopic count test	Preparation of histopathological tissue specimen		N000	160060010
		Gastroduodenal endoscopy	D308	160093810
		Endoscopic biopsy	D414	160098210
		Pathological diagnostic fee	N007	160062310
Microbial culture test	Identification by microbial culture (digestive tract)		D018	160058310
		Gastroduodenal endoscopy	D308	160093810
		Endoscopic biopsy	D414	160098210
		Pathological diagnostic fee	N007	160062310
		Microbiological test diagnostic fee	D026	160062210
Antibody measurement test	Antibody against <i>H. pylori</i> (qualitative, semi-quantitative) or Antibody against <i>H. pylori</i>		D012	160172450
		Venous blood collection	D400-00	160095710
		Immunological test diagnostic fee	D026	160062110
<sup>13</sup> C-Urea breath test	<sup>13</sup> C-Urea breath test		D023-02	160172850
		Microbiological test diagnostic fee	D026	160062210
		Diagnostic drug Pylonic <sup>®</sup> or Diagnostic drug Ubit <sup>®</sup> tablet 100 mg	ATC: T2X9 <sup>b</sup> ATC: T2X9 <sup>b</sup>	610462013 610462047
Stool antigen test	<i>H. pylori</i> antigen (qualitative)		D012	160175450
		Immunological test diagnostic fee	D026	160062110

12 **Note:** A diagnostic test was defined as a test that was included on a health insurance claim using one of the codes listed above. Diagnostic test costs were  
13 the sum of costs for defined diagnostic tests and defined related tests. <sup>a</sup>Referred to by the Medical Fee Information Service  
14 (<http://www.iryohoken.go.jp/shinryohoshu/>). <sup>b</sup>Referred to by the European Pharmaceutical Market Research Association  
15 (<https://www.ephmra.org/classification/anatomical-classification/>).

16 **Abbreviations:** ATC, anatomical therapeutic chemical system.  
17

18 **Table S4. Characteristics of patients treated with P-CAB + CAM 400 mg/day or P-CAB + CAM 800 mg/day, before and after propensity score**  
 19 **matching.**

Item	Unmatched			Matched		
	P-CAB + CAM 400 mg (n=35,625)	P-CAB + CAM 800 mg (n=14,771)	p-value <sup>a</sup>	P-CAB + CAM 400 mg (n=14,769)	P-CAB + CAM 800 mg (n=14,769)	p-value <sup>a</sup>
<b>Age, mean (years) ± SD</b>	51.0±10.2	50.5±10.0	<0.0001	50.5±10.0	50.5±10.0	0.893
<b>Male (%)</b>	20,377 (57.2%)	9,000 (60.9%)	<0.0001	8,997 (60.9%)	8,998 (60.9%)	0.991
<b>Indication, n (%)<sup>b</sup></b>						
<b>Gastritis</b>	12,732 (35.7%)	5,931 (40.2%)	<0.0001	5,927 (40.1%)	5,929 (40.1%)	0.981
<b>Peptic ulcer</b>	8,996 (25.3%)	3,986 (27%)	<0.0001	3,990 (27.0%)	3,986 (27.0%)	0.958
<b>Stomach Cancer</b>	191 (0.5%)	64 (0.4%)	0.139	48 (0.3%)	64 (0.4%)	0.130
<b>Idiopathic thrombocytopenic purpura</b>	30 (0.1%)	20 (0.1%)	0.097	13 (0.1%)	18 (0.1%)	0.369
<b>Gastric MALT lymphoma</b>	25 (0.1%)	3 (0%)	0.031	3 (0.0%)	3 (0.0%)	1.000
<b>GERD, n (%)</b>	7,116 (20%)	3,273 (22.2%)	<0.0001	3,027 (20.5%)	3,273 (22.2%)	0.001
<b>Triple-drug blister pack, n (%)</b>	18,942 (53.2%)	6,521 (44.1%)	<0.0001	7,981 (54.0%)	6,520 (44.1%)	<0.0001
<b>Patients in primary care, n (%)</b>	23,102 (64.9%)	8,972 (60.8%)	<0.0001	9,661 (65.5%)	8,971 (60.8%)	<0.0001

20 **Note:** <sup>a</sup>p-value P-CAB + CAM 400 mg vs. P-CAB + CAM 800 mg. <sup>b</sup>Indications, based on insurance name of disease, are totals including duplicates diagnosed  
 21 up to 6 months before the first eradication treatment. Since there are possible indications other than those listed, the total will not be 100%.

