Evidence-Based Guidelines for the Diagnosis and Treatment of Helicobacter pylori Infection in Korea: 2025 Revised Edition

Key change

1) A dual-pillar strategy of tailored therapy and empirical quadruple therapy (← multiple empirical regimens)

2) Restricted use of empirical clarithromycin-based triple therapy under specific conditions

3) Removal of sequential therapy (ST) and PAM

4) Use of P-CABs as alternatives to proton pump inhibitors

5) Expansion of eradication indications to include gastric cancer prevention in *H. pylori* gastritis and regression of hyperplastic polyps ≤10 mm

6) Positioning of bismuth quadruple therapy as a conditionally recommended first-line empirical option, with preference for reservation as salvage therapy, and introduction of modified bismuth quadruple therapy (addition of bismuth to conventional regimens) as an additional first-line empirical option.

Treatment algorithm (2020)

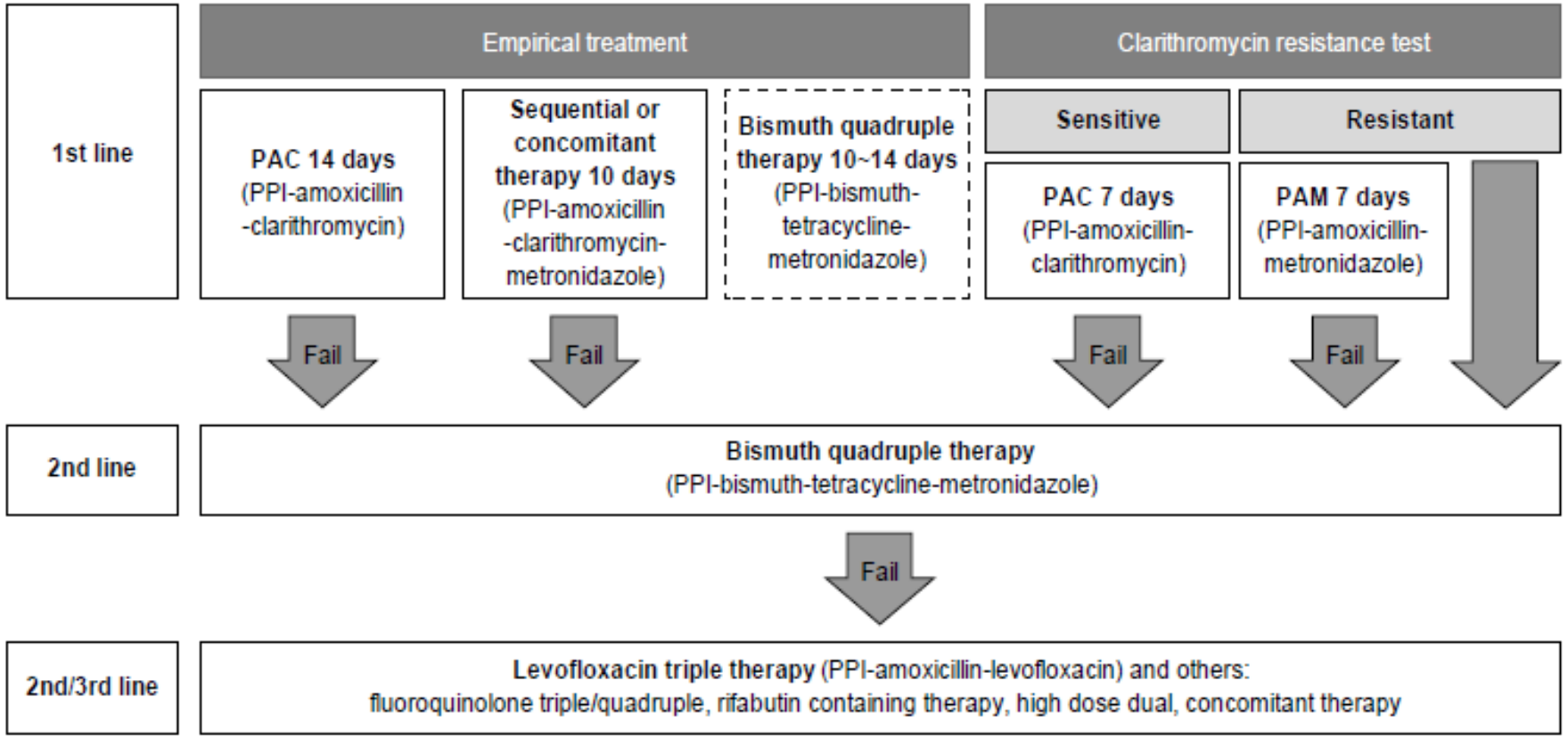
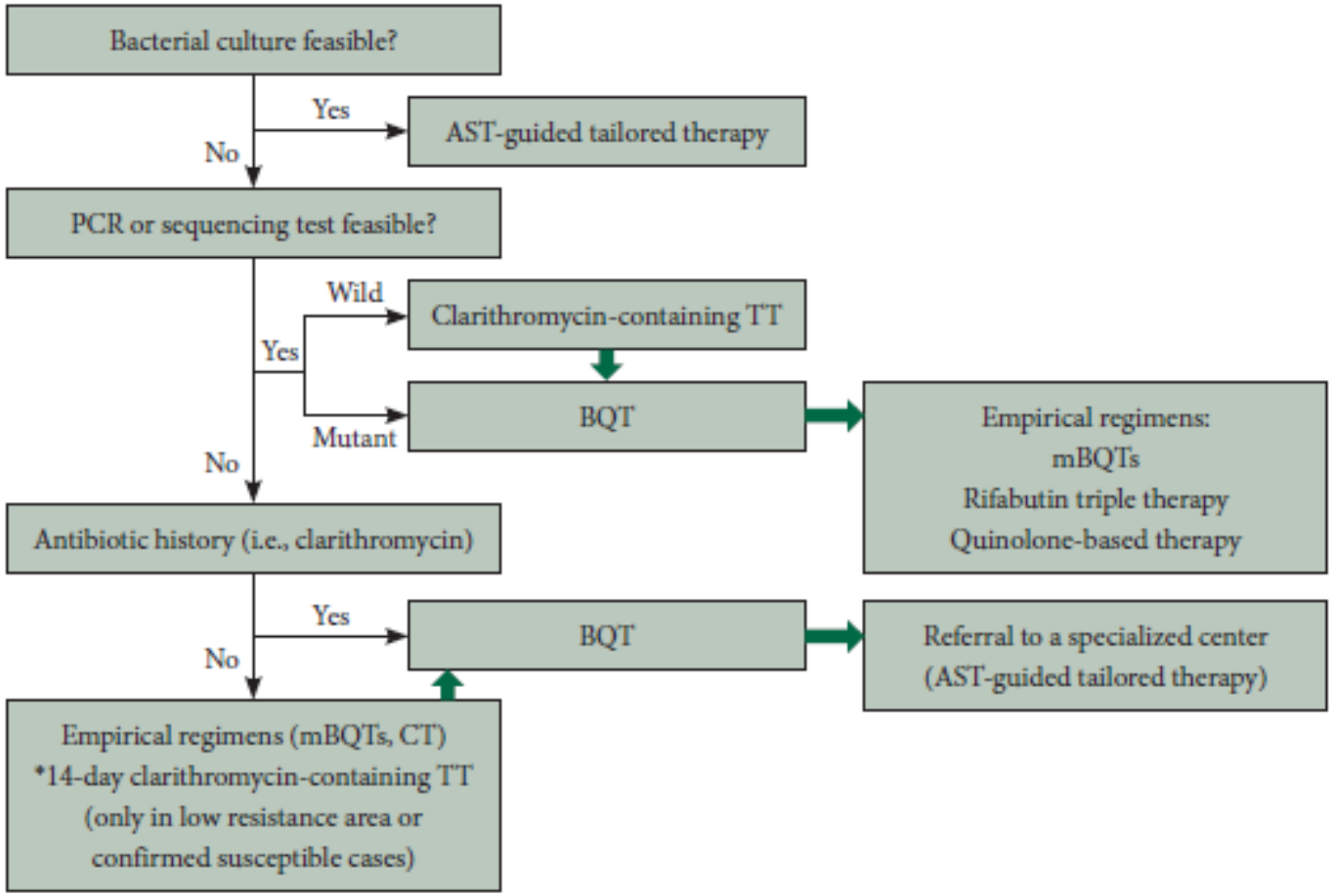


