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Review Article

Efficacy and safety of potassium-competitive acid blockers in eradicating *Helicobacter pylori* and treating gastro-esophageal reflux disease: A systematic review and meta-analysis

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Abstract

Background: This systematic review aimed to assess the efficacy and safety of PCAB versus PPI in eradicating *H. pylori* and GERD.

Methods: The studies were searched through databases of PubMed, ScienceDirect, Wiley Online Library, and CENTRAL. A random-effects meta-analysis was performed to evaluate the efficacy and safety of PCAB in eradicating *H. pylori* and treating GERD, using odds ratios (OR) and 95% confidence intervals (95%CI) as the effect measures.

Results: PCAB therapy demonstrated superior efficacy and safety compared to PPI-based therapy in eradicating *H. pylori* (efficacy OR 1.40 [95% CI 1.12–1.76]; safety OR 0.71 [0.52–0.95]) and treating GERD (efficacy OR 1.62 [1.01–2.61]; safety OR 0.90 [0.71–1.14]). Vonoprazan therapy, but not tegoprazan, particularly showed superiority, with ORs of 1.66 [1.24–2.23] for *H. pylori* eradication (safety OR 0.71 [0.52–0.95]) and 1.80 [1.00–3.25] for GERD (safety OR 1.03 [0.83–1.27]). For *H. pylori* eradication, vonoprazan triple therapy showed greater efficacy overall (OR 1.94 [1.19–3.17]) and compared to lansoprazole (OR 2.84 [1.97–4.11]) and rabeprazole (OR 2.63 [1.05–6.58]), though not compared to esomeprazole (OR 1.62 [0.69–3.81]). In GERD treatment, both short-term (8 weeks) and long-term (24 weeks) vonoprazan therapies were similarly effective (OR 2.55 [1.71–3.80] and OR 2.17 [1.00–4.72], respectively) and showed particular efficacy in patients with severe (grade C/D) reflux esophagitis (OR 3.51 [1.65–7.46]).

Conclusions: Vonoprazan had a superior efficacy than PPI in eradicating H. pylori and treating GERD, but not for tegoprazan. PCAB demonstrated a favorable safety profile.

Keywords: Gastro-esophageal reflux disease, Helicobacter pylori, Proton pump inhibitor, Tegoprazan, Vonoprazan.

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H*elicobacter pylori* is a microorganism responsible for a high prevalence of bacterial infections worldwide. *H. pylori* is the most common cause of chronic gastritis, gastric and duodenal peptic ulcer disease (PUD), gastric cancer, and gastric mucosa-associated lymphoid tissue (MALT) lymphoma (1). The prevalence of *H. pylori* is estimated to reach 11% in Sweden, 30% in the United States, 60% in Spain, and up to 83% in China (2). ERD is a chronic gastrointestinal disorder characterized by regurgitation of gastric contents into the esophagus. Based on a study by El-Serag, the prevalence of GERD in the US is estimated between 18.1% up to 27.8%, with a higher prevalence observed in men than women. Women tend to experience GERD symptoms associated with non-erosive reflux disease (NERD), while men more commonly exhibit erosive esophagitis. Additionally, men with long-term GERD have a higher incidence of Barrett's esophagus (23%) compared to women (14%) (3). H. pylori can be diagnosed using various methods, including invasive biopsy and non-invasive tests like the urea breath test (UBT), serology, and stool antigen tests.

UBT and stool antigen tests are popular due to their safety, accuracy, ease of use, and low-cost. However, their sensitivity decreases with active gastrointestinal bleeding or recent use of bismuth, antibiotics, or antisecretory drugs. Therefore, antibiotics and bismuth compounds should be discontinued at least four weeks before the UBT (4).Gastro-esophageal reflux disease (GERD) is different from other conditions because it typically causes heartburn and acid regurgitation, but can also present with chest pain. Rare symptoms, called atypical symptoms, include dysphagia, bleeding, chronic cough, asthma, and laryngitis, and hoarseness, teeth erosion, belching, and bloating. Due to the varied symptoms, diagnosing GERD can be challenging. To aid in diagnosis, several questionnaires have been developed, such as questionnaire for diagnosing reflux esophagitis (QUEST), the frequency scale for GERD symptoms (FSSG), the reflux questionnaire (ReQuest), the reflux disease questionnaire (RDQ), and the gastroesophageal reflux disease questionnaire (GERD-Q) (5-13). The gold standard for diagnosing GERD is endoscopy. Based on the results of endoscopy findings and histopathological appearance, GERD is classified into three phenotypes, namely non-erosive reflux disease (NERD), erosive esophagitis (EE), and Barrett's esophagus (BE). NERD is the most frequently found condition (60-70%), followed by erosive esophagitis (30%) and Barrett's esophagus (6-12%) (3, 14). Management of both GERD and H. pylori infection involves the use of PPI. PPI works by inhibiting hydrogen-potassium ATPase in the stomach's parietal cells, reducing the gastric contents' acidity level and usually alleviating GERD symptoms (13). Meanwhile, in the case of H. Pylori, a combination of PPI with antibiotics is commonly referred to as triple therapy. Apart from triple therapy, the commonly used therapy option is quadruple therapy consisting of PPI, tetracycline, metronidazole, and bismuth for 7-14 days (4, 15). Several recent studies have shown that vonoprazan, part of potassium-competitive acid blockers (PCAB) class, has greater effectiveness than proton pump inhibitor (PPIs) in eradicating H. pylori and alleviating GERD symptoms. The study by Chey (2022) demonstrated that vonoprazan is more effective than PPI triple-based therapy in eradicating H. pylori (16). Laine (2023) showed that vonoprazan is at least as effective as lansoprazole in healing and maintening therapy of erosive esophagitis (17). The latest study, Choi (2022), found that tegoprazan, another PCAB, has the same effectiveness and safety as PPI-based triple therapy in eradicating H. pylori (18). Similarly, Lee (2019) showed that tegoprazan (50 or 100 mg once daily) is no less effective than esomeprazole for treating erosive esophagitis (19, 20). Based on the above findings, the author is interested in studying the therapeutic applications of vonoprazan and tegoprazan in depth, particularly focusing on their effectiveness and safety in eradicating H. pylori compared to PPI-based therapy.

Methods

Study design: This study is designed as a meta-analysis.

Data sources and searches: We searched PubMed, Cochrane Register of Controlled Trials, WileyOnline, and ScienceDirect for studies on PCAB for H. pylori infection and GERD, published between January 2015 and November 2023. We used keywords related to H. pylori infection, vonoprazan (VPZ), tegoprazan (TPZ), and GERD, with the search terms ((Gastroesophageal Reflux Disease) AND ((Vonoprazan) OR (Tegoprazan)). We excluded reviews and systematic reviews, selecting only English-language studies involving humans.

Definition: Eradication of H. pylori infection was confirmed by supporting tests, such as the C-urea breath test (C-UBT) or stool antigen tests, showed that the infection was gone within the study's specified timeframe. The success was indicated by a delta over baseline (DOB) of less than 4 on the C-UBT. For GERD, a diagnosis was made if the patient had GERD symptoms and met the criteria of GERD questionnaires like GERD-Q and FSSG or if GERD was confirmed through endoscopy. Management was considered successful if endoscopic findings or symptom assessments improved based on these questionnaires.

Study selection: Eligible studies for this review included research on PCAB (vonoprazan and tegoprazan) therapy for H. pylori infection and GERD in adult patients (≥18 years old). There were no restrictions based on sex, race, viral genotype, or sample size. The review focused on randomized controlled trials (RCTs), cohort studies, and observational studies, excluding systematic reviews and case reports. Five reviewers (NNGKD, NLPYD, KMNP, and PISLD) independently evaluated titles and abstracts of the articles. Full-text documents were then thoroughly assessed.

Data extraction and quality assessment: Data extraction was conducted by five reviewers (NNGKD, NLPYD, KMNP, and PISLD) for studies from 2015 to 2023. Each reviewer read the full texts and recorded data into Google Sheets, including study details such as authors, year, location, design, and number of patients, diagnostic methods, drug regimens, and follow-up periods. Outcomes such as H. pylori eradication, GERD efficacy, and adverse effects were also recorded. Disagreements were resolved with input from third party reviewers (DAS and IKM).

Study quality was assessed using the "Critical Appraisal Skills Programme Tools (CASP)" checklist, which is available at https://casp-uk.net/casp-tools-checklists. Studies were classified as Good, Fair, or poor based on their validity, importance, and applicability.

Risk of bias assessment: The risk of bias was evaluated using either the Risk of Bias for Nonrandomized Studies (RoBANS) or Risk of Bias 2 (RoB2), depending on the study design. RoBANS evaluated six domains: participant selection, exposure measurement, control of confounding variables, blinding, and reporting completeness. RoB2 assessed five domains: randomization, deviation from intended interventions, outcome measurement, missing outcomes, and selective reporting.

Statistical analysis: The extracted data were tabulated and summarized narratively. To estimate the efficacy and safety of PCAB in eradicating *H. pylori* (separately for PP and ITT analysis) and treating GERD, we conducted random-effects meta-analyses, using odds ratio as the common effect measure. A random-effects model was selected due to potential heterogeneity arising from different dosage and regimens, duration of therapy, and grade of esophagitis. Furthermore, random-effects model was expected to give identical results when no heterogeneity was presented among the studies.

Between-studies heterogeneity was assessed with Cochran's Q (chi-square) tests and I^2 statistics, where a $P_{heterogeneity}$ of <0.100 or an I^2 of >50% denotes significant heteroskedasticity. To further explore PCAB efficacy across different groups and interventions, and to explore potential sources of heterogeneity, we performed subgroup analyses by drug type (vonoprazan vs tegoprazan; for both outcomes), follow-up duration (for GERD), dosage and regimens (for both outcomes), and esophagitis grade (for GERD). Subgroup analysis based on bias risk was not conducted as no study had high bias risk.

Sensitivity analysis and publication bias assessment was performed only for the overall PCAB models. Sensitivity analysis was conducted using leave-one-out meta-analysis – sequentially, excluding one study at each analysis. Potential publication bias was evaluated using funnel plots and Egger's test. Funnel plots were generated only when the model included ≥10 studies. All analyses were conducted using R Version 4.3.2.

Results

A total of 1,454 articles were screened from various databases. After removing duplicates and exclusions, 51 articles were reviewed for eligibility. Twenty-five articles were excluded from the meta-analysis because they either did not use PPI as a control in eradicating H. pylori or ongoing studies on tegoprazan for treating GERD. The final meta-analysis included 26 articles (refer to figure 1).

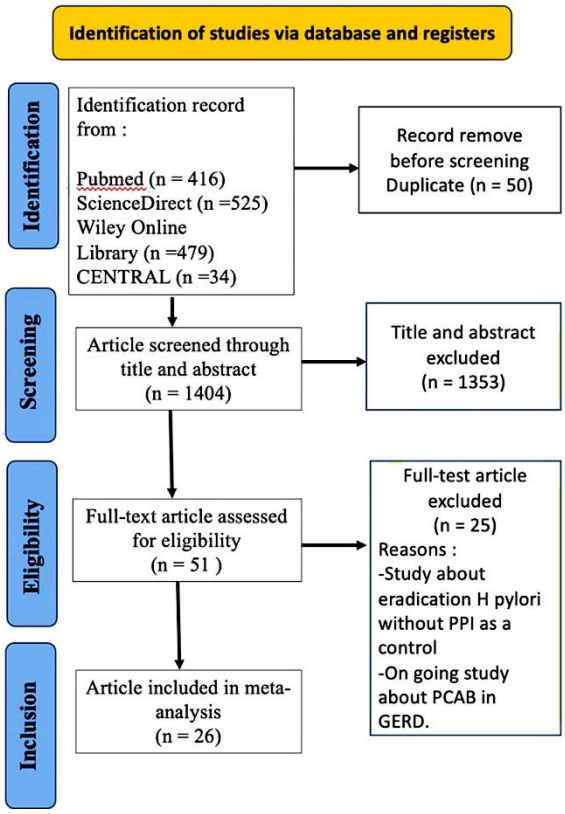

Figure 1. Study selection flow chart for systematic review and meta-analysis

Characteristic of studies: This summary highlights the key features of 26 studies. For H. pylori eradication, success was mainly measured using C-urea breath test (C-UBT), with some studies using *H. pylori* (HP) stool tests and Giemsa stain. Vonoprazan was commonly used at a dosage of 20 mg twice daily, while tegoprazan was typically dosed at 50 mg twice daily. For GERD therapy, the effectiveness of PCAB was assessed using endoscopy, gastroesophageal reflux disease questionnaire (GERD-Q), or frequency scale for the symtomps of GERD (FSSG), each with different criteria for evaluating improvement. Vonoprazan doses in the studies ranged from 10 mg to 20 mg, with treatment durations classified as short-term (less than 24 weeks) or long-term (24 weeks or more). Tegoprazan doses for GERD therapy varied between 25 mg, 50 mg, and 100 mg. More details are available in tables 1 and 2.

