

The Efficacy of Short-Course versus Standard-Course Proton Pump Inhibitor Therapy for Gastroesophageal Reflux Disease: A Systematic Review and Meta-Analysis

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Abstract:

This study aims to systematically evaluate the clinical efficacy and safety of short-course versus standard-course proton pump inhibitors (PPIs) for the treatment of gastroesophageal reflux disease (GERD), thereby providing an evidence-based foundation for the development of individualized clinical treatment regimens. Computerized searches were conducted in PubMed, Embase, Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang Database, and VIP Database to identify randomized controlled trials (RCTs) comparing short-course and standard-course PPI monotherapy for GERD, published up to February 1, 2026. Following literature screening and data extraction, study quality was assessed using the Cochrane risk-of-bias tool. Meta-analysis was performed with RevMan 5.4 software to compare clinical effective rate, symptom recurrence rate, symptom scores, and incidence of adverse reactions between the two groups. Five eligible RCTs were included, encompassing 1,045 patients (512 in the 6-8-week standard-course group and 510 in the 2-4-week short-course group). The meta-analysis revealed that the standard-course group had a significantly higher clinical effective rate than the short-course group (RR=1.10, 95% CI: 1.04-1.16, P=0.001) and a markedly lower symptom recurrence rate (RR=0.73, 95% CI: 0.62-0.85, P=0.0001). No statistically significant difference was observed in the incidence of adverse reactions between the groups (RR=1.96, 95% CI: 0.75-5.12, P=0.17). The overall quality of the included studies was moderate, with some domains showing unclear or high risk of bias. In conclusion, among GERD patients with good PPI tolerance, the 6-8-week standard course is superior to the 2-4-week short course in improving clinical efficacy and reducing recurrence risk, while demonstrating comparable safety. Short-course therapy may serve as an initial treatment strategy for PPI-hypersensitive individuals; however, treatment duration should be selected through comprehensive assessment of individual response and dynamically adjusted as needed.

Keywords:

Gastroesophageal Reflux Disease, Proton Pump Inhibitors, Short-course Therapy, Standard-course Therapy, Meta-analysis

1. Introduction

Gastroesophageal reflux disease (GERD) is a condition in which abnormal reflux of gastric contents causes troublesome symptoms and/or complications [1]. According to data from the Global Burden of Disease study, both the incidence and prevalence of GERD increased significantly between 1990 and 2021. The number of incident GERD cases rose from 180 million to 324.1 million (+80.1%), and the number of prevalent cases increased from 450 million to 825.6 million (+83.2%) [2,3].

The disease primarily manifests as reflux syndrome, including typical symptoms such as heartburn, acid regurgitation, and reflux. Patients may also experience various atypical symptoms, such as epigastric pain, chest pain resembling ischemic heart disease, and sleep disturbances. GERD can further lead to physiological and pathological changes in the oropharynx, including but not limited to hoarseness, globus sensation, frequent throat clearing, chronic cough, increased pharyngeal mucus, and dental enamel erosion, all of which severely impair patients' quality of life [4,5]. Current treatment for GERD mainly involves three major categories of acid-suppressive agents: antacids, proton pump inhibitors (PPIs), and histamine-2 receptor antagonists (H2RAs) [6]. PPIs are recommended as first-line therapy for GERD by multiple guidelines and have been shown to be significantly superior to H2RAs and prokinetic agents, with their efficacy and safety extensively confirmed [7].

However, no uniform standard exists for the optimal treatment duration of PPIs in GERD in clinical practice, and the choice between a 2-4-week short course and a 6-8-week standard course remains highly controversial. Some studies suggest that short-course PPIs can rapidly relieve acute GERD symptoms while reducing the potential risks associated with long-term medication [8,9]; in contrast, other studies indicate that standard-course PPIs achieve higher mucosal healing rates, lower symptom recurrence rates, and better long-term prognosis [10,11,12]. Conventional clinical decision-making for treatment regimens largely relies on physicians' personal experience and lacks robust evidence-based medical support.