Fig. 10. Proposed algorithm for the treatment of *Helicobacter pylori* infection. Bismuth quadruple therapy as a first-line therapy is dotted because it is less preferred than other regimens. PPI, proton pump inhibitor.

Treatment algorithm (2025 Revised Edition)



Treatment medication (2025 Revised Edition)

Table 6. Summary of recommended first-line, second-line, and third-line *H. pylori* treatments in the 2025 guidelines

Treatment line	Approach	Regimen components	Duration (day)	Key restrictions/considerations
First-line	Tailored (PCR-guided)	C-susceptible: PPI/P-CAB+A+C	14	Requires PCR/AST confirmation of susceptibility
		C-resistant: BQT (PPI/P-CAB+B+M+T)	10–14	Recommended precision approach; ITT ≥90%
First-line	Empirical	CT: PPI/P-CAB+A+M+C	10	Stewardship concern (3 antibiotics); reserve for high resistance risk
		BQT: PPI/P-CAB+B+M+T	10–14	Tetracycline availability/tolerability issues possible
		mBQT-PACB: PPI/P-CAB+A+C+B	14	Efficacy reduced in high-level clarithromycin resistance
		mBQT-PAMB: PPI/P-CAB+A+M+B	14	Preferred mBQT; bypasses clarithromycin resistance
Second-line	Empirical	BQT: PPI/P-CAB+B+M+T	10–14	Standard salvage; metronidazole resistance overcome by higher dose/duration
		Alternative: PAMB (PPI/P-CAB+A+M+B)	14	If tetracycline unavailable or not tolerated
Third-line	Empirical/ AST-guided	Rifabutin TT: PPI/P-CAB+A+rifabutin	10–14	Low resistance (0.8%); monitor for myelotoxicity; Tbc resistance concern
		mBQT with unused antibiotics: PPI/P-CAB+B+(A or L)+ (unused antibiotics)	14	Avoid previously used antibiotics except A/M
		Levofloxacin TT: PPI/P-CAB+A+L	10–14	Limited use; resistance 36%–43%; only if susceptible or no prior fluoroquinolone exposure
	AST-guided	Susceptibility-guided regimen	Per AST	Strongly recommended; referral to specialised centre; ITT ≥80%–90%

PCR, polymerase chain reaction; PPI, proton pump inhibitor; P-CAB, potassium-competitive acid blocker; PACB, PPI+amoxicillin+clarithromycin+bismuth; PAMB, PPI+amoxicillin+metronidazole+bismuth; TT, triple therapy; BQT, bismuth-quadruple therapy; mBQT, modified BQT; CT, concomitant therapy; AST, antibiotic susceptibility test; ITT, intention-to-treat; A, amoxicillin; C, clarithromycin; B, bismuth; M, metronidazole; T, tetracycline; L, levofloxacin.