Table 1. Characteristics of study about the eradication of H. pylori (16, 18, 21-37)

Author	Year of publication	Study design	Country	Patient number	Dosage of VPZ/ TGZ based therapy	Dosage of PPI based therapy	Duration	Confirmative test for eradication	Outcome
Chey, et al	2022	RCT	US and Europe	1046	VPZ 20 mg bid AMX 1 gr tid	LPZ 30 mg bid AMX 1 gr bid CLM 500 mg bid	14 days	C-UBT	Eradication H. pylori
Shinozaki, et al	2016	Cohort retrospec-tive	Japan	573	VPZ 20 mg bid CLM 200 mg bid AMX 750 mg bid	LPZ 30 mg or RPZ 10 mg or EPZ 20 mg bid CLM 200 mg bid AMX 750 mg bid	14 days	C-UBT	Eradication H. pylori
Maruyama, et al	2017	RCT	Japan	141	VPZ 20 mg bid CLM 200 mg or 400 mg bid AMX 750 mg bid	RPZ 20 mg or LPZ 30 mg bid + AMX 750 mg bid + CLM 200 or 400 mg bid	7 days	14C-UBT	Eradication H. pylori
Wang, et al	2023	RCT	China	151	VPZ 20 mg bid AMX 750 mg qid	RPZ 10 mg bid Bismuth pottasium citrate 220 mg bid AMX 1000 mg CLM bid500 mg bid	14 days	C-UBT	Eradication H. pylori
Li, et al	2023	CT	China	256	VPZ 20 mg bid AMX 750 mg tid	EPZ 20 mg bid AMX 1000 mg bid Furazolidone 100 mg bid Bismuth pottasium citrate 0.6 gram bid	14 days	C-UBT	Eradication H. pylori
Peng, et al	2023	RCT	China	316	VPZ 20 mg bid AMX 750 mg qid	EPZ 20 mg bid AMX 1 gram bid CLM 0.5 gram bid CBS 220 mg bid	14 days	C-UBT	Eradication H. pylori
Hojo, et al	2020	RCT	Japan	46	VPZ 20 mg bid AMX 750 mg bid MTZ 250 mg bid	RPZ 10 mg bid AMX 750 mg bid MTZ 250 mg bid	7 days	C-UBT	Eradication H. pylori
Ang, et al	2022	RCT	Singapore	244	VPZ 20 mg bid AMX 1 gram bid CLM 500 mg bid	OMZ or EPZ or RPZ 20 mg bid AMX 1 gram bid CLM 500 mg bid	14 days	C-UBT	Eradication H. pylori

Author	Year of publication	Study design	Country	Patient number	Dosage of VPZ/ TGZ based therapy	Dosage of PPI based therapy	Duration	Confirmative test for eradication	Outcome
Hou, et al	2022	RCT	China	531	VPZ 20 mg bid AMX 1 gram bid CLM 500 mg bid Bismuth potassium/tripotassium citrate 600 mg bid	LPZ 30 mg bid AMX 1 gram bid CLM 500 mg bid Bismuth potassium /tripotassium citrate 600 mg bid	14 days	C-UBT	Eradication H. pylori
Shichijo, et al	2016	Cohort retrospective	Japan	2715	VPZ 20 mg bid AMX 750 mg bid CLM 200/400 mg bid	LPZ 30 mg or RPZ 10 mg or EPZ 20 mg or OMZ 20 mg bid AMX 750 mg bid CLM 200/400 mg bid	7 days	C-UBT	Eradication H. pylori
Sue, et al	2017	RCT	Japan	147	VPZ 20 mg bid AMX 750 mg bid CLM 200 or 400 mg bid	LPZ 30 mg/ RPZ 10 mg/ EPZ 20 mg bid AMX 750 mg bid CLM 200 or 400 mg bid	7 days	C-UBT	Eradication H. pylori
Lu, et al	2022	RCT	China	234	VPZ 20 mg daily AMX 1000 mg bid Furazolidone 100 mg bid Colloidal bismuth 200 mg bid	EPZ 20 mg bid + AMX 1000 mg bid + furazolidone 100 mg bid + colloidal bismuth 200 mg bid	10 and 14 days	C-UBT	Eradication H. pylori
Zuberi, et al	2022	RCT	Pakistan	233	VPZ 20 mg bid, AMX 1 gr bid	AMX 1 grm bid, CLM 500 mg bid, OMZ 20 mg bid	4 weeks	Stool Hp antigen test and histologi on Giemsa Stain	Eradication H. pylori
Chen, et al	2023	RCT	China	300	VPZ 20 mg, AMX 1000 mg, CLM 500 mg, bismuth 220 mg bid	RPZ 10 mg, AMX 1000 mg, CLM 500 mg, bismuth 220 mg bid	14 days	13C/14C urea breath test (13C/14C-UBT), H. pylori stool antigen test (HpSAT), H. pylori histology, or H. pylori rapid urease test (RUT).	Eradication H. pylori
Tanabe, et al	2018	Restrospective cohort	Japan	1143	VPZ 20 mg bid, AMX 750 mg bid, CLM 200 or 400 mg bid	LPZ 30 mg or RPZ 10 mg or EPZ 20 mg bid, AMX 750 mg bid, CLM 200 or 400 mg bid	7 days	a rapid urease test, 13C-urease breath test, *H. pylori* immunoglobulin G serological test, or *H. pylori* stool antigen test.	Eradication H. pylori

Author	Year of publication	Study design	Country	Patient number	Dosage of VPZ/ TGZ based therapy	Dosage of PPI based therapy	Duration	Confirmative test for eradication	Outcome
Park, et al	2023	Retrospective cohort	Korea	961	Goup triple based therapy (854): TGZ 50 mg + AMX1000 mg + CLM 500 mg bid Group quadruple based therapy (107): TGZ 50 mg bid + bismuth 120 mg qid + MTZ 500 mg tid + TCL 500 mg qid	Group triple based therapy : EPZ/sodium bicarbonate 40/800 mg + AMX 1000 mg + CLM 500 mg bid Group quadruple therapy : RPZ 20 mg bid + bismuth 120 mg qid + MTZ 500 mg tid + TCL 500 mg qid	14 days	C-UBT	Eradication H. pylori
Kim, et al	2021	Retrospective Cohort	Korea	381	TGZ 50 mg bid + AMX 1000 mg bid + CLM 500 mg bid + bismuth tripotassium dicitrate 300 mg bid	LPZ 30 mg bid + AMX 1000 mg bid + CLM 500 mg bid + bismuth tripotassium dicitrate 300 mg bid	7 days	C-UBT	Eradication H. pylori
Jung, et al	2022	Retrospective Cohort	Korea	677	TGZ 50 mg bid + AMX 1000 mg bid + CLM 500 mg bid	RPZ 20 mg bid + AMX 1000 mg bid + CLM 500 mg bid	14 days	Rapid urease test, 13C-urea breath test (Korea Otsuka Pharmaceutical Co., Ltd., Seoul, Korea), and/or histologic evaluation with modified Giemsa staining.	Eradication H. pylori
Choi, et al	2022	RCT	Korea	350	TGZ 50 mg bid + AMX 1000 mg bid+ CLM 500 mg bid	LPZ 30 mg bid + AMX 1000 mg bid+ CLM 500 mg bid	7 days	C-UBT and biopsy	Eradication H. pylori

Abbreviations: VPZ, vonoprazan, TGZ, tegoprazan; PCAB, potassium-competitive acid blockers; OMZ, omeprazole; LZP, lansoprazole; RPZ, rabeprazole; EPZ, esomeprazole; AMX, amoxicillin; CLM, clarithromycin; MTZ, metronidazole; TCL, tetracycline CBS, colloidal bismuth subcitrate; PPI, proton pump inhibitor; bid, bis in die; tid, ter in die; RCT, randomised clinical trial; CT, clinical trial.

Table 2. Characteristics of study about GERD (17, 19, 38-42).

Author	Year of publication	Study design	Country	Patient number	Dosage of VPZ/ TGZ based therapy	Dosage of PPI based therapy	Duration	Confirmative test for eradication	Outcome
Laine, et al	2023	RCT	US and Europe	1027	VPZ 20 mg (healing phase) and VPZ 10 mg (maintenance therapy)	LPZ 30 mg (healing phase) and LPZ 15 mg (maintenance therapy)	8 weeks and 24 weeks	Endoscopy	GERD

Author	Year of publication	Study design	Country	Patient number	Dosage of VPZ/ TGZ based therapy	Dosage of PPI based therapy	Duration	Confirmative test for eradication	Outcome
Sakurai, et al	2018	RCT	Japan	60	VPZ 20 mg	EPZ 20 mg	4 weeks	GERD-Q	GERD
Ashida, et al	2018	RCT	Japan	607	VPZ 20 mg and 10 mg	LPZ 15 mg	24 weeks	Endoscopy	GERD
Ashida, et al	2016	RCT	Japan	409	VPZ 20 mg and 10 mg	LPZ 30 mg	8 weeks and 52 weeks	Endoscopy	GERD
Ashida, et al	2015	RCT	Japan	732	VPZ 5 mg, 10 mg, 20 mg, 40 mg	LPZ 30 mg	4 weeks	Endoscopy	GERD
Lee, et al	2018	RCT	Korea	302	TGZ 50 mg or 100 mg	EPZ 40 mg	4-8 weeks	Endoscopy	GERD
Cho, et al	2022	RCT	Korea	351	TGZ 25 mg	LPZ 15 mg	24 weeks	Endoscopy	GERD

Abbreviations: VPZ, vonoprazan, TGZ, tegoprazan; PCAB, potassium-competitive acid blockers; LPZ, lansoprazole; EPZ, esomeprazole; PPI, proton pump inhibitor; GERD, gastroesophageal reflux disease; RCT, randomised clinical trial.

Risk of bias assessment: Among the 20 randomized controlled trials (RCTs) reviewed, one had an unclear risk of bias related to the selection of reported results (Choi, 2022). Out of the six cohort studies, two had an unclear risk of bias concerning confounding variables (Shichijo, 2016; Jung, 2022). Figures 2 and 3 provide a detailed explanation of the risk of bias for each study in the meta-analysis.

Efficacy and safety of PCAB in eradicating H. pylori: PCAB was found to be effective and safe for eradicating *H. pylori* compared to PPIs (OR 1.40 [95%CI 1.12-1.76] in the ITT analysis and 1.77 [1.34-2.33] in the PP analysis), albeit with considerable heterogeneity (I^2=63% and 65% respectively, both $P_{heterogeneity}$<0.001). While vonoprazan showed consistent superiority compared to PPI-based therapy (OR 1.66 [95%CI 1.24-2.23; I^2=59%, $P_{heterogeneity}$=0.003] in the ITT analysis and 2.15 [1.56-2.97; I^2=57%, $P_{heterogeneity}$=0.003] in the PP analysis), tegoprazan was not superior to PPI-based therapy both in the ITT analysis (OR 1.02 [95%CI 0.84-1.23]; I^2=0%, $P_{heterogeneity}$=0.612) and the PP analysis in the PP analysis (1.08 [0.86-1.36]; I^2=0%, $P_{heterogeneity}$=0.786) (table 3). Both in the ITT and PP analysis, vonoprazan duplex therapy showed similar efficacy to PPI triple or quadruple therapy (figure 4a-b).

On the other hand, vonoprazan triple therapy showed superiority compared to PPI triple therapy both in the ITT (OR 1.94 [95%CI 1.19-3.17; I^2=66%, $P_{heterogeneity}$=0.008]) and PP analysis (2.61 [1.82-3.75; I^2=45%, $P_{heterogeneity}$=0.080]). The superiority of vonoprazan triple therapy was more apparent compared to rabeprazole- (ITT analysis: OR 2.63 [95%CI 1.05-6.58; I^2=67%, $P_{heterogeneity}$=0.029]; figure 5) and lansoprazole-based therapy (ITT analysis: OR 2.84 [95%CI 1.96-4.11; I^2=0%, $P_{heterogeneity}$=0.534]; figure 6), while the efficacy of vonoprazan triple therapy was similar to esomeprazole-based therapy (ITT analysis: OR 1.62 [95%CI 0.69-3.81; I^2=73%, $P_{heterogeneity}$=0.055]) (figure 7). Vonoprazan quadruple therapy showed similar efficacy to PPI quadruple therapy in the ITT analysis (OR 1.49 [95%CI 0.86-2.60; I^2=0%, $P_{heterogeneity}$=0.964]), while the opposite is true based on the PP analysis (OR 1.76 [95%CI 1.10-2.82; I^2=0%, $P_{heterogeneity}$=0.841]). However, it is worth noting that the estimates for vonoprazan quadruple therapy was based only on very few studies. On the other hand, the non-superior efficacy of tegoprazan was observed both in tegoprazan triple and quadruple therapy (figure 8a-b). Leave-one-out sensitivity analyses on the efficacy of PCAB in eradicating *H. pylori* were found to be robust both in the ITT and PP analysis (Supplementary figure S1a-b). Furthermore, we did not detect any potential publication bias (Egger's $P_{heterogeneity}$=0.305 in the ITT analysis and $P_{heterogeneity}$=0.553 in the PP analysis; Supplementary figure S2a-b). PCAB was

relatively safer than PPI-based therapy with a lower prevalence of adverse events (OR 0.71 [95%CI 0.52-0.95; I^2=79%, $P_{heterogeneity}$<0.001]). Specifically, vonoprazan was found to be safer than tegoprazan in eradicating *H. pylori* (OR 0.61 [95%CI 0.42-0.89; I^2=80%, $P_{heterogeneity}$<0.001] vs 1.00 [0.70-1.43; I^2=71%, $P_{heterogeneity}$=0.007]; table 4 and figure 9). Sensitivity analysis revealed robust estimates (Supplementary figure S3), and publication bias assessment showed no potential reporting bias (Egger's $P_{heterogeneity}$=0.318; Supplementary figure S4).