Therefore, this study aims to systematically integrate relevant clinical research data through meta-analysis, comparing the clinical efficacy and safety of short-course versus standard-course PPIs in the treatment of GERD, thereby providing a scientific basis for the formulation of individualized clinical treatment strategies.

2. Method

2.1. Search Strategy

All articles were retrieved from six databases including PubMed, Embase, Web of Science, CNKI, Wanfang and VIP before 01 February 2026. The reference list of all included articles were independently screened to identify additional studies left out in the initial search. Supplementary material provides the comprehensive search strategy.

2.2. Eligibility Criteria

2.2.1. Inclusion criteria

- (1) Patients meet the diagnostic criteria for GERD.
- (2) Studies comparing different courses of proton pump inhibitor therapy, with all other intervention conditions identical except for the duration of treatment.

(3) PPI agents included commonly used formulations such as omeprazole, lansoprazole, pantoprazole, rabeprazole, esomeprazole, etc.; standard dose or double dose was used as the defining criterion, with explicit description of administration route and frequency (e.g., once daily [qd] or twice daily [bid]).

(4) Randomized controlled trials only.

2.2.2. Exclusion criteria

(1) Studies for which full text was not available or duplicate publications.

(2) Study types including reviews, editorials, letters, unpublished research, conference abstracts, case reports, dissertations etc.

(3) Studies lacking defined primary or secondary outcome measures.

(4) Studies involving combination drug therapy (i.e., interventions other than PPI monotherapy as defined).

2.3. Study Selection

All studies retrieved from databases were imported into Endnote X9 and removed duplicates. The screening process was conducted in two phases. In the first phase, researcher screened relevant studies based on titles and abstracts. In the second phase, researcher further assessed whether the relevant articles met the inclusion or exclusion criteria.

2.4. Quality Assessment

One investigator independently assessed the quality and risk of bias of the included studies. The quality assessment scale was developed based on the Cochrane Risk of Bias tool in Review Manager (RevMan) 5.4. The main criteria were risk of random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), incomplete outcome data (attribution bias), selective outcome reporting (reporting bias) and other bias. The Cochrane Risk of Bias tool describes the bias as “low risk”, “high risk” and “unclear risk”.

2.5. Data Extraction and Analysis

Data extraction was performed independently by one investigator. Missing or insufficient data was obtained by contacting the corresponding author of the article by E-mail, and if no response was received after one month, the study would be excluded from this systematic review.

Study characteristics extracted clinical characteristics (i.e., author/year, sample size, treatment course, outcome, effective rate and conclusion). For the three-arm randomized controlled trial (Wu 2012), which included 4-week, 6-week, and 8-week treatment groups, only data from the 4-week short-course group and the 8-week standard-course group were extracted for analysis, ensuring consistency with the study’s predefined comparison of short versus standard treatment durations.

All data were analyzed by the Revman 5.4 statistical software. For outcomes were continuous data, we used mean difference (MD) and 95% confidence intervals (CIs). For dichotomous outcomes relative risk (RR) and 95% confidence intervals (CIs) were used, as all included studies were randomized controlled trials (RCTs) and RR can directly reflect the ratio of event rates between groups for intuitive clinical interpretation. Statistical significance was reported at $P < 0.05$.

3. Results

3.1. Article Screening Results

This search retrieved a total of 1,939 relevant articles. After duplicate removal using EndNote, 1,605 articles remained. Following title and abstract screening, 1,583 articles were excluded. Upon full-text review, 17 additional articles were excluded, ultimately resulting in the inclusion of 5 randomized controlled trials. The literature screening process is illustrated in Figure 1.