Table 5. Comparison of the main components between the 2025 and 2020 guidelines

Category	2020 guideline	2025 guideline
Treatment philosophy	Multiple empirical regimen choices (TT, BQT, ST, CT)	Dual-pillar strategy: precision (PCR-guided)+pragmatic empirical quadruple therapy
Tailored therapy (PCR-based)	Mentioned as optional approach	Primary recommended strategy; core pillar of dual-pillar framework
Clarithromycin-containing TT	Primary empirical first-line (14 days recommended over 7 days)	Not recommended empirically; only with confirmed clarithromycin susceptibility (tailored therapy)
Sequential therapy	Recommended first-line option	Excluded (poor adherence, salvage selection difficulty, inferior to CT/BQT)
Metronidazole TT (PAM)	Alternative for clarithromycin-resistant strains (7 days)	Not recommended (high metronidazole resistance 29.5%; may compromise future BQT efficacy)
CT	Recommended first-line option (10 days)	Effective empirical option (10–14 days); stewardship concerns noted
Bismuth-based regimens	BQT as first-line alternative	Emphasised: BQT+new mBQTs (PACB, PAMB) as preferred empirical options
Acid suppressant	PPI-based regimens	P-CAB formally incorporated as alternative/preferred option
Second-line therapy (salvage)	BQT (10–14 days)	BQT reaffirmed; PAMB as alternative if tetracycline unavailable
Third-line therapy	Limited guidance (levofloxacin TT)	Clarified algorithm: rifabutin TT, mBQTs with unused antibiotics, levofloxacin TT (limited); AST-guided therapy strongly recommended
Gastric cancer prevention indication	Atrophic gastritis/intestinal metaplasia did not reach expert consensus	*H. pylori* gastritis patients: eradication suggested for gastric cancer prevention (weak; moderate)
Hyperplastic polyps	Not included	Eradication suggested for hyperplastic polyps ≤10 mm (weak; low)

PCR, polymerase chain reaction; PPI, proton pump inhibitor; P-CAB, potassium-competitive acid blocker; PAM, PPI+amoxicillin+metronidazole; PACB, PPI+amoxicillin+clarithromycin+bismuth; PAMB, PPI+amoxicillin+metronidazole+bismuth; TT, triple therapy; BQT, bismuth-quadruple therapy; mBQT, modified BQT; CT, concomitant therapy; ST, sequential therapy; AST, antibiotic susceptibility testing.

Summary of recommendations

- **Statement 4**
- Tailored therapy based on clarithromycin resistance testing (antibiotic susceptibility testing) is recommended as first-line eradication therapy for *H. pylori* infection.

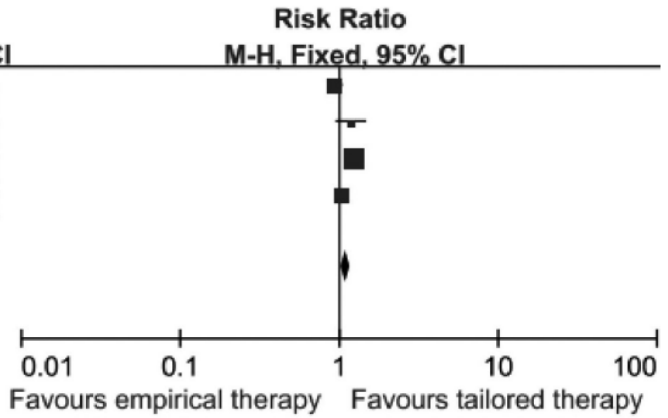
- Based on clarithromycin resistance testing, 10-day BQT is recommended for resistant strains, and 7-day clarithromycin-based triple therapy for susceptible strains.

Statement 4

Study or Subgroup	Tailored therapy Events	Total	Empirical therapy Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cho JH 2022	114	141	121	141	26.2%	0.94 [0.85, 1.05]
Kim JL 2020	32	36	27	36	5.8%	1.19 [0.95, 1.48]
Kim JS 2024	235	287	201	306	42.1%	1.25 [1.13, 1.37]
Kim SJ 2022	124	145	120	145	25.9%	1.03 [0.93, 1.14]
Total (95% CI)		**609**		**628**	**100.0%**	**1.11 [1.05, 1.17]**
Total events	505		469			

Heterogeneity: Chi² = 17.05, df = 3 (P = 0.0007); I² = 82%

Test for overall effect: Z = 3.48 (P = 0.0005)