Table 3. Summary of meta-analysis on the efficacy of PCAB in eradicating *H. pylori*

Variable	ITT analysis					PP analysis				
	Effect size			Heterogeneity		Effect size			Heterogeneity	
	Event/N (PCAB vs PPI)	OR (95%CI)	P-value	I^2	P-value	Event/N (PCAB vs PPI)	OR (95%CI)	P-value	I^2	$P_{heterogeneity}$
Overall vs PPI-based therapy	2481/3010 vs 2906/3759	1.40 (1.12-1.76)	0.004	63%	<0.001	3057/3440 vs 4699/5922	1.77 (1.34-2.33)	<0.001	65%	<0.001
Vonoprazan vs PPI-based therapy	1593/1839 vs 1995/2561	1.66 (1.24-2.23)	0.001	59%	0.003	2180/2386 vs 3812/4849	2.15 (1.56-2.97)	<0.001	57%	0.003
VPZ duplex										
vs PPI triple therapy	208/265 vs 201/255	0.98 (0.64-1.49)	0.926	NA	NA	263/310 vs 247/299	1.47 (0.52-4.11)	0.468	72%	0.061
vs PPI quadruple therapy	270/307 vs 254/310	1.62 (0.88-3.00)	0.124	37%	0.204	269/279 vs 257/277	1.95 (0.33-11.66)	0.465	72%	0.028
VPZ triple										
vs PPI triple therapy	889/1011 vs 1398/1818	1.94 (1.19-3.17)	0.008	66%	0.007	1231/1347 vs 2989/3904	2.61 (1.82-3.75)	<0.001	45%	0.080
vs Esomeprazole triple therapy	429/480 vs 199/243	1.62 (0.69-3.81)	0.269	73%	0.055	797/877 vs 381/473	2.12 (0.85-5.30)	0.107	78%	0.010
vs Lansoprazole triple therapy	429/480 vs 291/405	2.84 (1.96-4.11)	<0.001	0%	0.534	797/877 vs 1407/1931	3.16 (2.03-4.93)	<0.001	52%	0.125
vs Rabeprazole triple therapy	515/575 vs 510/670	2.63 (1.05-6.58)	0.039	67%	0.029	881/966 vs 870/1117	3.43 (2.00-5.88)	<0.001	58%	0.051
VPZ quadruple										
vs PPI quadruple therapy	226/256 vs 142/178	1.49 (0.86-2.60)	0.157	0%	0.964	417/450 vs 319/369	1.76 (1.10-2.82)	0.018	0%	0.841
Tegoprazan vs PPI-based therapy	888/1171 vs 911/1198	1.02 (0.84-1.23)	0.876	0%	0.612	877/1054 vs 887/1073	1.08 (0.86-1.36)	0.496	0%	0.786
TGZ triple vs PPI triple therapy	716/954 vs 698/927	0.98 (0.79-1.21)	0.866	0%	0.508	706/862 vs 678/832	1.02 (0.80-1.31)	0.864	0%	0.946
TGZ quadruple vs PPI quadruple therapy	172/217 vs 213/271	1.18 (0.75-1.84)	0.474	0%	0.368	171/192 vs 209/241	1.50 (0.83-2.73)	0.177	0%	0.631

Abbreviations: ITT, intention-to-treat; OR, odds ratio; PP, per protocol; PPI, proton pump inhibitor; TGZ, tegoprazan.

Table 4. Summary of meta-analysis on the safety of PCAB in eradicating *H. pylori*

Variable	Effect size			Heterogeneity	
	Event/N (Intervention vs Control)	OR (95%CI)	P-value	I^2	$P_{heterogeneity}$
Overall vs PPI-based therapy	999/3356 vs 1275/5099	0.71 (0.52-0.95)	0.024	79%	<0.001
Vonoprazan vs PPI-based therapy	593/2151 vs 881/3981	0.61 (0.42-0.89)	0.011	80%	<0.001
Tegoprazan vs PPI-based therapy	406/1205 vs 394/1118	1.00 (0.70-1.43)	0.990	71%	0.007

Abbreviations: OR, odds ratio; PCAB, potassium-competitive acid blockers, PPI, proton pump inhibitor; TGZ, tegoprazan; VPZ, vonoprazan.

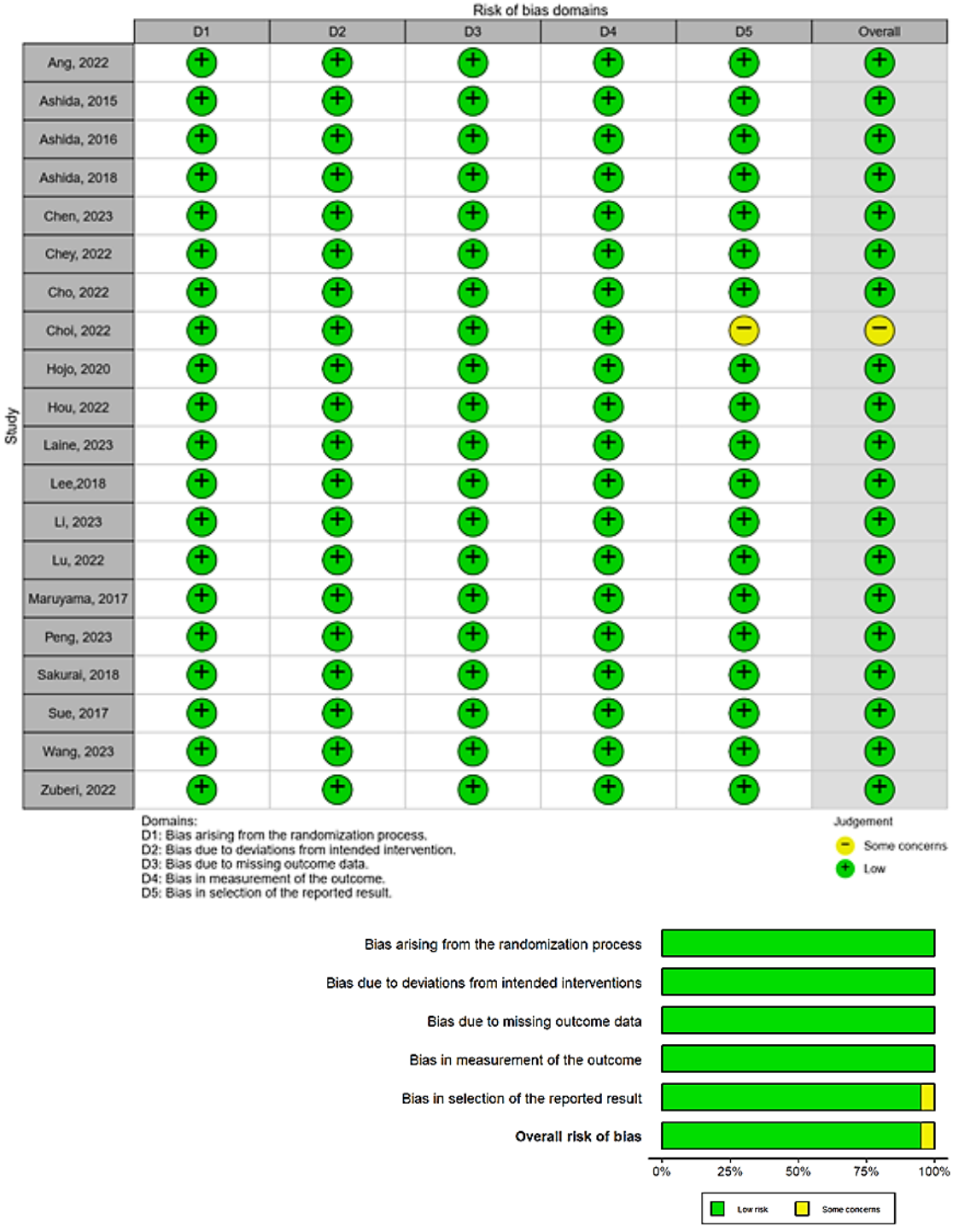

Figure 2. Risk of bias of the included randomized controlled trials

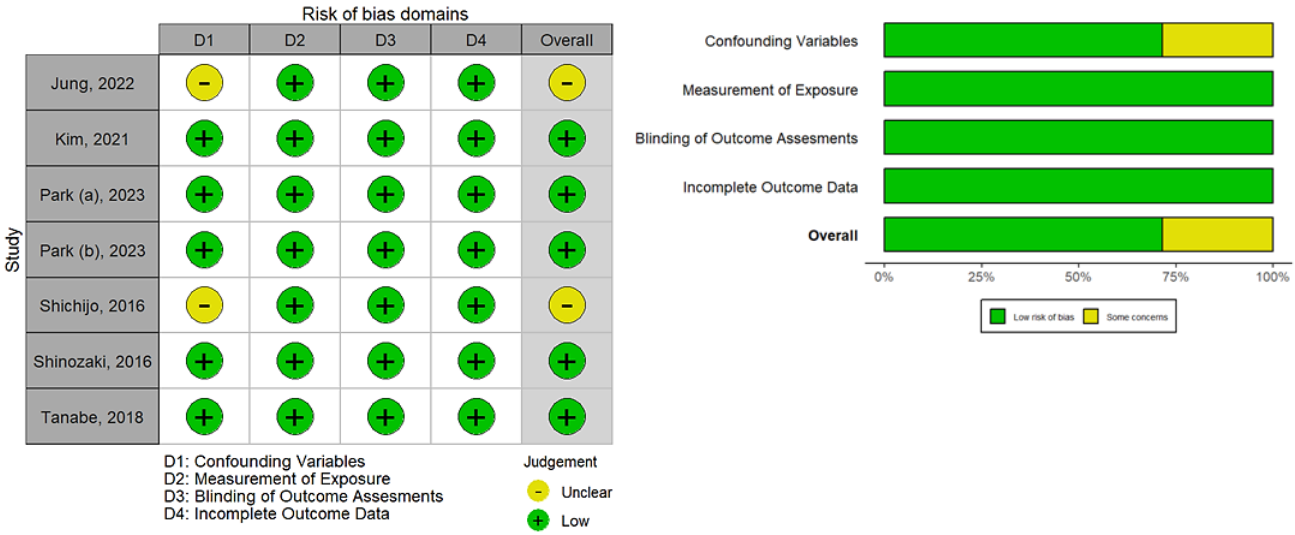

Figure 3. Risk of bias of the included cohort studies

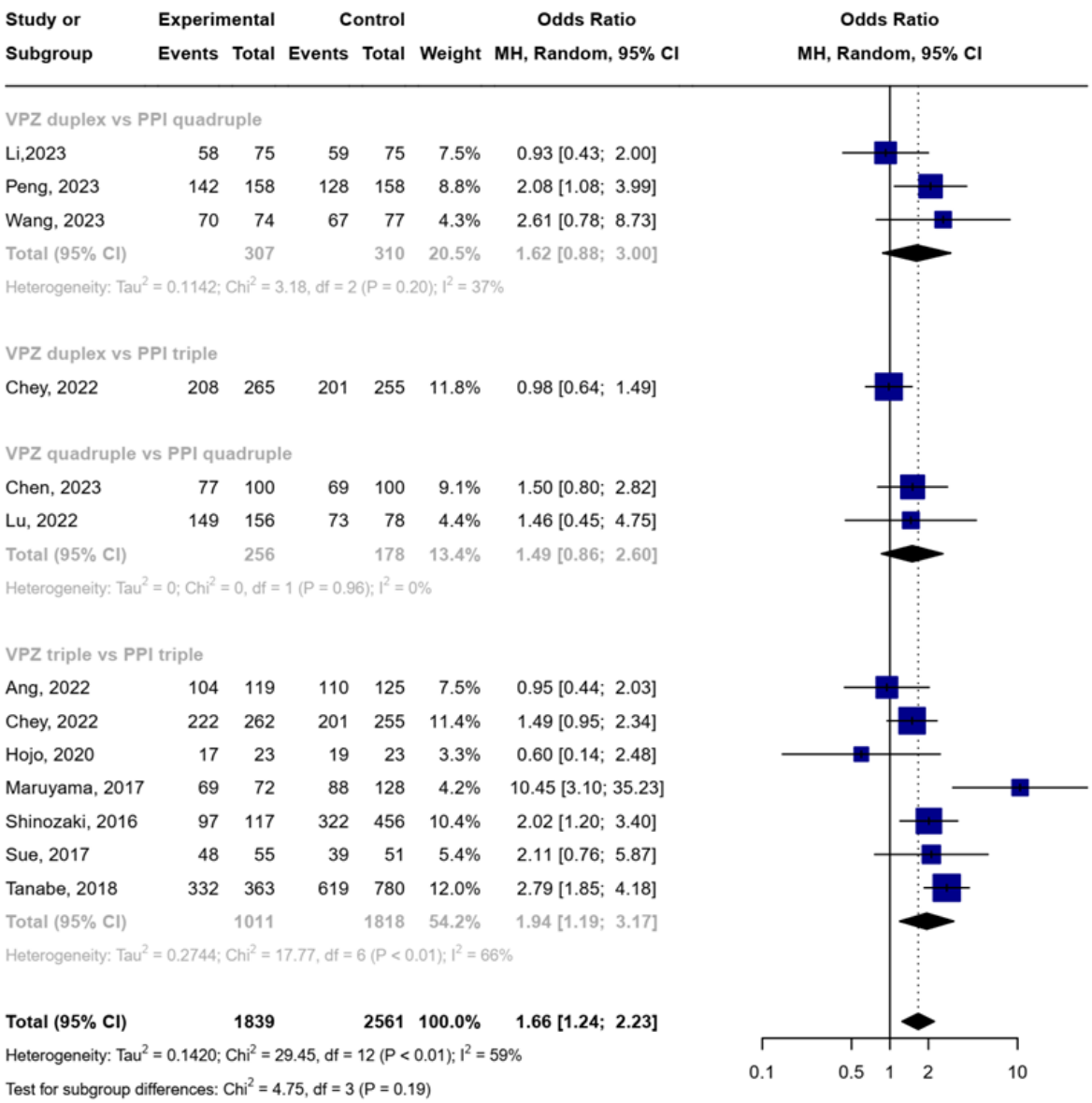

Figure 4a. Efficacy of Vonoprazan versus PPI in the eradication of *H. pylori* (ITT Analysis)