22 **Abbreviations:** CAM, clarithromycin; GP, general practitioner; GERD, gastroesophageal reflux disease; JPY, Japanese yen; MALT, mucosa-associated  
 23 lymphoid tissue; P-CAB, potassium-competitive acid blocker; SD, standard deviation.

24

25 **Table S5. Characteristics of patients treated with PPI + CAM 400 mg/day or PPI + CAM 800 mg/day, before and after propensity score matching.**

Item	Unmatched			Matched		
	PPI + CAM 400 mg (n=14,211)	PPI + CAM 800 mg (n=7,794)	p-value <sup>a</sup>	PPI + CAM 400 mg (n=7,794)	PPI + CAM 800 mg (n=7,794)	p-value <sup>a</sup>
<b>Age, mean (years) ± SD</b>	51.8±10.1	51.3±10.0	0.0004	51.4±10.0	51.3±10.0	0.883
<b>Male, n (%)</b>	8,002 (56.3%)	4,622 (59.3%)	<0.0001	4,647 (59.6%)	4,622 (59.3%)	0.683
<b>Indication, n (%)<sup>b</sup></b>						
<b>Gastritis</b>	4,238 (29.8%)	2,485 (31.9%)	0.002	2,484 (31.9%)	2,485 (31.9%)	0.986
<b>Peptic ulcer</b>	4,193 (29.5%)	2,446 (31.4%)	0.004	2,439 (31.3%)	2,446 (31.4%)	0.904
<b>Stomach Cancer</b>	81 (0.6%)	16 (0.2%)	<0.0001	16 (0.2%)	16 (0.2%)	1.000
<b>Idiopathic thrombocytopenic purpura</b>	24 (0.2%)	14 (0.2%)	0.854	3 (0.0%)	14 (0.2%)	0.008
<b>Gastric MALT lymphoma</b>	4 (0.0%)	3 (0.0%)	0.681	2 (0.0%)	3 (0.0%)	0.655
<b>GERD, n (%)</b>	2,980 (21.0%)	1,823 (23.4%)	<0.0001	1,656 (21.2%)	1,823 (23.4%)	0.001
<b>Triple-drug blister pack, n (%)</b>	10,973 (77.2%)	5,798 (74.4%)	<0.0001	5,979 (76.7%)	5,798 (74.4%)	0.001
<b>Patients in primary care, n (%)</b>	9,149 (64.9%)	5,019 (64.6%)	0.724	5,049 (65.3%)	5,019 (64.6%)	0.375

26 **Note:** <sup>a</sup>p-value PPI + CAM 400 mg vs. PPI + CAM 800 mg. <sup>b</sup>Indications, based on insurance name of disease, are totals including duplicates diagnosed up to  
27 6 months before the first eradication treatment. Since there are possible indications other than those listed, the total will not be 100%.

28 **Abbreviations:** CAM, clarithromycin; GP, general practitioner; GERD, gastroesophageal reflux disease; JPY, Japanese yen; MALT, mucosa-associated  
29 lymphoid tissue; PPI, proton pump inhibitor; SD, standard deviation.

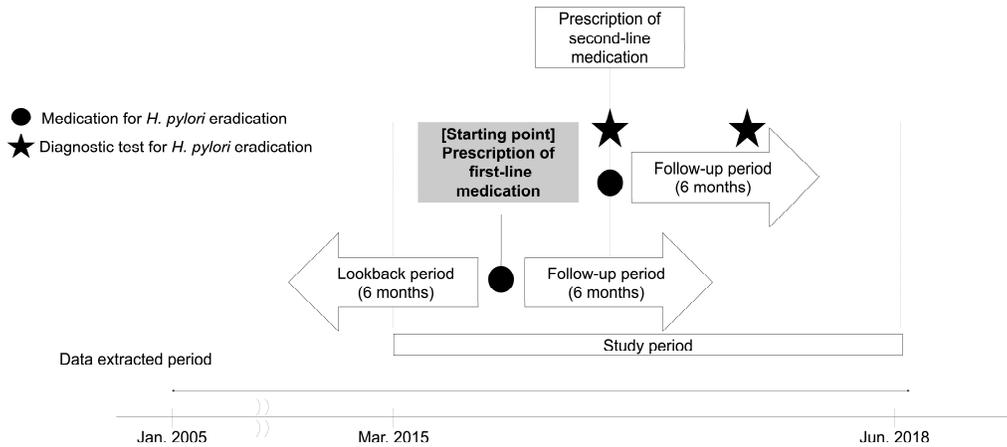
31 **Table S6. Characteristics of patients treated with P-CAB + CAM 400 mg/day or PPI + CAM 400 mg/day, before and after propensity score matching.**