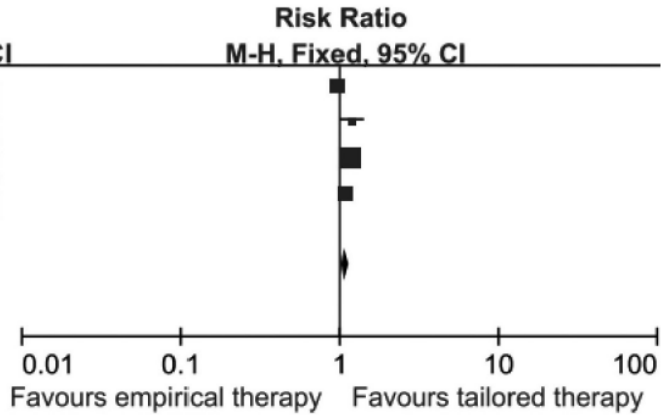


A

Study or Subgroup	Tailored therapy Events	Total	Empirical therapy Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cho JH 2022	113	127	116	124	25.3%	0.95 [0.88, 1.03]
Kim JL 2020	32	33	27	33	5.8%	1.19 [1.00, 1.41]
Kim JS 2024	235	274	201	268	43.9%	1.14 [1.05, 1.24]
Kim SJ 2022	122	129	117	132	25.0%	1.07 [0.99, 1.15]
Total (95% CI)		**563**		**557**	**100.0%**	**1.08 [1.03, 1.13]**
Total events	502		461			

Heterogeneity: Chi² = 13.37, df = 3 (P = 0.004); I² = 78%

Test for overall effect: Z = 3.12 (P = 0.002)



B

Statement 4

- The eradication rates of clarithromycin-based TT have continuously decreased.
  - From 2007 to 2016 : 71.6% ~ 79.6%
  - Post-2018 : 66.9% ~ 76.2%

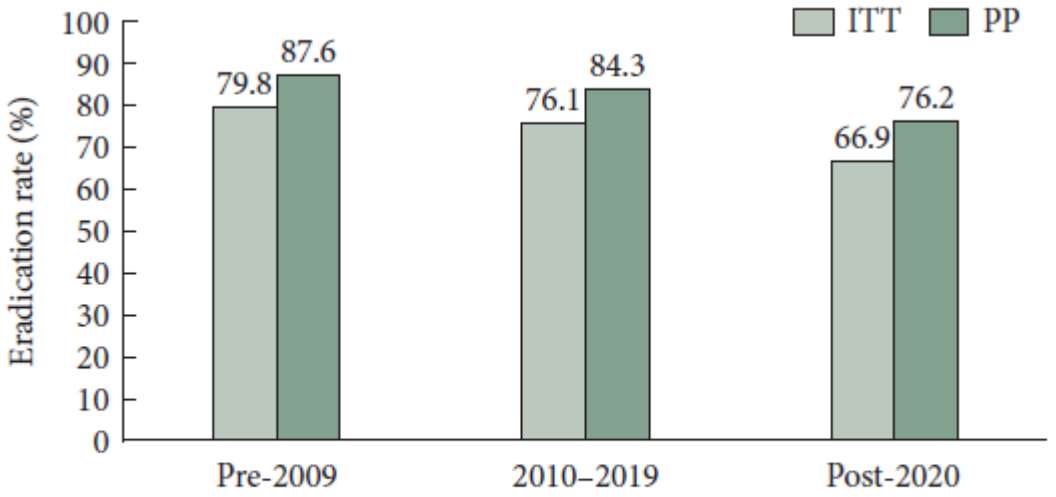


Fig. 7. *H. pylori* eradication rates with 14-day standard triple therapy by study period (Korean randomized controlled trials). ITT, intention-to-treat analysis; PP, per-protocol analysis.

Statement 4

- Dual resistance to clarithromycin and metronidazole : 9.2% → 37.9%
- Dual resistance to clarithromycin and quinolone : 2.8% → 41.7%
- Triple resistance (clarithromycin, MTZ, quinolone) : 1.4% → 28.2%
- Levofloxacin resistance : 7.3% → 35.7%

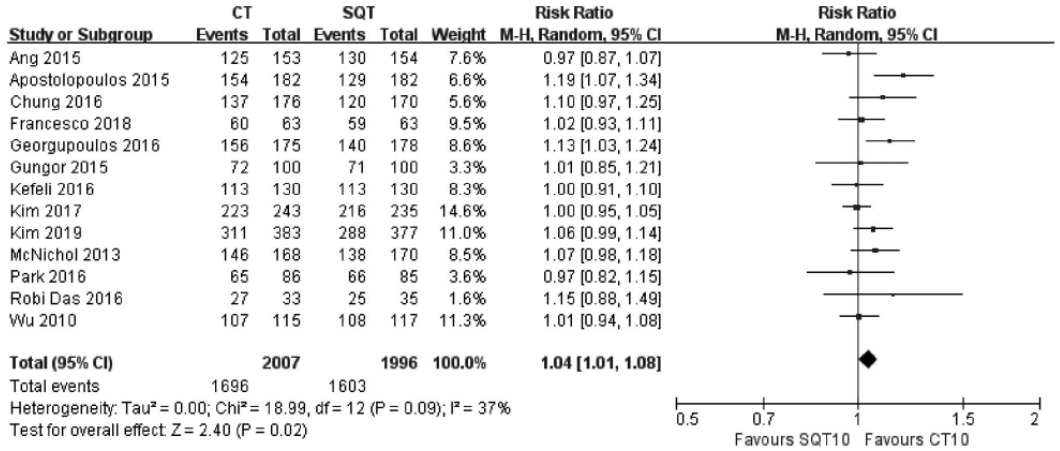
- In contrast, resistance rates against amoxicillin and tetracycline remain low.
- Bismuth partially overcomes metronidazole resistance through cell wall destrabilization.

Summary of recommendations

- **Statement 5**
- Ten-day concomitant therapy is recommended as first-line empirical eradication therapy for *H. pylori* infection.