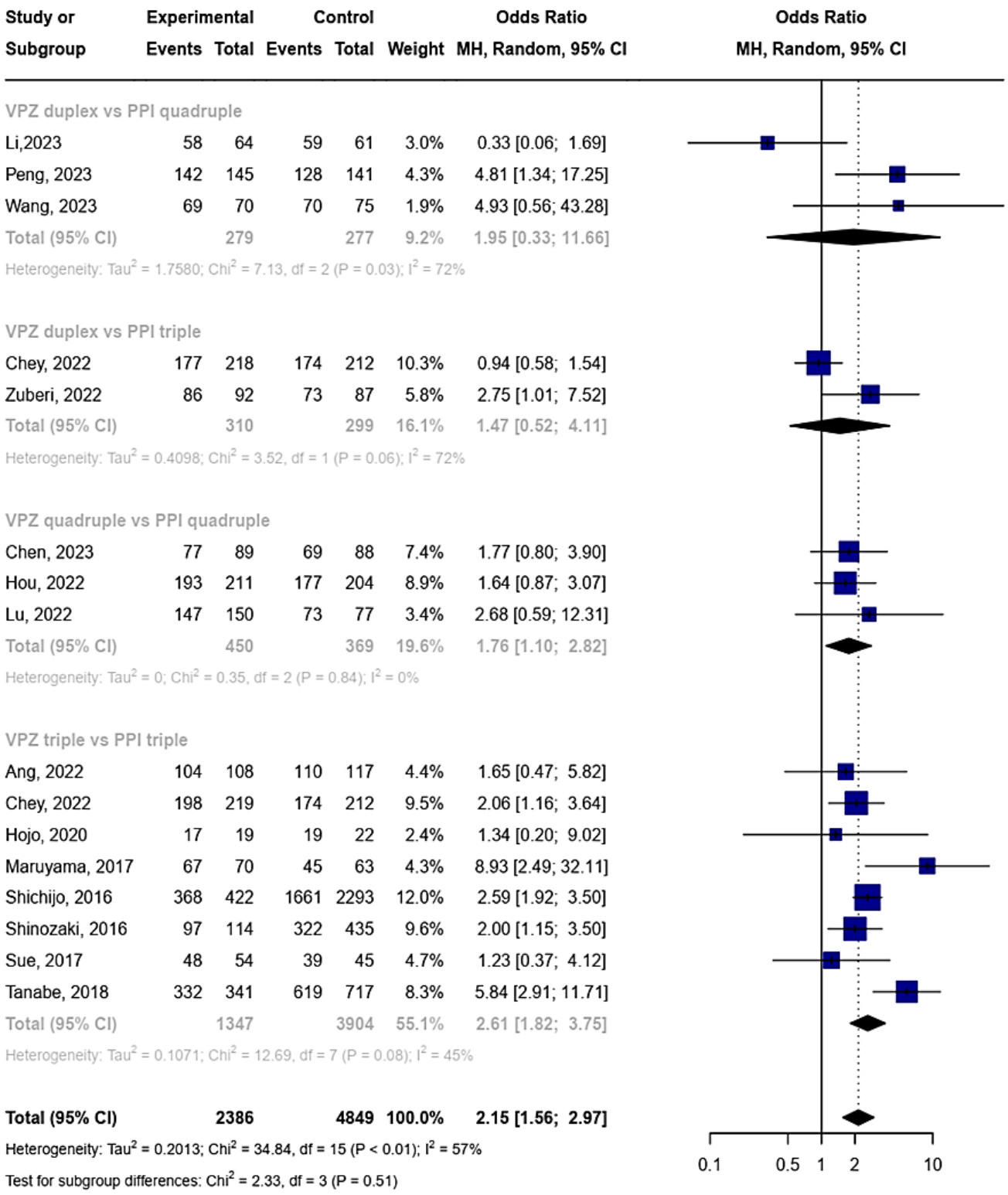

Figure 4b. Efficacy of Vonoprazan versus PPI in eradication of *H. Pylori* (PP Analysis)

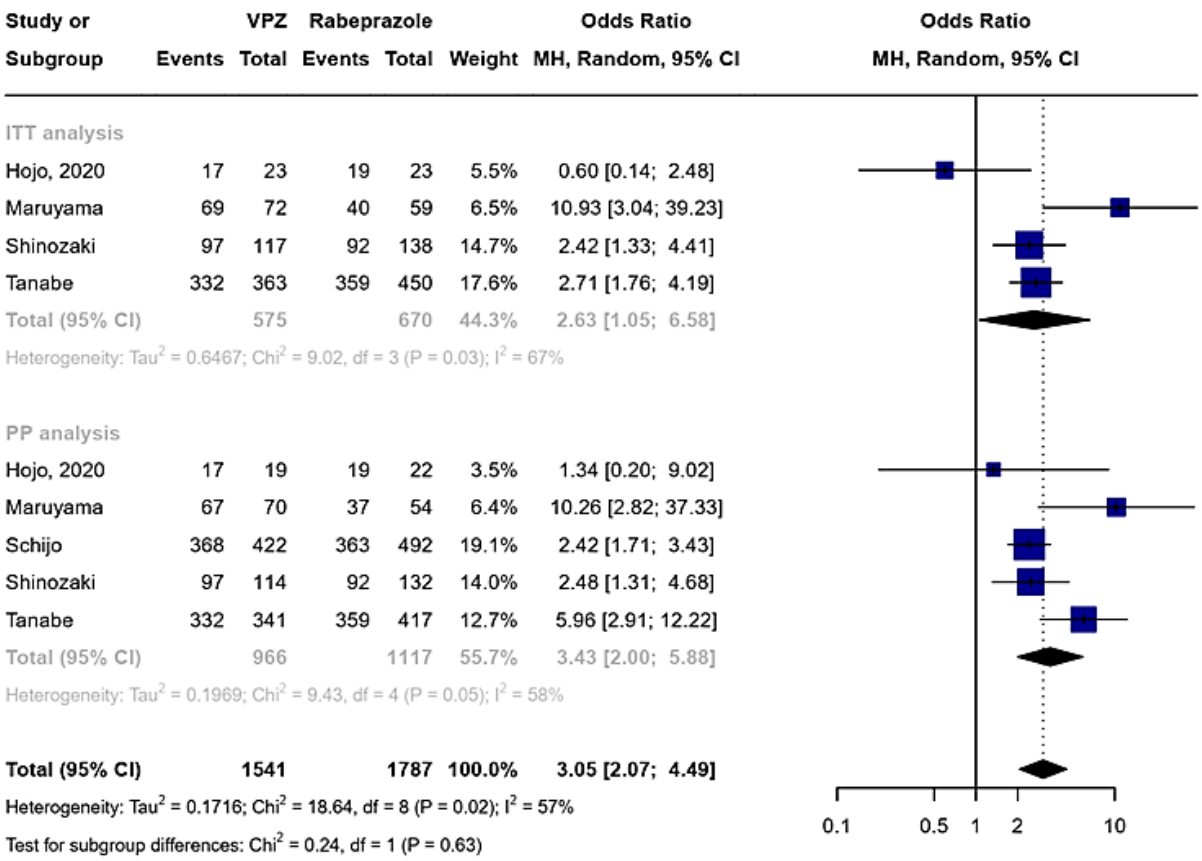

Figure 5. Efficacy of Vonoprazan-based versus Rabeprazole-based therapy in the eradication of *H. pylori*

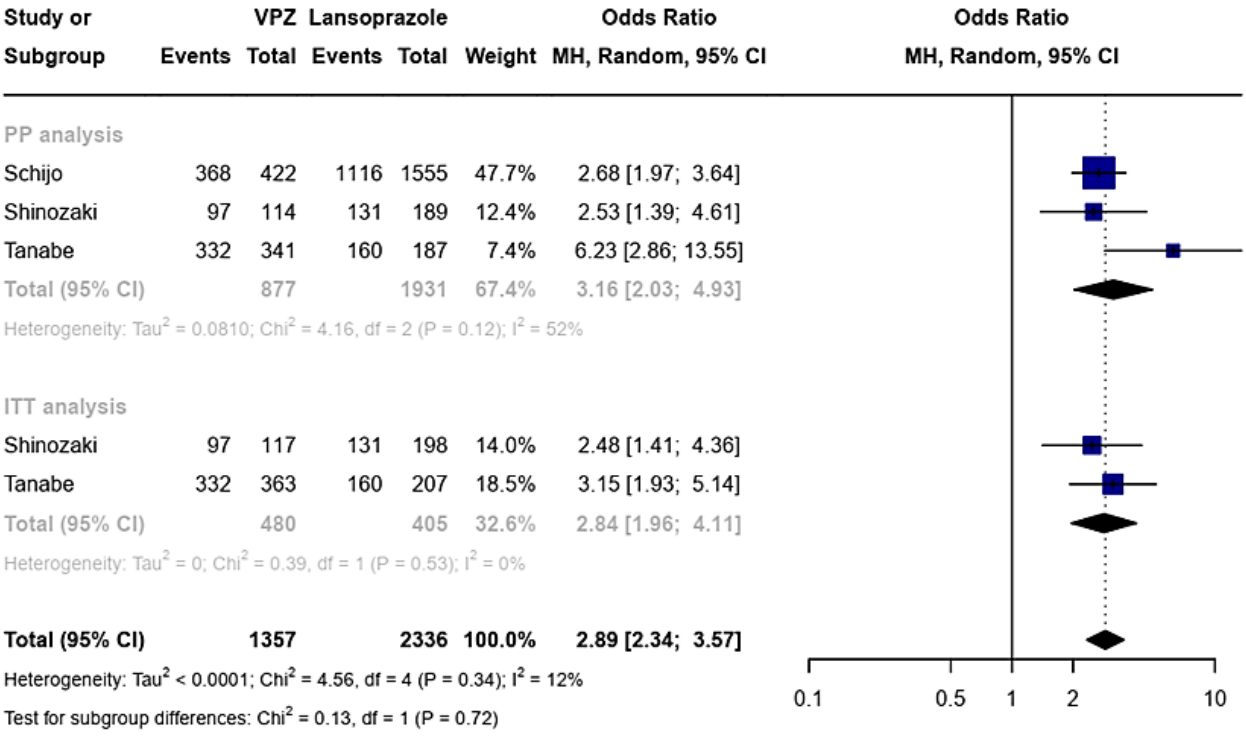

Figure 6. Efficacy of Vonoprazan-based versus Lansoprazole-based therapy in the eradication of *H. pylori*

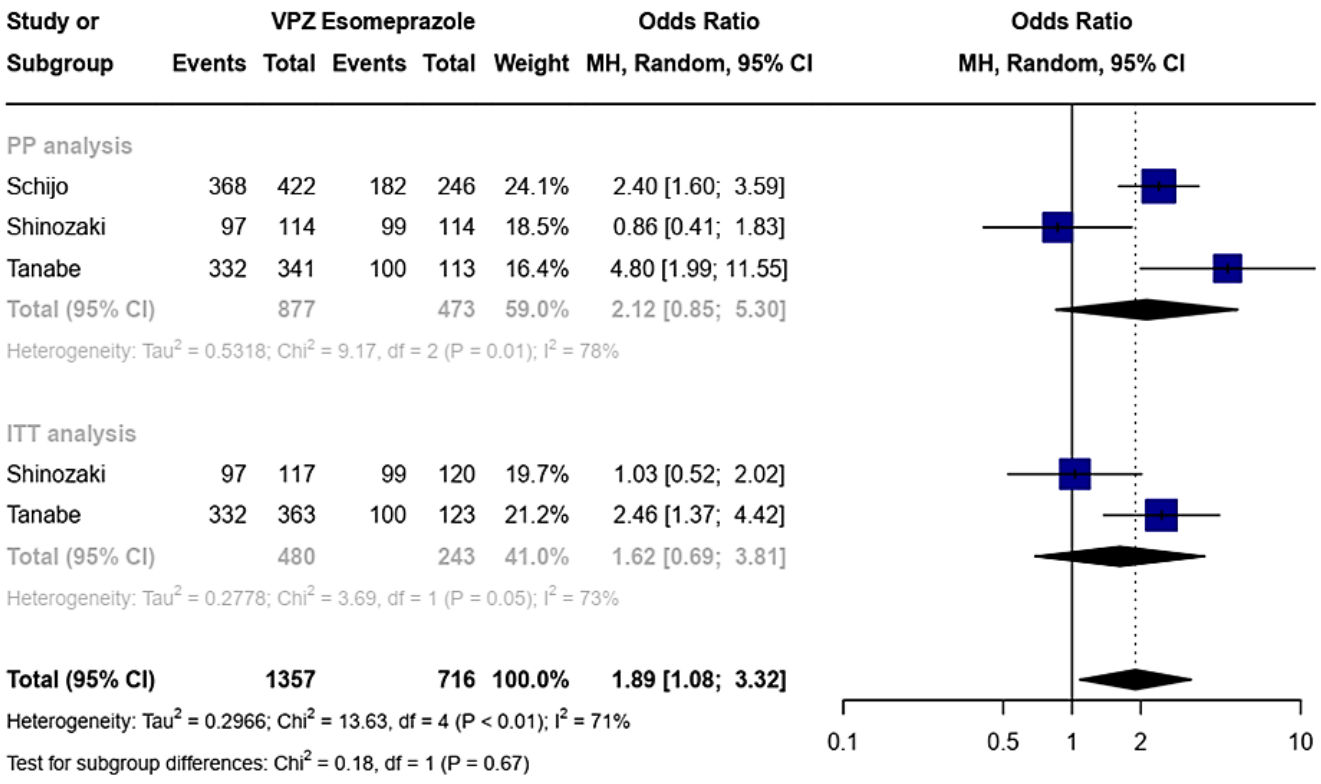

Figure 7. Efficacy of Vonoprazan-based versus Esomeprazole-based therapy in the eradication of *H. pylori*