Item	Unmatched			Matched		
	P-CAB + CAM 400 mg (n=35,625)	PPI + CAM 400 mg (n=14,211)	p-value <sup>a</sup>	P-CAB + CAM 400 mg (n=14,206)	PPI + CAM 400 mg (n=14,206)	p-value <sup>a</sup>
<b>Age, mean (years) ± SD</b>	51±10.2	51.8±10.1	<0.0001	51.8±10.1	51.8±10.1	0.966
<b>Male (%)</b>	20,377 (57.2%)	8,002 (56.3%)	0.070	7,998 (56.3%)	8,000 (56.3%)	0.981
<b>Indication, n (%)<sup>b</sup></b>						
<b>Gastritis</b>	12,732 (35.7%)	4,238 (29.8%)	<0.0001	4,259 (30%)	4,238 (29.8%)	0.786
<b>Peptic ulcer</b>	8,996 (25.3%)	4,193 (29.5%)	<0.0001	4,206 (29.6%)	4,193 (29.5%)	0.866
<b>Stomach Cancer</b>	191 (0.5%)	81 (0.6%)	0.643	52 (0.4%)	81 (0.6%)	0.012
<b>Idiopathic thrombocytopenic purpura</b>	30 (0.1%)	24 (0.2%)	0.010	19 (0.1%)	19 (0.1%)	1.000
<b>Gastric MALT lymphoma</b>	25 (0.1%)	4 (0%)	0.079	4 (0%)	4 (0%)	1.000
<b>GERD</b>	7,116 (20%)	2,980 (21%)	0.013	2,951 (20.8%)	2,980 (21%)	0.672
<b>Triple-drug blister pack</b>	18,942 (53.2%)	10,973 (77.2%)	<0.0001	7,466 (52.6%)	10,971 (77.2%)	<0.0001
<b>Patients in primary care, n (%)</b>	23,102 (64.9%)	9,149 (64.9%)	0.921	9,159 (64.5%)	9,147 (64.9%)	0.565

32 **Note:** <sup>a</sup>p-value P-CAB CAM 400 mg vs. PPI CAM 400 mg. <sup>b</sup>Indications, based on insurance name of disease, are totals including duplicates diagnosed up to 6  
33 months before the first eradication treatment. Since there are possible indications other than those listed, the total will not be 100%.

34 **Abbreviations:** CAM, clarithromycin; GP, general practitioner; GERD, gastroesophageal reflux disease; JPY, Japanese yen; MALT, mucosa-associated  
35 lymphoid tissue; P-CAB, potassium-competitive acid blocker; PPI, proton pump inhibitor; SD, standard deviation.

36 **Supplementary figures:**



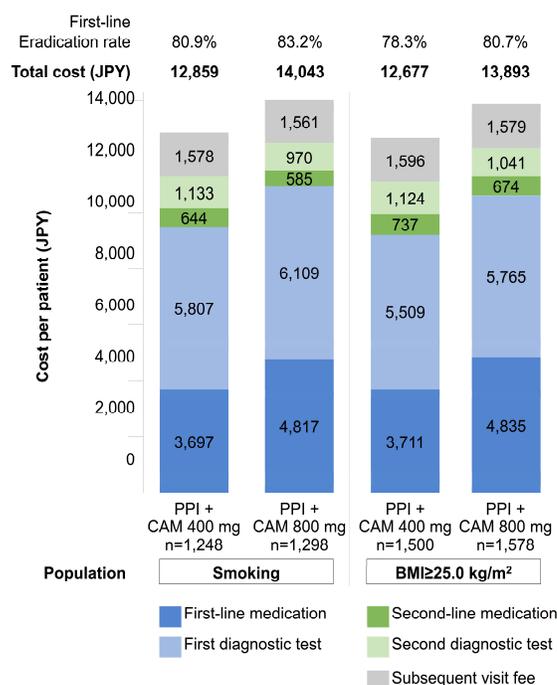
37

38 **Figure S1. Definitions of study period and successful first-line eradication therapy.**

39 This analysis included patients who were prescribed medication for *H. pylori* first-line eradication  
40 therapy from March 2015 to June 2018. Successful first-line eradication therapy was defined as  
41 patients who completed any diagnostic tests within 6 months after a prescription for first-line  
42 eradication medication and who had not been prescribed any medications for second-line eradication  
43 therapy.