Statement 5

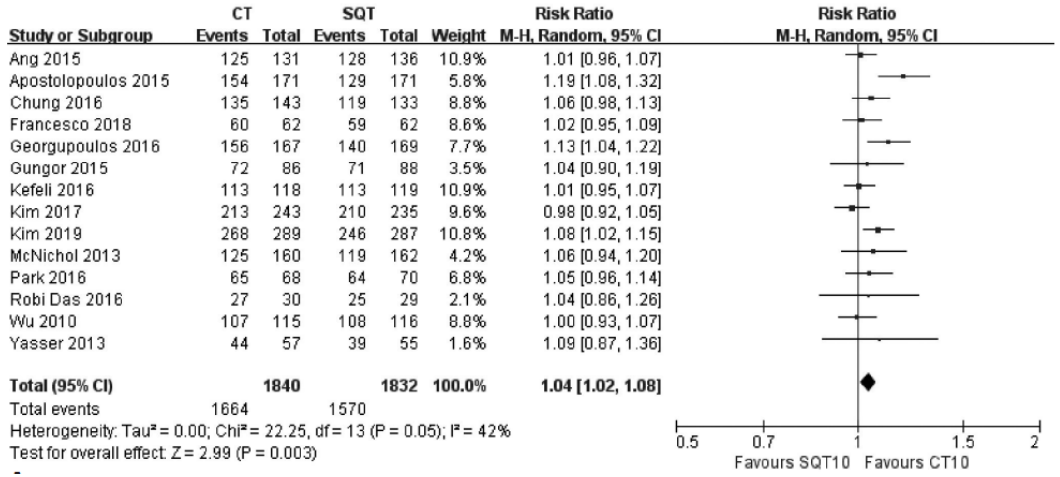
- 10-day CT showed marginally higher eradication rates than 10-day ST



Study or Subgroup	CT Events	CT Total	SQT Events	SQT Total	Weight	Risk Ratio M-H, Random, 95% CI
Ang 2015	125	153	130	154	7.6%	0.97 [0.87, 1.07]
Apostolopoulos 2015	154	182	129	182	6.6%	1.19 [1.07, 1.34]
Chung 2016	137	176	120	170	5.6%	1.10 [0.97, 1.25]
Francesco 2018	60	63	59	63	9.5%	1.02 [0.93, 1.11]
Georgupoulos 2016	156	175	140	178	8.6%	1.13 [1.03, 1.24]
Gungor 2015	72	100	71	100	3.3%	1.01 [0.85, 1.21]
Kefeli 2016	113	130	113	130	8.3%	1.00 [0.91, 1.10]
Kim 2017	223	243	216	235	14.6%	1.00 [0.95, 1.05]
Kim 2019	311	383	288	377	11.0%	1.06 [0.99, 1.14]
McNichol 2013	146	168	138	170	8.5%	1.07 [0.98, 1.18]
Park 2016	65	86	66	85	3.6%	0.97 [0.82, 1.15]
Robi Das 2016	27	33	25	35	1.6%	1.15 [0.88, 1.49]
Wu 2010	107	115	108	117	11.3%	1.01 [0.94, 1.08]
Total (95% CI)		**2007**		**1996**	**100.0%**	**1.04 [1.01, 1.08]**
Total events	1696		1603			

Heterogeneity: Tau² = 0.00; Chi² = 18.99, df = 12 (P = 0.09); I² = 37%
Test for overall effect: Z = 2.40 (P = 0.02)

ITT



Study or Subgroup	CT Events	CT Total	SQT Events	SQT Total	Weight	Risk Ratio M-H, Random, 95% CI
Ang 2015	125	131	128	136	10.9%	1.01 [0.96, 1.07]
Apostolopoulos 2015	154	171	129	171	5.8%	1.19 [1.08, 1.32]
Chung 2016	135	143	119	133	8.8%	1.06 [0.98, 1.13]
Francesco 2018	60	62	59	62	8.6%	1.02 [0.95, 1.09]
Georgupoulos 2016	156	167	140	169	7.7%	1.13 [1.04, 1.22]
Gungor 2015	72	86	71	88	3.5%	1.04 [0.90, 1.19]
Kefeli 2016	113	118	113	119	10.9%	1.01 [0.95, 1.07]
Kim 2017	213	243	210	235	9.6%	0.98 [0.92, 1.05]
Kim 2019	268	289	246	287	10.8%	1.08 [1.02, 1.15]
McNichol 2013	125	160	119	162	4.2%	1.06 [0.94, 1.20]
Park 2016	65	68	64	70	6.8%	1.05 [0.96, 1.14]
Robi Das 2016	27	30	25	29	2.1%	1.04 [0.86, 1.26]
Wu 2010	107	115	108	116	8.8%	1.00 [0.93, 1.07]
Yasser 2013	44	57	39	55	1.6%	1.09 [0.87, 1.36]
Total (95% CI)		**1840**		**1832**	**100.0%**	**1.04 [1.02, 1.08]**
Total events	1664		1570			

Heterogeneity: Tau² = 0.00; Chi² = 22.25, df = 13 (P = 0.05); I² = 42%
Test for overall effect: Z = 2.99 (P = 0.003)

PP

Statement 5

- An analysis restricted to Korean studies showed no significant difference between the 10-day and 14-day regimens.