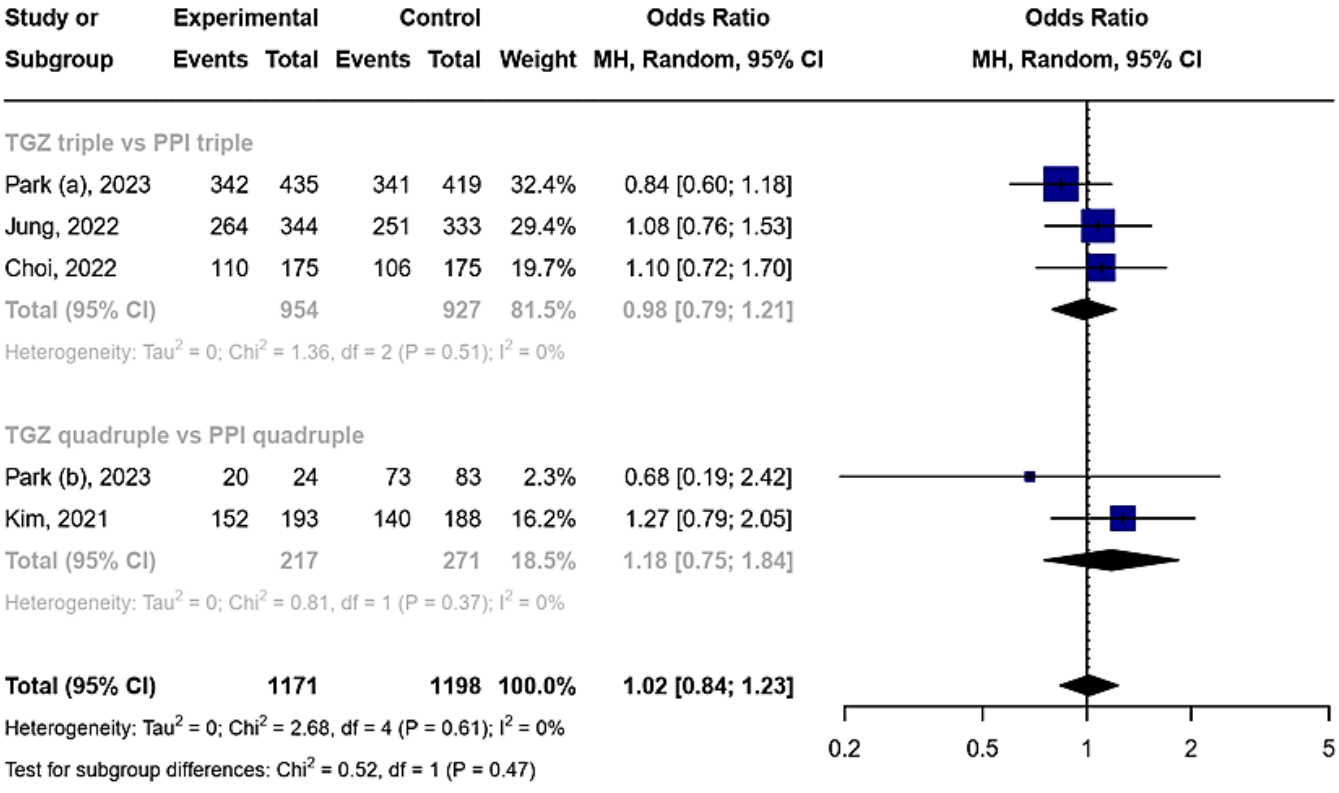

Figure 8a. Efficacy of Tegoprazan versus PPI in eradication of *H. Pylori* (ITT Analysis)

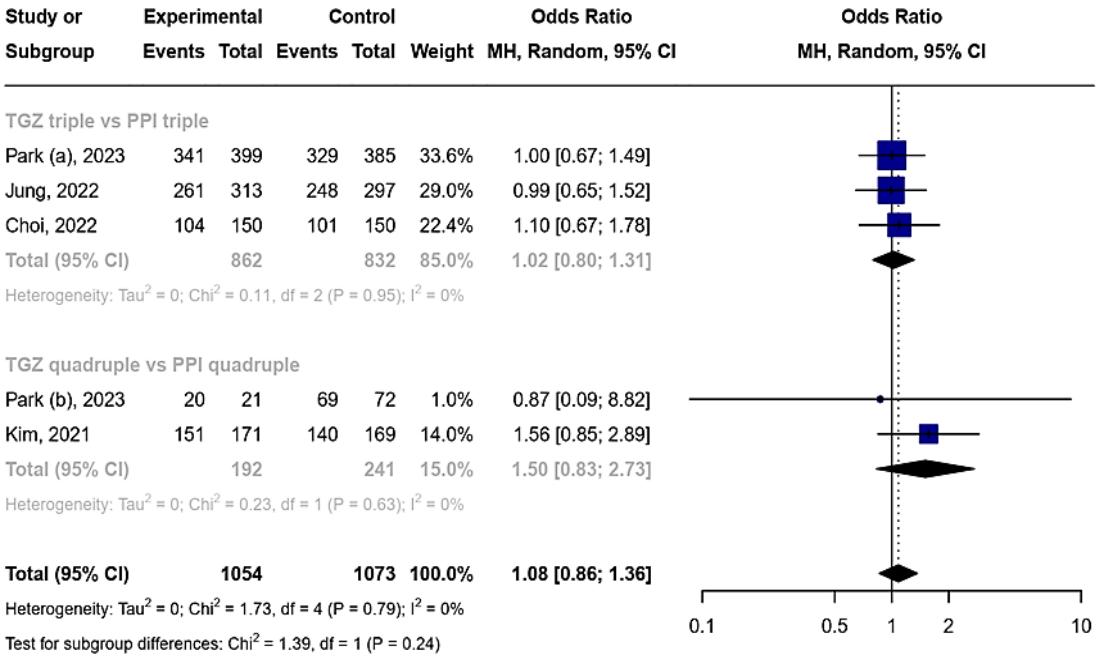

Figure 8b. Efficacy of Tegoprazan versus PPI in eradication of *H. pylori* (PP Analysis)

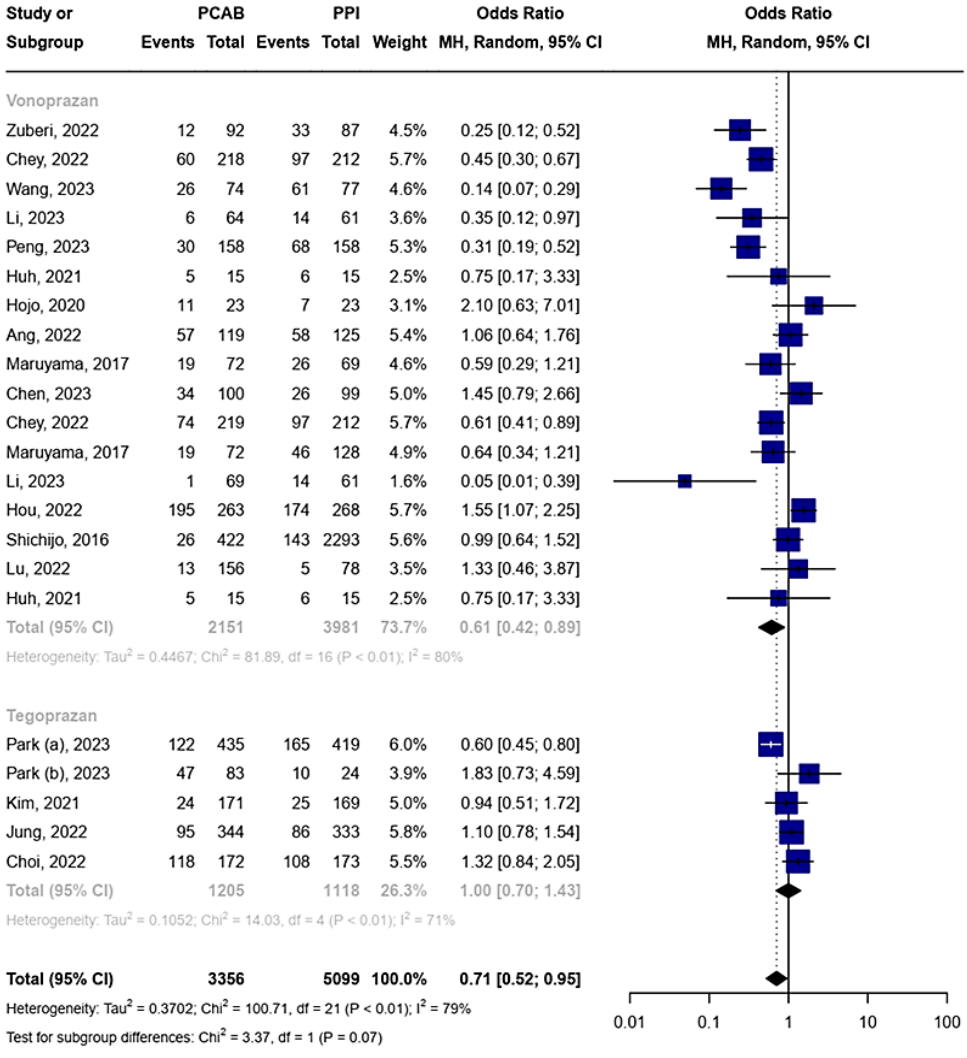

Figure 9. Adverse event of PCAB versus PPI in Eradication of H Pylori

Efficacy and safety of PCAB in GERD: PCAB was also found to be more efficacious and safer than PPI-based therapy in treating GERD. Overall, PCAB had a superior efficacy compared to PPI-based therapy (OR 1.62 [95%CI 1.01-2.61; I^2=39%, $P_{heterogeneity}$=0.149]), which is more apparent in vonoprazan (1.80 [1.00-3.25; I^2=52%, $P_{heterogeneity}$=0.101]) than in tegoprazan (1.12 [0.52-2.41; I^2=0%, $P_{heterogeneity}$=0.951]; table 5 and figure 10). Sensitivity analysis revealed that the exclusion of Ashida 2015, Ashida 2016, or Laine 2023 nullified the superiority of PCAB in treating GERD, indicating that the results were relatively not robust (supplementary figure S5).

Vonoprazan demonstrated higher efficacy both in the short-term (8 weeks: OR 2.55 [95%CI 1.71-3.80; I^2=0%, $P_{heterogeneity}$=0.404]) and long-term use (24 weeks; OR 2.17 [95%CI 1.00-4.72; I^2=76%, $P_{heterogeneity}$=0.040]) (figure 11). Furthermore, the efficacy of long-term vonoprazan use was higher in vonoprazan 10 mg compared to vonoprazan 20 mg (OR 1.64 [95%CI 1.11-2.43; I^2=13%, $P_{heterogeneity}$=0.283] vs. 2.86 [0.79-10.38; I^2=81%, $P_{heterogeneity}$=0.023]) (Figure 12). The efficacy of vonoprazan was more apparent in treating severe GERD (Los Angeles [LA] grade C/D: OR 3.51 [95%CI 1.65-7.46; I^2=44%, $P_{heterogeneity}$=0.170]) compared to mild-to-moderate GERD (1.14 (0.57-2.26; I^2=0%, $P_{heterogeneity}$=0.390]) (figure 13).

PCAB was relatively safe with a similar prevalence of adverse events compared to PPI-based therapy (OR 0.90 [95%CI 0.71-1.14; I^2=4%, $P_{heterogeneity}$=0.393]). Specifically, tegoprazan was had a lower adverse event rate than PPI-based therapy in treating GERD (OR 0.57 [95%CI 0.36-0.92; I^2=0%, $P_{heterogeneity}$=0.726]), while the safety profile between vonoprazan and PPI-based therapy was similar (1.03 [0.83-1.27; I^2=0%, $P_{heterogeneity}$=0.866]; figure 14). Sensitivity analysis revealed similar trends and estimates (supplementary figure S6). Funnel plots for publication bias assessment on the efficacy and safety of PCAB in treating GERD were not generated as the number of studies were less than 10.

Table 5. Summary of meta-analysis on the efficacy of PCAB in treating GERD

Variable	Effect size			Heterogeneity	
	Event/N (Intervention vs Control)	OR (95%CI)	P-value	I^2	$P_{heterogeneity}$
Overall	1532/1624 vs 977/1094	1.62 (1.01-2.61)	0.046	39%	0.149
Vonoprazan vs PPI-based therapy	1226/1303 vs 779/882	1.80 (1.00-3.25)	0.050	52%	0.101
by duration of therapy					
Short-term therapy - 8 weeks	681/719 vs 621/709	2.55 (1.71-3.80)	<0.001	0%	0.404
Long-term therapy - 24 weeks	859/990 vs 391/495	2.17 (1.00-4.72)	0.051	76%	0.040
Long-term therapy - VPZ 10 mg vs Lansoprazole 15 mg	424/495 vs 391/495	1.64 (1.11-2.43)	0.013	13%	0.283
Long-term therapy - VPZ 20 mg vs Lansoprazole 15 mg	435/495 vs 391/495	2.86 (0.79-10.38)	0.111	81%	0.023
by esophagitis grade					
LA classification - Grade A/B	782/822 vs 516/549	1.14 (0.57-2.26)	0.710	0%	0.390
LA classification - Grade C/D	421/451 vs 228/292	3.51 (1.65-7.46)	0.001	44%	0.170
Tegoprazan vs PPI-based therapy	306/321 vs 198/212	1.12 (0.52-2.41)	0.777	0%	0.951

Abbreviation: OR, odds ratio; PCAB, potassium-competitive acid blockers, PPI, proton pump inhibitor; VPZ, vonoprazan.

Table 6. Summary of meta-analysis on the safety of PCAB in treating

Variable	Effect size			Heterogeneity	
	Event/N (Intervention vs Control)	OR (95%CI)	P-value	I^2	$P_{heterogeneity}$
Overall vs PPI-based therapy	321 vs 2123 vs 271/1355	0.90 (0.71-1.14)	0.384	4%	0.393
Vonoprazan vs PPI-based therapy	284/1749 vs 223/1082	1.03 (0.83-1.27)	0.816	0%	0.866
Tegoprazan vs PPI-based therapy	37/374 vs 48/273	0.57 (0.36-0.92)	0.020	0%	0.726

Abbreviations: OR, odds ratio; PCAB, potassium-competitive acid blockers, PPI, proton pump inhibitor.