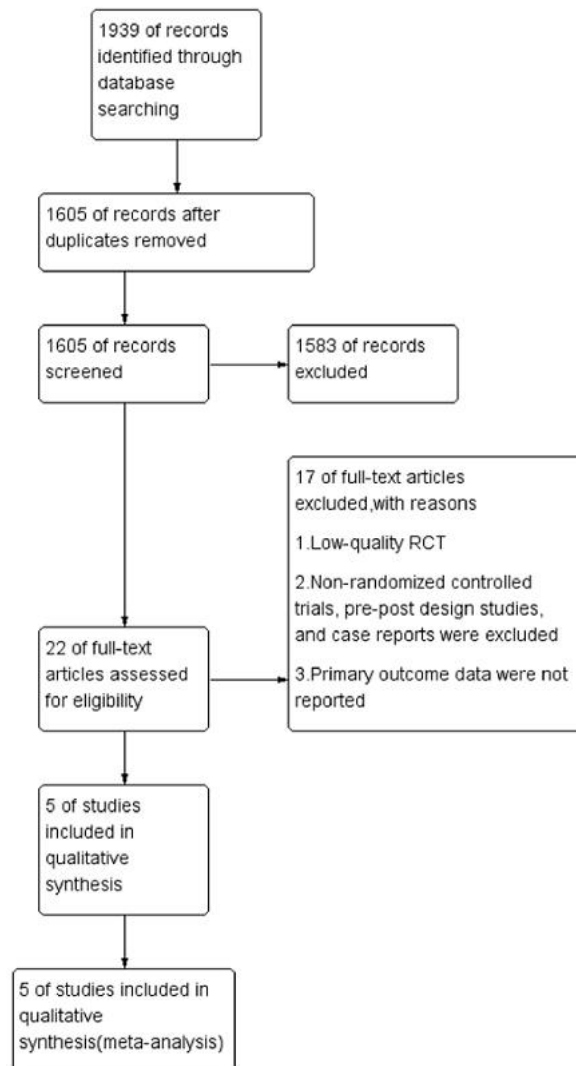


Figure 1. PRISMA flow diagram of study retrieval and selection.

3.2. Basic Characteristics of Included Studies

This study included a total of 5 randomized controlled trials involving 1,045 patients (512 in the experimental group [standard course] and 510 in the control group [short course]). The PPIs used across the studies included commonly employed proton pump inhibitors such as omeprazole and esomeprazole. The experimental group received a 6-8-week course, while the control group received a 2-4-week course. The primary outcome measures reported in each study included clinical effective rate, symptom scores, symptom recurrence rate, and incidence of adverse reactions. In all studies, the GERD diagnostic criteria, baseline patient characteristics, and medication dosages were consistent between the experimental and control groups, ensuring

intergroup comparability. The basic characteristics of the included studies are presented in Table 1.

Table 1. Study characteristics of the included studies.

Author /Year	Sample size (Experimental group / Control group)	Treatment Course (Experimental Group / Control Group)	Outcome	Effective Rate (Experimental Group / Control Group)	Conclusion
Hsu 2015	201/207	8 weeks/ 4weeks	Complete symptom relief rate, 12-week symptom recurrence rate, symptom control failure rate, sustained esophagitis healing rate	Complete symptom relief rate: 82.1%/77.9%; 12-week symptom recurrence rate: 47.8%/62.5%; symptom control failure rate: 57.3%/71.1%; sustained esophagitis healing rate: 40.9%/49.6%	8-week proton pump inhibitor (PPI) therapy did not improve the complete symptom relief rate in patients with mild erosive esophagitis, but reduced the symptom recurrence rate
Feng 2018	92/90	6 weeks/ 4weeks	Symptom score, total effective rate of symptom improvement, total effective rate of endoscopic improvement, adverse reaction rate	Post-treatment symptom score: 1.85±0.14 / 2.94±0.15; total effective rate of symptom improvement: 90.22%/76.67%; total effective rate of endoscopic improvement: 89.13%/73.33%; adverse reaction rate: 3.26%/3.33%	6-week omeprazole therapy is more effective than 4-week therapy for gastroesophageal reflux disease (GERD), with comparable safety
Su 2019	44/43	6 weeks/ 4weeks	Clinical total effective rate, complication rate, symptom score, endoscopic examination score	Clinical total effective rate: 97.73%/83.72%; complication rate: 9.30%/4.55%; post-treatment symptom score: 1.01±0.17 / 1.42±0.24; post-treatment endoscopic score: 0.96±0.08 / 1.37±0.18	6-week omeprazole therapy for GERD has higher efficacy, fewer adverse reactions, and better symptom/endoscopic outcomes
Wu 2012	21/23/19	8 weeks/ 6weeks/ 4weeks	Clinical symptom relief rate, 24-hour esophageal pH monitoring results	Clinical effective rate: 85.71% (8 weeks)/78.26% (6 weeks)/68.42% (4 weeks); number of reflux episodes with pH<4: 43.42±3.51 (8	8-week PPI therapy for GERD is more effective than 6-week and 4-week courses