A

	ITT	PP
	Effect size (95% CI)	Effect size (95% CI)
10D CT, overall (n=23)	0.85 (0.82-0.88)	0.91 (0.88-0.93)
10D CT, Korea (n=7)	0.84 (0.77-0.89)	0.92 (0.88-0.94)
14D CT, overall (n=6)	0.86 (0.76-0.92)	0.94 (0.88-0.97)
14D CT, Korea (n=2)	0.79 (0.72-0.85)	0.94 (0.50-0.99)

B

	ITT	PP
	Effect size (95% CI)	Effect size (95% CI)
10D CT, overall (n=10)	84.97%	93.0% (937/1008)
10D CT, Korea (n=4)	81.9% (576/703)	92.9% (526/566)
14D CT, overall (n=19)	85.5% (1543/1806)	90.7% (1309/1443)
14D CT, Korea (n=3)	83.9% (343/409)	90.1% (328/364)

C

Summary of recommendations

- **Statement 6**
- Ten to 14-day BQT may be used as first-line empirical eradication therapy for *H. pylori* infection.
- BQT is associated with higher adverse event rates and potential utility as salvage therapy; its use as first-line therapy is suggested when other eradication regimens cannot be used.

Summary of recommendations

- **Statement 7**
- Clarithromycin-based triple therapy may be used in a limited fashion when antibiotic susceptibility testing is unavailable and regional clarithromycin resistance is expected to be below 15%.

Summary of recommendations

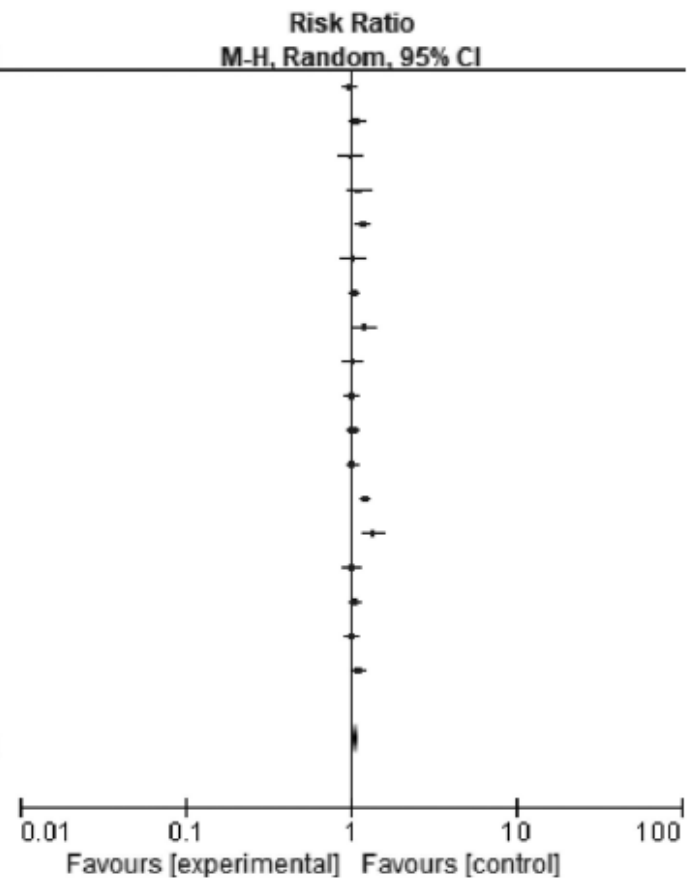
- **Statement 8**
- P-CAB-based antibiotic combination therapy may substitute for PPI-based antibiotic combination therapy as first-line eradication treatment for *H. pylori* infection.

Statement 8

Study or Subgroup	PCAB Events	PCAB Total	PPI Events	PPI Total	Weight	Risk Ratio M-H, Random, 95% CI
Ang 2022	104	119	110	125	6.0%	0.99 [0.90, 1.09]
Bunchorntavakul 2021	59	61	54	61	5.6%	1.09 [0.99, 1.21]
Chen 2023	38	45	38	45	2.9%	1.00 [0.84, 1.19]
Chen 2024	77	100	69	100	3.1%	1.12 [0.94, 1.32]
Chey 2022	273	338	226	330	6.3%	1.18 [1.08, 1.29]
Choi 2022	110	175	106	175	3.2%	1.04 [0.88, 1.22]
Han 2023	308	345	293	345	8.2%	1.05 [0.99, 1.11]
Huang 2023	39	40	32	40	3.3%	1.22 [1.04, 1.43]
Kim 2023	84	105	82	106	4.0%	1.03 [0.90, 1.19]
Kong 2024	158	184	155	184	6.5%	1.02 [0.94, 1.11]
Lee 2024	176	202	171	204	6.8%	1.04 [0.96, 1.13]
Lu 2023	151	156	73	78	7.8%	1.03 [0.97, 1.10]
Maruyama 2017	300	324	243	320	7.5%	1.22 [1.14, 1.31]
Murakami 2016	69	72	48	69	3.2%	1.38 [1.17, 1.62]
Su 2023	65	73	64	73	4.9%	1.02 [0.90, 1.14]
Tan 2024	252	287	236	286	7.5%	1.06 [0.99, 1.14]
Waqar 2024	58	61	57	61	6.4%	1.02 [0.93, 1.11]
Zhou 2024	245	287	217	283	6.8%	1.11 [1.03, 1.21]
Total (95% CI)		**2974**		**2885**	**100.0%**	**1.08 [1.04, 1.12]**
Total events	2566		2274			

Heterogeneity: Tau² = 0.00; Chi² = 40.85, df = 17 (P = 0.0010); I² = 58%

Test for overall effect: Z = 4.27 (P < 0.0001)