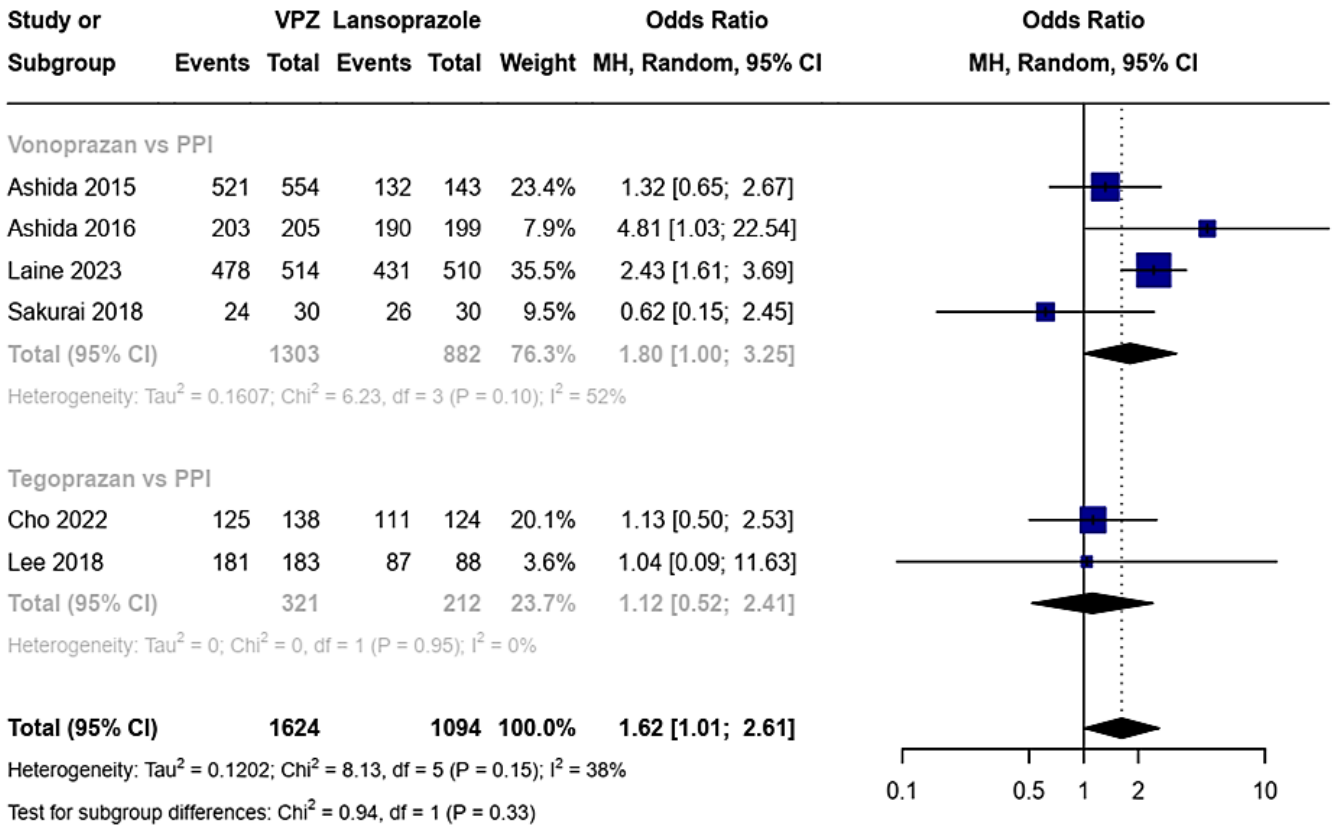

Figure 10. Efficacy of PCAB versus PPI in treating GERD

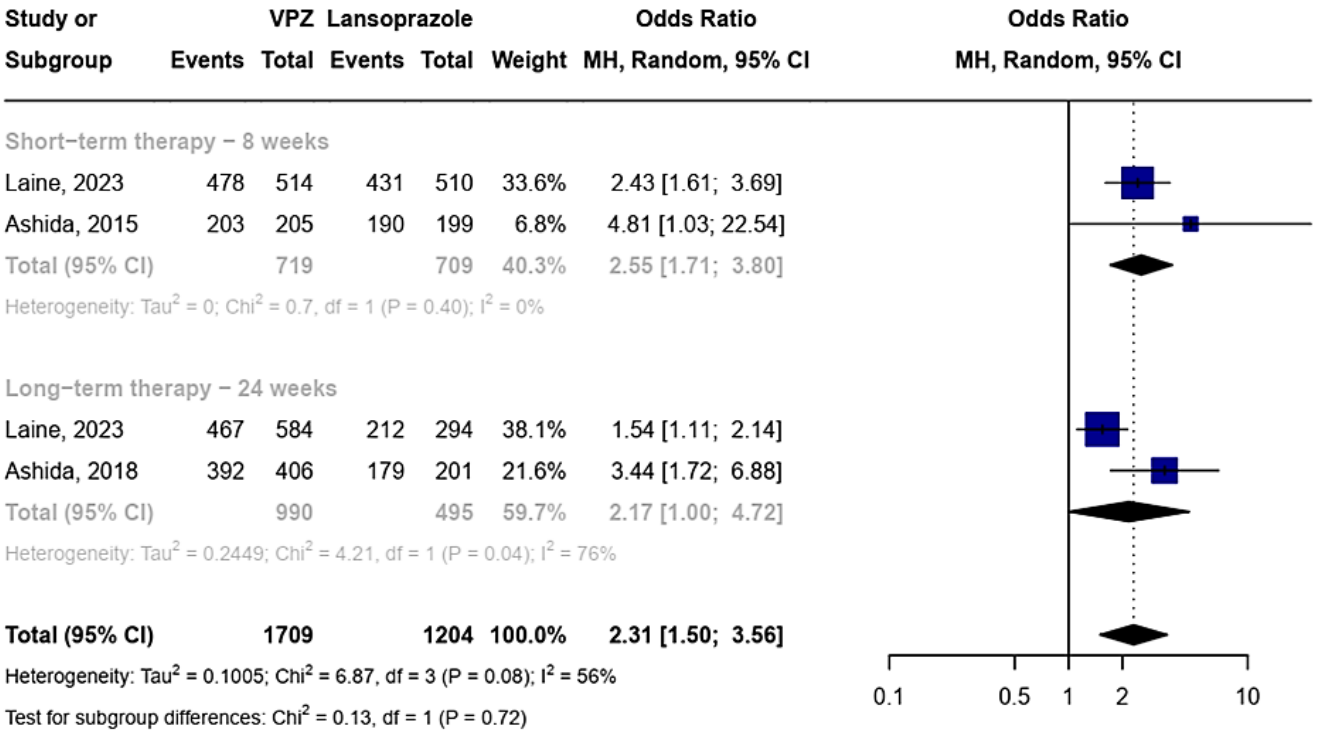

Figure 11. Efficacy of Vonoprazan (VPZ) versus PPI in treating GERD

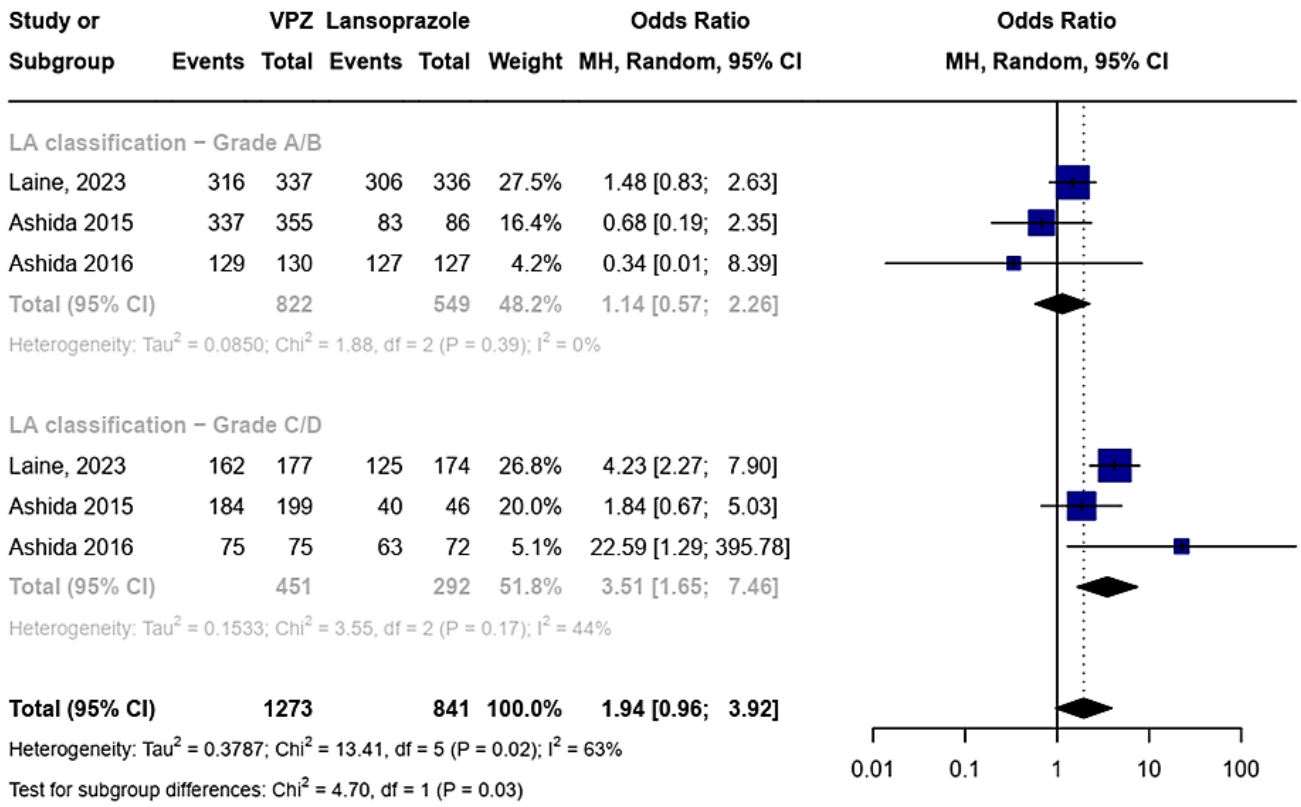

Figure 12. Efficacy of Vonoprazan (VPZ) versus Lansoprazole in treating GERD

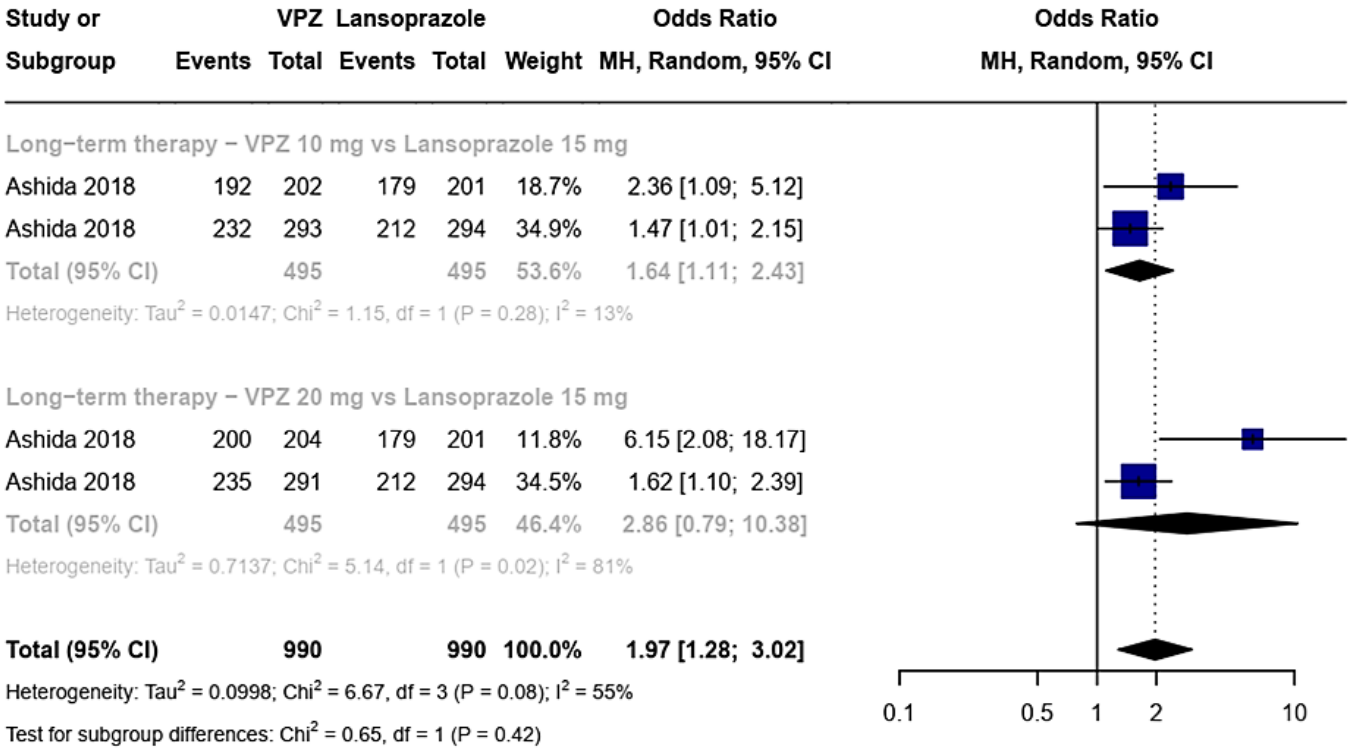

Figure 13. Efficacy of Vonoprazan versus Lansoprazole as maintenance therapy in treating GERD