			(number of reflux episodes with pH<4, total time percentage of pH<4)	weeks)/47.23±3.32 (6 weeks)/50.36±3.78 (4 weeks); total time percentage of pH<4: 6.16±1.93% (8 weeks)/8.29±1.87% (6 weeks)/11.41±1.34 % (4 weeks)	
Sun 2015	154/151	8 weeks/ 2weeks	24-week maintenance symptom control rate, initial treatment symptom relief rate, total success rate, time to first recurrence, patient satisfaction	24-week symptom control rate: 94.9%/87.3%; initial symptom relief rate: 88.3%/83.4%; total success rate: 83.8%/72.8%; risk of first recurrence: reduced by 46% (HR=0.543); satisfaction: 100% (satisfied)/96% (satisfied)	8-week esomeprazole therapy has better symptom control and relief effects than 2-week therapy in Chinese GERD patients, with similar safety

3.3. Quality Assessment Results

This study employed the Cochrane risk-of-bias tool to independently evaluate the quality of the 5 included randomized controlled trials comparing short-course versus standard-course PPIs for GERD treatment across seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases.

Of the 5 included RCTs, 1 explicitly adopted a method for random sequence generation (4 were unclear); 1 study provided a detailed description of allocation concealment (4 were unclear); 2 studies explicitly used an open-label design without blinding of participants and personnel and were rated as high risk (3 were uncertain); blinding of outcome assessment was uncertain in all articles. Four studies completely reported outcome data with no evidence of selective reporting; 1 study was unclear regarding other sources of bias, while the risk of other bias was low. Overall, the quality of the included studies was moderate, with some domains showing unclear or high risk of bias. The risk-of-bias summary is presented in Figure 2 and Figure 3.

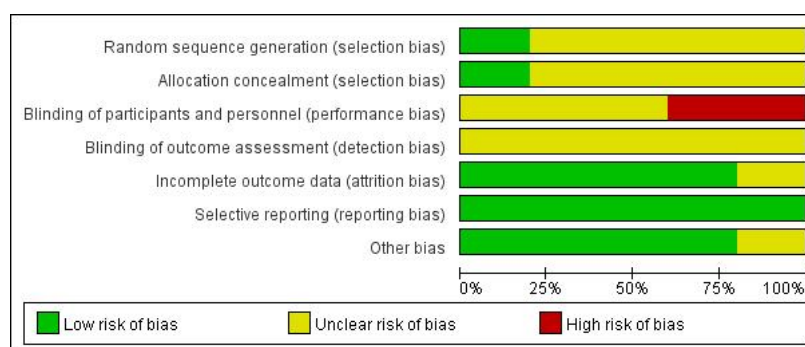


Figure 2. Summary of Risk of Bias Across Included Studies.

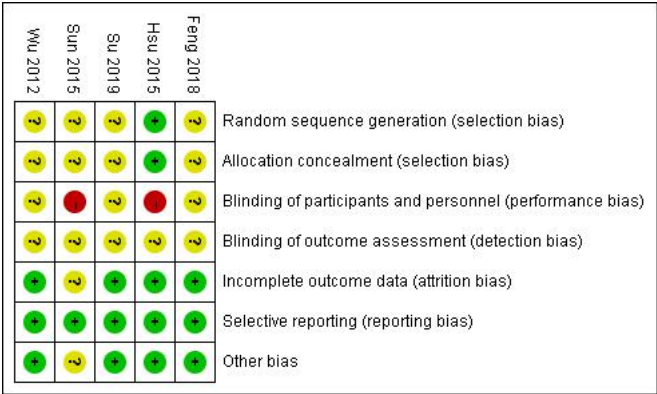


Figure 3. Risk of Bias Graph for Each Included Study.