A

P-cab vs PPI

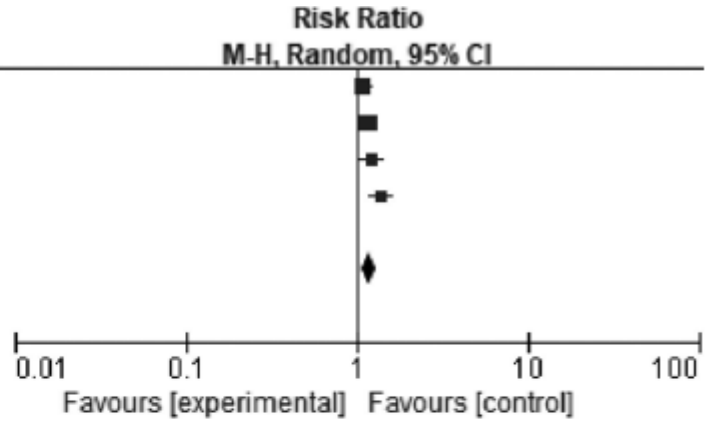
Statement 8

Vonoprazan

Study or Subgroup	PCAB Events	PCAB Total	PPI Events	PPI Total	Weight	Risk Ratio M-H, Random, 95% CI
Bunchorntavakul 2021	59	61	54	61	30.1%	1.09 [0.99, 1.21]
Chey 2022	273	338	226	330	33.0%	1.18 [1.08, 1.29]
Huang 2023	39	40	32	40	18.5%	1.22 [1.04, 1.43]
Maruyama 2017	69	72	48	69	18.4%	1.38 [1.17, 1.62]
Total (95% CI)		**511**		**500**	**100.0%**	**1.19 [1.09, 1.30]**
Total events	440		360			

Heterogeneity: Tau² = 0.00; Chi² = 6.09, df = 3 (P = 0.11); I² = 51%

Test for overall effect: Z = 3.94 (P < 0.0001)



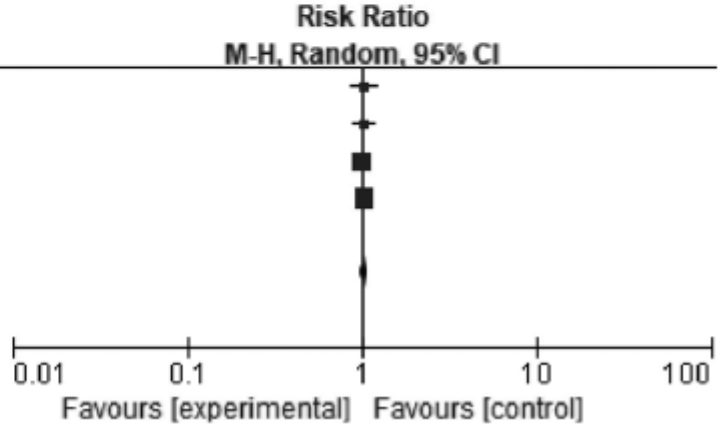
B

Tegoprazan

Study or Subgroup	PCAB Events	PCAB Total	PPI Events	PPI Total	Weight	Risk Ratio M-H, Random, 95% CI
Choi 2022	110	175	106	175	9.7%	1.04 [0.88, 1.22]
Kim 2023	84	105	82	106	13.4%	1.03 [0.90, 1.19]
Kong 2024	158	184	155	184	36.0%	1.02 [0.94, 1.11]
Lee 2024	176	202	171	204	41.0%	1.04 [0.96, 1.13]
Total (95% CI)		**666**		**669**	**100.0%**	**1.03 [0.98, 1.09]**
Total events	528		514			

Heterogeneity: Tau² = 0.00; Chi² = 0.12, df = 3 (P = 0.99); I² = 0%

Test for overall effect: Z = 1.18 (P = 0.24)