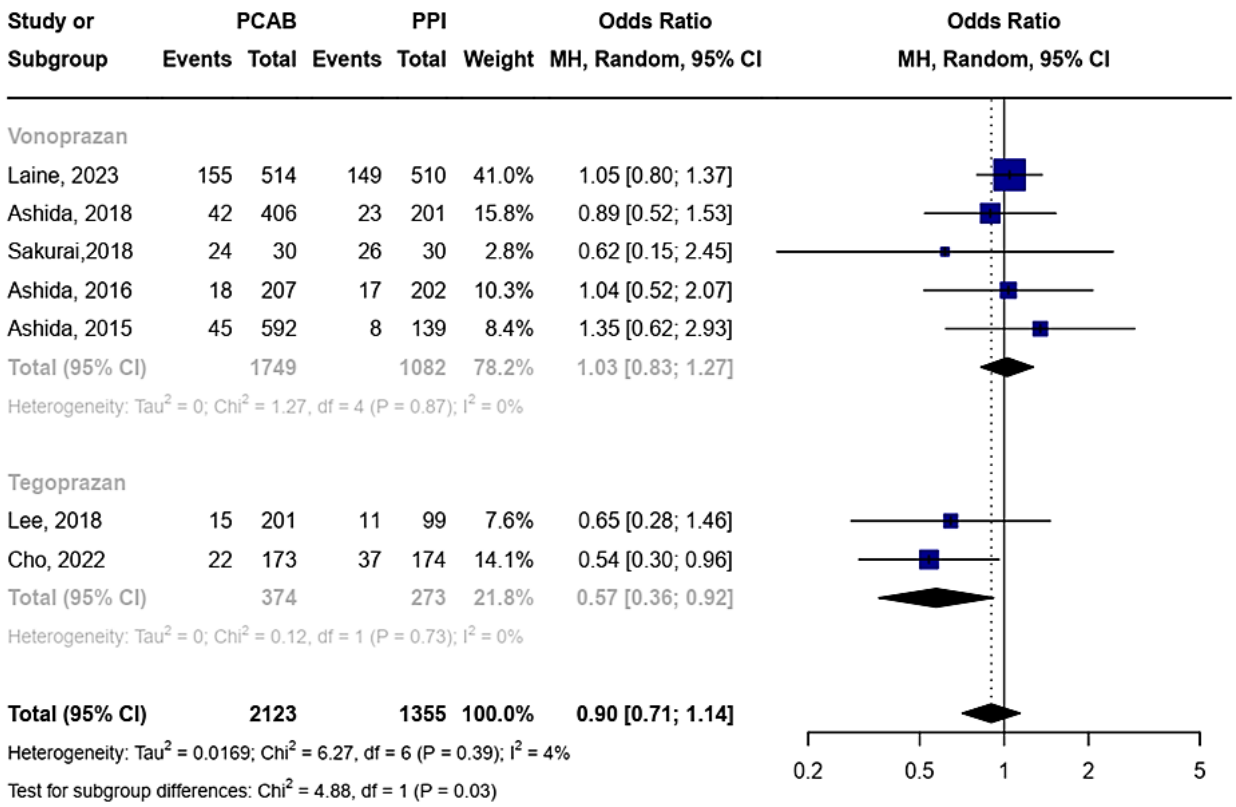

Figure 14. Adverse event of PCAB versus PPI in treating GERD

Discussion

Vonoprazan versus PPI in eradication of H. pylori: This study found no significant difference between vonoprazan duplex therapy and PPI triple or quadruple therapy for eradicating H. pylori. All studies used amoxicillin and vonoprazan, with amoxicillin disrupting bacterial cell walls and effectively working when the intragastric pH exceeds 6 (43-45). Dual therapy with vonoprazan and amoxicillin maintains intragastric pH above 5 throughout the day (46). Several studies comparing vonoprazan-amoxicillin (VA) dual therapy with standard triple therapy or bismuth-containing quadruple therapy have shown that the VA dual therapy is non-inferior and safe (47-49).

A study by Hojo and Sue found no significant difference in the efficacy of vonoprazan compared to PPIs. However, our study showed that triple or quadruple therapy with vonoprazan was more effective than with PPIs, as both PP and ITT analyses indicated (26, 30).The addition of clarithromycin to triple therapy was crucial for H. pylori eradication, although resistance to clarithromycin is high and increasing, particularly in Japan (50). A recent meta-analysis by Jung hasfound no significant difference between vonoprazan-based and PPI-based therapies (51). Another meta-analysis by Li showed similar eradication rates for vonoprazan and PPI therapies in both high-quality RCTs and non-RCTs, though results varied somewhat between the two types of studies (52).

The study found that vonoprazan triple therapy was significantly more effective than lansoprazole and rabeprazole in both ITT and PP analyses. However, there was no significant difference between vonoprazan triple therapy and esomeprazole in either ITT or PP analysis. The vonoprazan 10 mg regimen, even with a shorter treatment duration, achieved a good eradication rate compared to the esomeprazole 14 mg regimen. Shortening the treatment to 10 days, rather than the usual 14 days, has been shown to improve patient adherence, reduce antibiotic resistance, and lower costs (31, 53, 54).

Earlier studies in Asia reported over 95% healing rates for vonoprazan in patients with H. pylori-positive duodenal ulcers, outperforming lansoprazole (55). Vonoprazan was also as effective as lansoprazole in treating peptic ulcers and infections resistant to clarithromycin (56). A trial comparing vonoprazan and rabeprazole showed no significant differences after failed first-line therapy (26) Overall, vonoprazan, especially at 20 mg twice a day, demonstrated superior efficacy in eradicating H. pylori, maintaining a stomach pH of 6.8 over 24 hours (49, 57-59).

Tegoprazan versus PPI in eradication H. pylori: The study found no significant difference in H. pylori eradication between tegoprazan-based and PPI therapies, whether used as triple or quadruple therapy. Both the PP and ITT analyses showed similar results, with odds ratios of 1.08 and 1.02, respectively. Park (2023) reported no significant difference between tegoprazan and esomeprazole, a strong PPI, and also found no difference between tegoprazan and rabeprazole. Tegoprazan can quickly raise intragastric pH, but it does not maintain Ph levels as well as vonoprazan or esomeprazole (35). Kim (2021) also found no significant difference between tegoprazan and lansoprazole (36). Jung (2022) found no significant difference in H. pylori eradication between tegoprazan and rabeprazole. This might be due to the study not testing for CYP2C19 cytochrome status. Most PPIs are metabolized by CYP2C19, but rabeprazole is metabolized through different pathways. Tegoprazan is processed by P450 3A4, so its effectiveness in eradicating H. pylori is similar to rabeprazole in patients with specific CYP2C19 genetic polymorphism (37).

The study found that vonoprazan was more effective than PPI in eradicating H. pylori, whereas tegoprazan showed no significant difference compared to PPI. Increasing the tegoprazan dose from 100 mg to 200 mg once daily raised the median intragastric pH from 5.2 to 6.4. Thus, tegoprazan 100 mg taken twice daily could be effective for H. pylori eradication (37, 60). However, the studies included in this meta-analysis used a lower dose of tegoprazan, which might explain why its results were similar to those of PPI.

Adverse event of used PCAB in the eradication of H. Pylori: The PCAB group experienced fewer adverse events compared to the PPI group, with an odds ratio (OR) of 0.71. Specifically, in the vonoprazan-based group, adverse events were lower than in the PPI group (OR 0.61). In contrast, the tegoprazan-based group showed no significant difference (OR 1.00). Huh's study (2021) noted that PPI therapy often led to dark stools, nausea, dizziness, and vomiting. It found that vonoprazan's safety and tolerability were comparable to those of PPI (61, 62). Ang's study (2022) also showed that side effects like watery stools and flatulence were similar between PPI and vonoprazan groups (27). Choi's study (2022) found more upper abdominal pain with tegoprazan, though the symptoms were mild and improved on their own (18). Park's study (2023) reported that esomeprazole/sodium bicarbonate led to more stomach discomfort and diarrhea compared to tegoprazan, possibly due to sodium bicarbonate's effects on stomach pH and intestinal health. Overall, these studies suggest that tegoprazan is safe to use (35).

Vonoprazan (short-term therapy, long-term therapy) in treating GERD: Our study found that vonoprazan was significantly more effective than PPIs in treating GERD, both in the short term and long term. The study also showed that vonoprazan was significantly better than PPIs in treating severe erosive esophagitis (type C/D) but showed no significant difference compared to PPIs for mild erosive esophagitis (grade A/B). Vonoprazan works by blocking H+, K+-ATPase in gastric cells, leading to stronger and more sustained acid suppression compared to PPIs. This effect is less dependent on the stomach's pH and continues even in acidic conditions. Vonoprazan also reduced the recurrence of erosive esophagitis more effectively in patients with the CYP2C19 genotype, who metabolize PPIs rapidly (41, 63).

In short-term therapy, vonoprazan was notably more effective than PPIs, showing a higher 24-hour intragastric pH > 4 compared to esomeprazole. Although symptom relief after four weeks of treatment was similar for both vonoprazan and esomeprazole, vonoprazan achieved optimal gastric suppression in just one day, whereas PPIs took 3 to 5 days (20, 38). For long-term therapy, vonoprazan's longer half-life (7-8 hours vs. 1-2 hours for PPIs) and its ability to bind to proton pumps in any form make it easier to use and more effective (17). Vonoprazan does not impact liver function and is better tolerated (39). Studies show vonoprazan is as effective as lansoprazole in preventing esophageal erosive recurrence, with better healing rates for severe cases (41).

Tegoprazan in treating GERD: This study found that tegoprazan was similar to PPIs in treating GERD. Tegoprazan, a new PCAB, binds reversibly to the H+/K+-ATPase in parietal cells. Kim's study showed that the time to the first nighttime heartburn-free interval was shorter with tegoprazan compared to esomeprazole, though the difference was not statistically. There was also no significant difference in sleep disorder improvement within 7 days (64). Another study found that tegoprazan 50 mg worked faster at night than both vonoprazan 20 mg and esomeprazole 40 mg (65). Yang's study showed that tegoprazan 50 mg quickly increased intragastric pH within an hour, faster than vonoprazan 20 mg and esomeprazole 40 mg, highlighting the rapid action of tegoprazan in suppressing gastric acid and its potential for treating acute GERD symptoms (65).

Adverse event PCAB in treating GERD: In this study, there was no significant difference in adverse events between vonoprazan and PPI. Common issues in both groups included nasopharyngitis and diarrhea, with complaints generally being mild (17, 41). However, TGZ

showed a lower incidence of adverse events compared to PPI, with 4.5% of patients on TGZ and 4.2% on esomeprazole reporting issues. The most common complaints were mild gastrointestinal symptoms, such as diarrhea, indicating that TGZ is well tolerated (19, 42). This meta-analysis found that vonoprazan is more effective than PPIs for eradicating H. pylori and superior to lansoprazole, and rabeprazole in this regard. In GERD therapy, vonoprazan outperformed PPIs for both short-term and long-term treatment, and was notably better than lansoprazole for managing grade C/D reflux esophagitis. In contrast, tegoprazan showed no significant difference from PPIs in eradicating H. pylori or managing GERD. Both vonoprazan and tegoprazan had fewer adverse events compared to PPIs, with mild side effects making them well tolerated.

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Ethics approval: This meta-analysis study used data from previously published studies, each of which adhered to ethical standards and obtained the necessary ethical approvals. As no new data was collected from human or animal subjects, additional ethical approval was not required for this analysis. The study was conducted in line with established guidelines for systematic reviews and meta-analyses, maintaining respect for data privacy and upholding ethical integrity.

Conflict of interests: The authors have no conflicts of interest to declare.

Authors' contribution: Conceptualization: NNGKD, Data curation: NNGKD, NLPYD, PISLD, KMNP, Formal analysis: NNGKD, NLPYD, PISLD, KMNP, Funding acquisition: IKM, Investigation: NNGKD, NLPYD, PISLD, KMNP, Methodology: NNGKD, NLPYD, PISLD, KMNP, Project administration: NNGKD, Resources: NNGKD, NLPYD, PISLD, KMNP, Software: NNGKD, NLPYD, PISLD, KMNP, Supervision: DAS, IKM, Validation: DAS, IKM, Visualization: DAS, IKM, Writing – original draft: NNGKD, NLPYD, PISLD, KMNP, Writing – review & editing: DAS, IKM, Approval of final manuscript: DAS, IKM.