44 **Abbreviations:** ICD, International Classification of Diseases; P-CAB, potassium-competitive acid  
45 blocker; PPI, proton pump inhibitor.

46



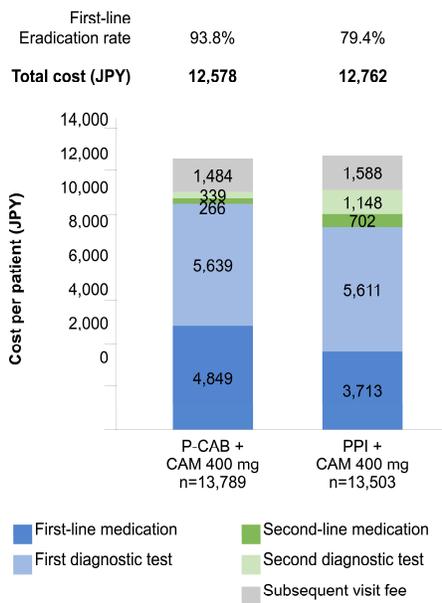
47

48 **Figure S2. Total costs for *Helicobacter pylori* eradication therapy per patient between CAM 400**  
 49 **mg/day and 800 mg/day in PPI-treated patients with smoking habit or overweight/obese.**

50 Total costs are presented as mean values per patient.

51 **Abbreviations:** BMI, body mass index; CAM, clarithromycin; JPY, Japanese yen; PPI, proton pump  
 52 inhibitor.

53



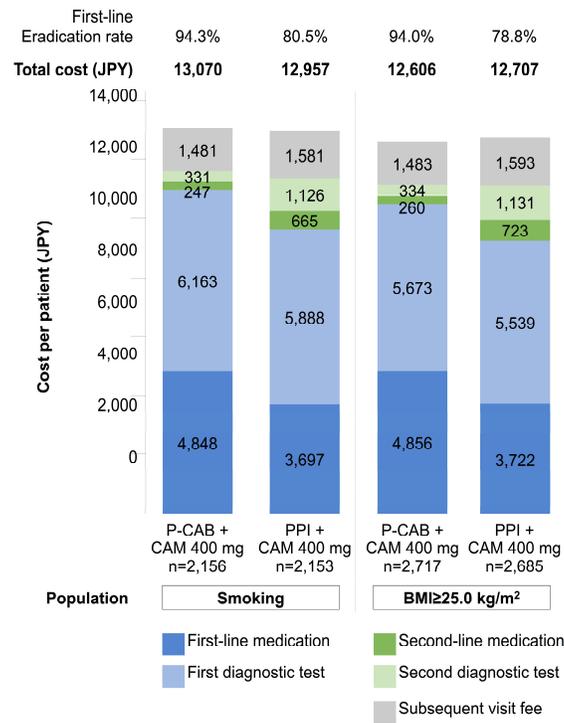
54

55 **Figure S3. Total costs for *Helicobacter pylori* eradication therapy between the P-CAB + CAM**  
 56 **400 mg/day and PPI + CAM 400 mg/day regimens.**

57 Total costs are presented as mean values per patient.

58 **Abbreviations:** CAM, clarithromycin; JPY, Japanese yen; P-CAB, potassium-competitive acid  
 59 blocker; PPI, proton pump inhibitor.

60



61

62 **Figure S4. Total costs for *Helicobacter pylori* eradication therapy per patient between P-CAB +**  
 63 **CAM 400 mg/day and PPI + CAM 400 mg/day-treated patients with smoking habit or**  
 64 **overweight/obese.**

65 Total costs are presented as mean values per patient.

66 **Abbreviations:** BMI, body mass index; CAM, clarithromycin JPY, Japanese yen; P-CAB, potassium-  
 67 competitive acid blocker; PPI, proton pump inhibitor.

68