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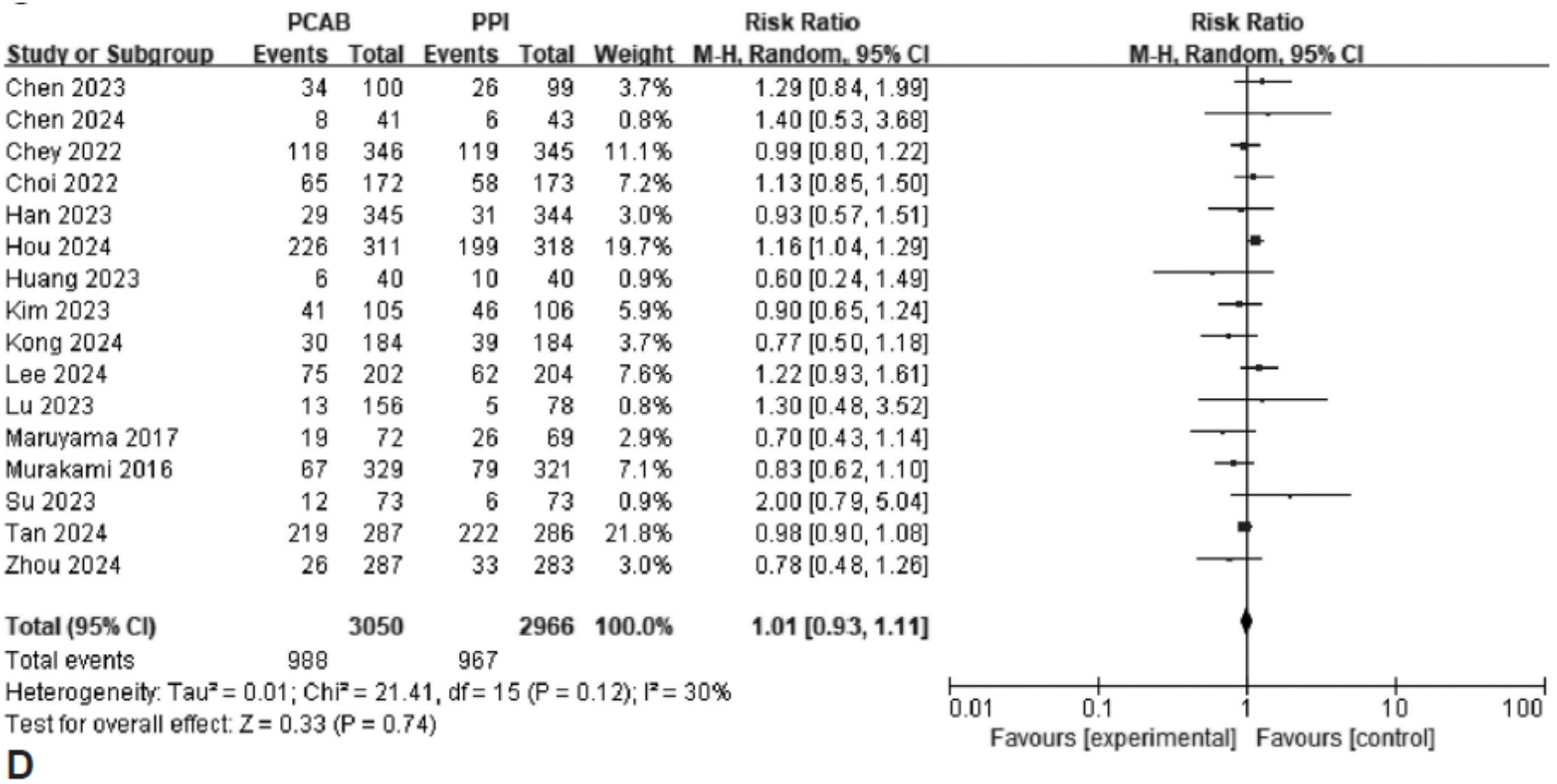
Statement 8



Study or Subgroup	PCAB Events	PCAB Total	PPI Events	PPI Total	Weight	Risk Ratio M-H, Random, 95% CI
Chen 2023	34	100	26	99	3.7%	1.29 [0.84, 1.99]
Chen 2024	8	41	6	43	0.8%	1.40 [0.53, 3.68]
Chey 2022	118	346	119	345	11.1%	0.99 [0.80, 1.22]
Choi 2022	65	172	58	173	7.2%	1.13 [0.85, 1.50]
Han 2023	29	345	31	344	3.0%	0.93 [0.57, 1.51]
Hou 2024	226	311	199	318	19.7%	1.16 [1.04, 1.29]
Huang 2023	6	40	10	40	0.9%	0.60 [0.24, 1.49]
Kim 2023	41	105	46	106	5.9%	0.90 [0.65, 1.24]
Kong 2024	30	184	39	184	3.7%	0.77 [0.50, 1.18]
Lee 2024	75	202	62	204	7.6%	1.22 [0.93, 1.61]
Lu 2023	13	156	5	78	0.8%	1.30 [0.48, 3.52]
Maruyama 2017	19	72	26	69	2.9%	0.70 [0.43, 1.14]
Murakami 2016	67	329	79	321	7.1%	0.83 [0.62, 1.10]
Su 2023	12	73	6	73	0.9%	2.00 [0.79, 5.04]
Tan 2024	219	287	222	286	21.8%	0.98 [0.90, 1.08]
Zhou 2024	26	287	33	283	3.0%	0.78 [0.48, 1.26]
Total (95% CI)		**3050**		**2966**	**100.0%**	**1.01 [0.93, 1.11]**
Total events	988		967			

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 21.41$, df = 15 (P = 0.12); $I^2 = 30\%$

Test for overall effect: Z = 0.33 (P = 0.74)

D

Adverse event rates

Summary of recommendations

- **Statement 9-1**
- Ten to 14-day BQT is recommended as second-line eradication therapy when clarithromycin-based triple therapy or concomitant therapy has failed.

- Metronidazole resistance can be largely overcome by increasing the dose and duration of bismuth-containing regimens

Summary of recommendations

- **Statement 9-2**
- When BQT has failed as first-line or second-line therapy, rifabutin-based triple therapy or modified BQT incorporating previously unused antibiotics may be considered. Levofloxacin-based therapy may be attempted in a limited fashion, considering regional resistance patterns.

Summary of recommendations

- **Statement 9-3**
- Referral to a specialized *H. pylori* center capable of antibiotic susceptibility testing-guided tailored therapy is suggested when two or more lines of eradication therapy have failed.

Medication

- TT : PAC
- CT : PACM
- BQT : PBMT
- mBQT : PAM+B, PAC+B
- mBQT with unused antibiotics : PB+(A or L)+(unused antibiotic)
- Levofloxacin based mBQT : PALB
- Levofloxacin based TT : PA+L
- Rifabutin TT : PA+rifabutin

Treatment algorithm (2025 Revised Edition)