3.4. Clinical Effective Rate

All 5 studies reported the clinical effective rate, encompassing 1,014 patients (507 in the experimental group [standard-course PPIs] and 507 in the control group [short-course PPIs]). Heterogeneity testing yielded $X^2=4.05$, $P=0.40$, $I^2=1\%$, indicating minimal heterogeneity among studies; therefore, a fixed-effects model was used for meta-analysis. The pooled results showed that the clinical effective rate with standard-course PPIs was significantly higher than with short-course therapy ($RR=1.10$, 95% CI: 1.04-1.16, $P=0.001$), indicating that the standard course confers an advantage in improving clinical response rates (see Figure 4).

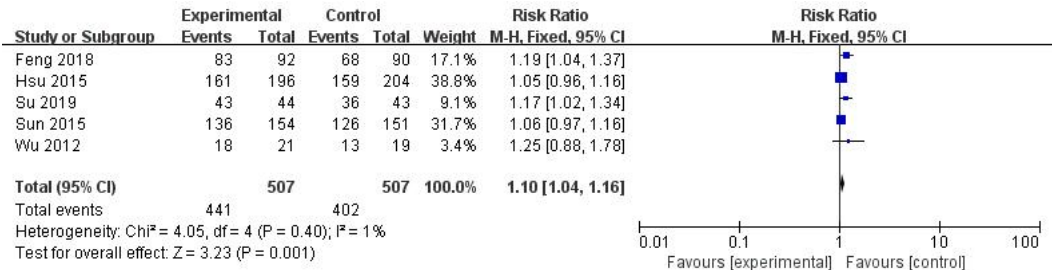


Figure 4. Forest plot of the treatment effect of PPIs therapy on clinical effective rate.

3.5. Symptom Recurrence Rate

Two studies reported the symptom recurrence rate, involving 571 patients (293 in the experimental group [standard-course PPIs] and 278 in the control group [short-course PPIs]). Heterogeneity testing showed $X^2=0.50$, $P=0.48$, $I^2=0\%$, indicating minimal heterogeneity; a fixed-effects model was therefore applied for meta-analysis. The pooled results demonstrated that the symptom recurrence rate in the standard-course group was significantly lower than in the short-course group ($RR=0.73$, 95% CI: 0.62-0.85, $P=0.0001$), indicating that standard-course PPIs can effectively reduce the long-term risk of symptom recurrence in GERD patients (see Figure 5).



Figure 5. Forest plot of the treatment effect of PPIs therapy on Symptom Recurrence Rate.

3.6. Symptom Scores

Two studies reported post-treatment symptom scores, including 269 patients (136 in the experimental group [standard-course PPIs] and 133 in the control group [short-course PPIs]). Heterogeneity testing yielded $X^2=122.99$, $P<0.00001$, $I^2=99\%$, indicating substantial heterogeneity among studies. The pooled results showed that symptom scores in the standard-course group were lower than in the short-course group (SMD=-4.71, 95% CI: -10.13-0.70, $P=0.09$), suggesting superior symptom improvement with the standard course; however, the difference was not statistically significant, and inter-study heterogeneity was extremely high (see Figure 6).

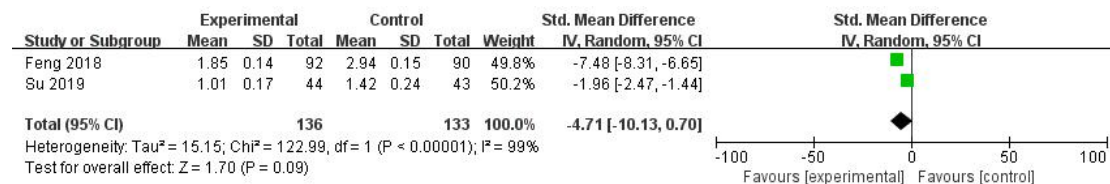


Figure 6. Forest plot of the treatment effect of PPIs therapy on Symptom Index Score.