References

1. Malfertheiner P, Camargo MC, El-Omar E, et al. Helicobacter pylori infection. Nat Rev Dis Primers 2023; 9: 19.
2. Matsumoto H, Shiotani A, Graham DY. Current and future treatment of helicobacter pylori infections. Adv Exp Med Biol 2019; 1149: 211-25.
3. Antunes C, Aleem A, Curtis SA. Gastroesophageal reflux disease. In: StatPearls. Treasure Island (FL): StatPearls Publishing 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441938/. Accessed Nov, 2023.
4. Garza-González E, Perez-Perez GI, Maldonado-Garza HJ, Bosques-Padilla FJ. A review of Helicobacter pylori diagnosis, treatment, and methods to detect eradication. World J Gastroenterol 2014; 20:1438-49.
5. Stanghellini V, Armstrong D, Monnikes H, Bardhans KD. Systematic review: do we need a new gastro-oesophageal reflux disease questionnaire. Aliment Pharmacol Ther 2004; 19: 463-79.
6. Carlsson R, Dent J, Bolling-Sternevald E, et al. The usefulness of a structured questionnaire in assessing symptomatic gastroesophageal reflux disease. Scand J Gastroenterol. 1998; 33: 1023-9.
7. Kusano M, Shimoyama Y, Sugimoto S, et al. Development and evaluation of FSSG: frequency scale for the symptoms of GERD. J Gastroenterol 2004; 39: 888-91.
8. Bardhan KD, Berghofer P. Look but also listen! Request: an assay on a new validated scale to access the outcome of GERD treatment. Digestion 2007; 75: 87-100.
9. Shaw M, Talley NJ, Beebe T, et al. Initial validation of a diagnostic questionnaire for gastroesophageal reflux disease. Am J Gastroenterol 2001; 96: 52-7
10. Shaw M, Dent J, Beebe T, et al. The reflux disease questionnaire: a measure for the assessment of treatment response in clinical trials. Health Qual Life Outcomes 2008; 6: 31.
11. Danjo A, Yamaguchi K, Fujimoto K, et al. Comparison of endoscopic findings with symptom assessment systems (FSSG and QUEST) for gastroesophageal reflux disease in Japanese centers. J Gastroenterol Hepatol 2009; 24: 633-8.
12. Jones R, Junghard O, Dent J, et al. Development of the GerdQ, a tool for the diagnosis and management of gastroesophageal reflux disease in primary care. Aliment Pharmacol Ther 2009; 30: 1030-8.
13. Saragih RH, Rey I. FSSG scale system in comparison with GERD questionnaires in predicting endoscopic

findings with reflux esophagitis. Indonesian J Gastroenterol Hepatol Dig Endosc 2012; 13: 136-40.
14. Maret-Ouda J, Markar SR, Lagergren J. Gastroesophageal reflux disease: a review. JAMA 2020; 324: 2536-47.
15. Roberts LT, Issa PP, Sinnathamby ES, et al. Helicobacter pylori: A review of current treatment options in clinical practice. Life 2022; 12: 2038.
16. Chey WD, Mégraud F, Laine L, et al. Vonoprazan triple and dual therapy for Helicobacter pylori infection in the United States and Europe: randomized clinical trial. Gastroenterology 2022; 163: 608-19.
17. Laine L, DeVault K, Katz P, et al. Vonoprazan versus lansoprazole for healing and maintenance of healing of erosive esophagitis: a randomized trial. Gastroenterology 2023; 164: 61-71.
18. Choi YJ, Lee YC, Kim JM, et al. Triple therapy-based on tegoprazan, a new potassium-competitive acid blocker, for first-line treatment of Helicobacter pylori infection: a randomized, double-blind, phase III, clinical trial. Gut Liver 2022; 16: 535-46.
19. Lee KJ, Son BK, Kim GH, et al. Randomized phase 3 trial: tegoprazan, a novel potassium-competitive acid blocker, vs. esomeprazole in patients with erosive oesophagitis. Aliment Pharmacol Ther 2019; 49: 864-72.
20. Simadibrata DM, Syam AF, Lee YY. A comparison of efficacy and safety of potassium-competitive acid blocker and proton pump inhibitor in gastric acid-related diseases: A systematic review and meta-analysis. J Gastroenterol Hepatol 2022; 37: 2217–28.
21. Shinozaki S, Nomoto H, Kondo Y, et al. Comparison of vonoprazan and proton pump inhibitors for eradication of Helicobacter pylori. Kaohsiung J Med Sci 2016; 32: 255-60.
22. Maruyama M, Tanaka N, Kubota D, et al. Vonoprazan-based regimen is more useful than ppi-based one as a first-line helicobacter pylori eradication: a randomized controlled trial. Can J Gastroenterol Hepatol 2017; 2017: 4385161.
23. Wang X, Teng G, Dong X, Dai Y, Wang W. Efficacy and safety of vonoprazan-amoxicillin dual therapy for Helicobacter pylori first-line treatment: a single-center, randomized, controlled trial. Therap Adv Gastroenterol 2023; 16: 17562848231190976.
24. Li J, Lv L, Zhu Y, Zhou Z, He S. A Modified 14-day dual therapy with vonoprazan and amoxicillin amplified the advantages over conventional therapies for eradication of helicobacter pylori: a non-inferiority clinical trial. Infect Drug Resist 2023; 16: 5637-45.
25. Peng X, Chen HW, Wan Y, et al. Combination of vonoprazan and amoxicillin as the first-line Helicobacter pylori eradication therapy: a multicenter, prospective, randomized, parallel-controlled study. Clin Exp Med 2023; 23: 4011-19.
26. Hojo M, Asaoka D, Takeda T, et al. A randomized controlled study on the effects of triple therapy including vonoprazan or rabeprazole for the second-line treatment of Helicobacter pylori infection. Therap Adv Gastroenterol 2020; 13: 175628482096624.
27. Ang D, Koo SH, Chan YH, et al. Clinical trial: seven-day vonoprazan- versus 14-day proton pump inhibitor-based triple therapy for first-line Helicobacter pylori eradication. Aliment Pharmacol Ther 2022; 56: 436-49.
28. Hou X, Meng F, Wang J, et al. Vonoprazan non-inferior to lansoprazole in treating duodenal ulcer and eradicating Helicobacter pylori in Asian patients. J Gastroenterol Hepatol 2022; 37: 1275-83.
29. Shichijo S, Hirata Y, Niikura R, et al. Vonoprazan versus conventional proton pump inhibitor-based triple therapy as first-line treatment against Helicobacter pylori: A multicenter retrospective study in clinical practice. J Dig Dis 2016; 17: 670-5.
30. Sue S, Ogushi M, Arima I, et al. Vonoprazan- vs proton-pump inhibitor-based first-line 7-day triple therapy for clarithromycin-susceptible Helicobacter pylori: A multicenter, prospective, randomized trial. Helicobacter 2017; 23: e12456.
31. Lu L, Wang Y, Ye J, et al. Quadruple therapy with vonoprazan 20 mg daily as a first-line treatment for Helicobacter pylori infection: A single-center, open-label, noninferiority, randomized controlled trial. Helicobacte 2022; 28: e12940.
32. Zuberi BF, Ali FS, Rasheed T, et al. Comparison of vonoprazan and amoxicillin dual therapy with standard triple therapy with proton pump inhibitor for helicobacter pylori eradication: a randomized control trial. Pak J Med Sci 2022; 38: 965-9.
33. Chen S, Shen W, Liu Y, Dong Q, Shi Y. Efficacy and safety of triple therapy containing berberine, amoxicillin, and vonoprazan for Helicobacter pylori initial treatment: A randomized controlled trial. Chin Med J (Engl) 2023; 136: 1690-8
34. Tanabe H, Yoshino K, Ando K, et al. Vonoprazan-based triple therapy is non-inferior to susceptibility-guided proton pump inhibitor-based triple therapy for Helicobacter pylori eradication. Ann Clin Microbiol Antimicrob 2018; 17: 29.
35. Park CH, Park JH, Jung YS. Comparative efficacy of tegoprazan vs esomeprazole/sodium bicarbonate for the

treatment of Helicobacter pylori infection. Clin Transl Gastroenterol 2023; 14: e00632.
36. Kim JY, Lee SY, Kim H, et al. Efficacy of seven-day potassium-competitive acid blocker-based first-line helicobacter pylori eradication therapy administered with bismuth. Yonsei Med J 2021; 62: 708-16.
37. Jung YS, Kim S, Kim HY, et al. Efficacy and tolerability of 14-day tegoprazan- versus rabeprazole-based triple therapy for eradication of helicobacter pylori: a real-world evidence study. Gut Liver 2022; 17: 711-21.
38. Sakurai K, Suda H, Fujie S, et al. Short-term symptomatic relief in gastroesophageal reflux disease: A comparative study of Esomeprazole and Vonoprazan. Dig Dis Sci 2018; 64: 815–22.
39. Ashida K, Sakurai Y, Nishimura A, et al. Randomized clinical trial: A dose-ranging study of Vonoprazan, a novel potassium-competitive acid blocker, vs. Lansoprazole for the treatment of erosive oesophagitis. Aliment Pharmacol Ther 2015; 42: 685–95.
40. Ashida K, Sakurai Y, Hori T, et al. Randomised clinical trial: vonoprazan, a novel potassium-competitive acid blocker, vs. lansoprazole for the healing of erosive oesophagitis. Aliment Pharmacol Ther 2016; 43: 240-51.
41. Ashida K, Iwakiri K, Hiramatsu N, et al. Maintenance for healed erosive esophagitis: Phase III comparison of vonoprazan with Lansoprazole. World J Gastroenterol 2018; 24: 1550–61.
42. Cho YK, Kim JH, Kim HS, et al. Randomised clinical trial: comparison of tegoprazan and lansoprazole as maintenance therapy for healed mild erosive oesophagitis. Aliment Pharmacol Ther 2022; 57: 72-80.
43. Windham IH and Merrell DS. The interplay between amoxicillin resistance and osmotic stress in Helicobacter pylori. J Bacteriol 2022; 204: e0004522.
44. Song Z, Zhou L, Xue Y, et al. A comparative study of 14-day dual therapy (esomeprazole and amoxicillin four times daily) and triple plus bismuth therapy for first-line Helicobacter pylori infection eradication: a randomized trial. Helicobacter 2020; 25: e12762.
45. Li C, Shi Y, Suo B, et al. PPI-amoxicillin dual therapy four times daily is superior to guidelines recommended regimens in the Helicobacter pylori eradication therapy within Asia: A systematic review and meta-analysis. Helicobacter 2021; 26: e12816.
46. Sakurai Y, Nishimura A, Kennedy G, et al. Safety, tolerability, pharmacokinetics, and pharmacodynamics of Single Rising TAK-438 (Vonoprazan) doses in healthy male Japanese/ non-Japanese subjects. Clin Transl Gastroenterol 2015; 6: e94.
47. Qian HS, Li WJ, Dang YN, et al. Ten-day vonoprazan-amoxicillin dual therapy as a first-line treatment of Helicobacter pylori infection compared with bismuth-containing quadruple therapy. Rom J Gastroenterol 2023; 118: 627–34.
48. Lin Y, Xu H, Yun J, et al. The efficacy of vonoprazan combined with different dose amoxicillin on eradication of Helicobacter pylori: an open, multicenter, randomized clinical study. Ann Transl Med 2022; 10: 987.
49. Suzuki S, Gotoda T, Kusano C, et al. Seven-day vonoprazan and low-dose amoxicillin dual therapy as first-line Helicobacter pylori treatment: A multicentre randomised trial in Japan. Gut 2020; 69: 1019–26.
50. Sugimoto M, Ban H, Hira D, et al. Letter: CYP3A4/5 genotype status and outcome of vonoprazan-containing Helicobacter pylori eradication therapy in Japan. Aliment Pharmacol Ther 2017; 45: 1009-10.
51. Jung YS, Kim EH, Park CH. Systematic review with meta-analysis: the efficacy of vonoprazan-based triple therapy on Helicobacter pylori eradication. Aliment Phamarcol Ther 2017; 46: 106–14.
52. Li M, Oshima T, Horikawa T, et al. Systemic review with meta-analysis: Vonoprazan, a potent acid blocker, is superior to proton pump inhibitors for eradication of clarithromycin-resistant strains of Helicobacter pylori. Helicobacter 2018; 23: 1–8.
53. Dore MP, Farina V, Cuccu M, et al. Twice-a-day bismuth-containing quadruple therapy for Helicobacter pylori eradication: a randomized trial of 10 and 14 days. Helicobacter 2011; 16: 295-300.
54. Jheng GH, Wu IC, Shih HY, et al. Comparison of second-line quadruple therapies with or without bismuth for Helicobacter pylori infection. Biomed Res Int 2015; 2015: 163960.
55. Hooi JKY, Lai WY, Ng WK, et al. Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis. Gastroenterology 2017; 153: 420–9.
56. Murakami K, Sakurai Y, Shiino M, et al. Vonoprazan, a novel potassium-competitive acid blocker, as a component of first-line and second-line triple therapy for Helicobacter pylori eradication: a phase III, randomised, double-blind study. Gut 2016; 65: 1439–46.
57. Sakurai Y, Mori Y, Okamoto H, et al. Acid-inhibitory effects of vonoprazan 20 mg compared with esomeprazole 20 mg or rabeprazole 10 mg in healthy

adult male subjects–a randomised open-label cross-over study. Aliment Pharmacol Ther 2015; 42: 719–30.
58. Jenkins H, Sakurai Y, Nishimura A, et al. Randomised clinical trial: Safety, tolerability, pharmacokinetics and pharmacodynamics of repeated doses of TAK-438 (vonoprazan), a novel potassium-competitive acid blocker, in healthy male subjects. Aliment Pharmacol Ther 2015; 41: 636–48.
59. Sakurai K, Suda H, Ido Y, et al. Comparative study: Vonoprazan and proton pump inhibitors in Helicobacter pylori eradication therapy. World J Gastroenterol 2017; 23: 668–75.
60. Han S, Choi HY, Kim YH, et al. Randomised clinical trial: safety, tolerability, pharmacokinetics, and pharmacodynamics of single and multiple oral doses of tegoprazan (CJ-12420), a novel potassium-competitive acid blocker, in healthy male subjects. Aliment Pharmacol Ther 2019; 50: 751-9.
61. Liou JM, Fang YJ, Chen CC, et al. Concomitant, bismuth quadruple, and 14-day triple therapy in the first-line treatment of Helicobacter pylori: a multicentre, open-label, randomised trial. Lancet 2016; 388: 2355-65.
62. Huh KY, Chung H, Kim YK, et al. Evaluation of safety and pharmacokinetics of bismuth-containing quadruple therapy with either vonoprazan or lansoprazole for Helicobacter pylori eradication. Br J Clin Pharmacol 2022; 88: 138-44.
63. Oshima T, Miwa H. Potent potassium-competitive acid blockers: a new era for the treatment of acid-related diseases. J Neurogastroenterol Motil 2018; 24: 334–44.
64. Kim JS, Seo SI, Kang SH, et al. Effects of tegoprazan versus esomeprazole on nighttime heartburn and sleep quality in gastroesophageal reflux disease: A multicenter double-blind randomized controlled trial. J Neurogastroenterol Motil 2023; 29: 58-64.
65. Yang E, Kim S, Kim B, et al. Night-time gastric acid suppression by tegoprazan compared to vonoprazan or esomeprazole. Br J Clin Pharmacol 2022; 88: 3288–96.