3.7. Adverse Reaction Rate

Three studies reported the incidence of adverse reactions, involving 574 patients (290 in the experimental group [standard-course PPIs] and 284 in the control group [short-course PPIs]). Heterogeneity testing showed $X^2=1.46$, $P=0.48$, $I^2=0\%$, indicating minimal heterogeneity; a fixed-effects model was used for meta-analysis. The pooled results revealed no statistically significant difference in adverse reaction rates between standard-course and short-course PPIs (RR=1.96, 95% CI: 0.75-5.12, $P=0.17$), indicating comparable safety profiles for the two regimens in GERD treatment (see Figure 7).

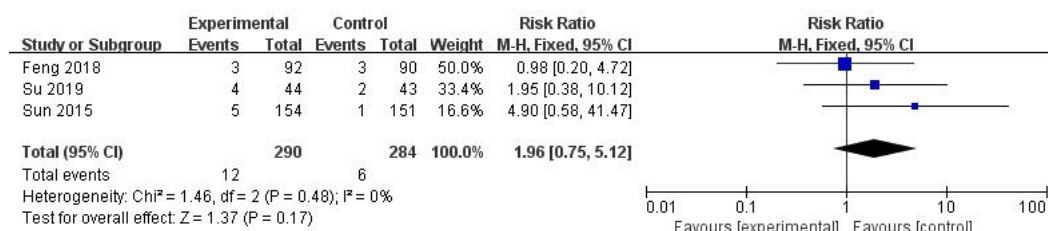


Figure 7. Forest plot of the treatment effect of PPIs therapy on Adverse Effects Rate.

4. Discussion

This meta-analysis systematically integrated data from 5 randomized controlled trials comparing short-course versus standard-course PPIs for GERD treatment. The results demonstrated that the 6-8-week standard course of PPIs achieved a significantly higher clinical effective rate than the 2-4-week short course, effectively reduced symptom recurrence rates, and provided superior symptom improvement, while the incidence of adverse reactions did not differ significantly between the groups. These findings support the extension of treatment to 6-8 weeks for more stable symptom control, with safety comparable to that of the short course.

The meta-analysis of symptom scores indicated superiority of the standard course, although the difference was not statistically significant. This result may be attributable to inconsistencies in the symptom scoring scales used across studies, which affected the pooled effect size. According to the literature data, the overall effective rate for short-course therapy reached 77.8%, while that for standard-course therapy reached 88.9%; the symptom recurrence rate with standard-course therapy was 17.4% lower

than with short-course therapy, and safety profiles were equivalent. Therefore, for patients with good PPI tolerance, the standard course is recommended as the preferred option. Given that the overall effective rate of short-course therapy already reaches 77.8%, short-course treatment may be prioritized as an initial strategy for PPI-hypersensitive individuals, with close monitoring of efficacy and drug response, followed by individualized adjustment of treatment duration and regimen.

PPIs are widely used in GERD treatment. Their mechanism of action involves acid-activated conversion into a reactive cationic sulfenic acid or sulfonamide intermediate, which then forms a disulfide bond with cysteine residues on the accessible outer surface of the H^+/K^+ -ATPase in gastric parietal cells, thereby covalently inhibiting the final key step of gastric acid secretion [13]. The core mechanism of H2RAs is competitive inhibition of H2 receptors on gastric parietal cells, blocking histamine binding and thereby reducing gastric acid and pepsin secretion, which alleviates acid stimulation of the esophageal mucosa. PPIs achieve sustained acid suppression through covalent inhibition of H^+/K^+ -ATPase and are far more potent than H2RAs. Prokinetic agents are a heterogeneous class of compounds acting on various gastrointestinal receptors; their core mechanism involves improving esophageal and gastric motility. Lacking high target selectivity, they frequently exhibit off-target effects, demonstrate limited efficacy as monotherapy for GERD, and are more suitable as adjunctive therapy to PPIs [14]. Consequently, PPIs remain the first-line core agent and gold standard for acid-suppressive therapy in GERD.

Several previous reviews have examined the impact of treatment duration on PPI efficacy in GERD. Huang et al. demonstrated that, within the 2-8-week range, each additional day of therapy was associated with a relative increase in healing rate ($\beta=0.0163$ per day, $p<0.0001$), indirectly supporting the conclusions of the present study [15]. Zhang et al. similarly showed that, in GERD patients receiving twice-daily PPIs, the 8-week course produced significantly superior mucosal healing compared with the 4-week course, further confirming the superiority of standard-course therapy [16].

In recent years, potassium-competitive acid blockers (P-CABs) have gradually been applied in GERD treatment. P-CABs competitively and reversibly bind to potassium ions, inhibiting H^+/K^+ -ATPase on gastric parietal cells and thereby blocking acid secretion [17,18]. Compared with traditional PPIs, they exhibit faster onset and are unaffected by CYP2C19 polymorphism. They demonstrate superiority in healing moderate-to-severe erosive esophagitis, *Helicobacter pylori* eradication, and refractory GERD, and can also be used for extra-esophageal manifestations such as GERD-related chronic cough, with safety comparable to that of traditional PPIs. P-CABs are particularly suitable for patients requiring rapid symptom control, those with poor medication adherence, or non-responders to PPIs, and have become an important option for individualized GERD therapy [19, 20]. Future studies are needed to further clarify the long-term efficacy of P-CABs in non-erosive reflux disease and Barrett's esophagus, optimize dosing regimens for varying disease severity, and accumulate more long-term follow-up data to confirm their efficacy and safety across different GERD phenotypes.

In summary, this study demonstrates that, in patients with gastroesophageal reflux disease, a 6-8-week standard course of proton pump inhibitor therapy yields a significantly higher clinical effective rate and lower symptom recurrence rate than a 2-4-week short course, with comparable safety. Short-course therapy may serve as an

initial regimen for hypersensitive populations, yet the standard course remains the preferred overall option. Mechanistically, PPIs achieve potent acid suppression by blocking the key step in gastric acid secretion and constitute the core drug for GERD treatment. Novel agents such as potassium-competitive acid blockers, as highlighted in recent research, provide new options for individualized therapy.

4.1. Limitations

Although the currently available randomized controlled trials preliminarily confirm the superiority of standard-course therapy over short-course therapy for GERD, the overall sample size remains relatively small, limiting the generalizability and statistical power of the findings. Future research should include large-scale, multicenter, double-blind, high-quality randomized controlled trials to further validate the reliability and stability of these conclusions, while supplementing richer stratified data. Such studies will help confirm and update the present findings, thereby providing higher-level evidence-based medical support for clinical practice.

4.2. Prospects for Future Research

This study explored differences in efficacy and safety between standard-course and short-course therapy for GERD. However, existing research still exhibits limitations such as inconsistent definitions of treatment duration, insufficient patient stratification, and relatively short follow-up periods. Future investigations should include large-sample, multicenter, long-term follow-up randomized controlled trials to further clarify treatment duration requirements across different disease courses, severity levels, and clinical phenotypes—including newly diagnosed versus recurrent patients, LA grades A-D, and erosive versus non-erosive gastroesophageal reflux disease. In addition, the interactive effects of treatment duration with dosing regimens and drug classes should be examined to provide more precise individualized treatment strategies for GERD duration selection.

5. Conclusions

This meta-analysis demonstrates that the 6-8-week standard course of PPIs for GERD yields a significantly higher clinical effective rate than the 2-4-week short course, effectively reduces symptom recurrence rates, and shows no statistically significant difference in adverse reaction incidence between the groups. These findings indicate that the standard course offers statistical advantages in clinical effective rate and recurrence rate while maintaining comparable safety. Although short-course therapy may serve as an initial choice for PPI-hypersensitive populations, the standard course remains the preferred recommendation for GERD treatment overall. Meanwhile, novel agents represented by P-CABs offer superior options for individualized GERD therapy; their long-term efficacy and safety in patients with varying disease severity still require further clarification in future studies.

Conflicts of Interest

The author declares that there is no conflict of interest regarding the publication of this article.

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