Evaluating Multiple Dosing Regimens for Proton Pump Inhibitors (PPI) for the Treatment of Gastroesophageal Reflux Disease (GERD): Systematic Review and Meta-Analysis

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Introduction

- Several PPI dosing options are used to treat GERD with respect to dose (standard, half standard, double standard) and frequency (once or twice daily).
- We performed a systematic review to assess resolution of GERD symptoms, resolution of heartburn, and esophageal healing in regard to various PPI dosages and frequencies.

Methods

- EMBASE and PubMed Search in October 2021 yielded 1381 unique records. (**Figure 1**)
- 51 studies were included in the systematic review, and 37 RCTs were included in the quantitative analysis
- Primary outcomes: resolution of GERD symptoms, resolution of heartburn, esophageal healing ≤ 12 weeks.
- Data abstraction and analysis was performed using Systematic Review Data Repository+, Cochrane Risk of Bias tool (v2), and Stata (**Figure 2**).
- Studies were excluded from quantitative review if they did not report outcomes of interest, only assessed outcomes after 12 weeks, or compared out-of-practice dosages

Figure 1: Study Flow Chart
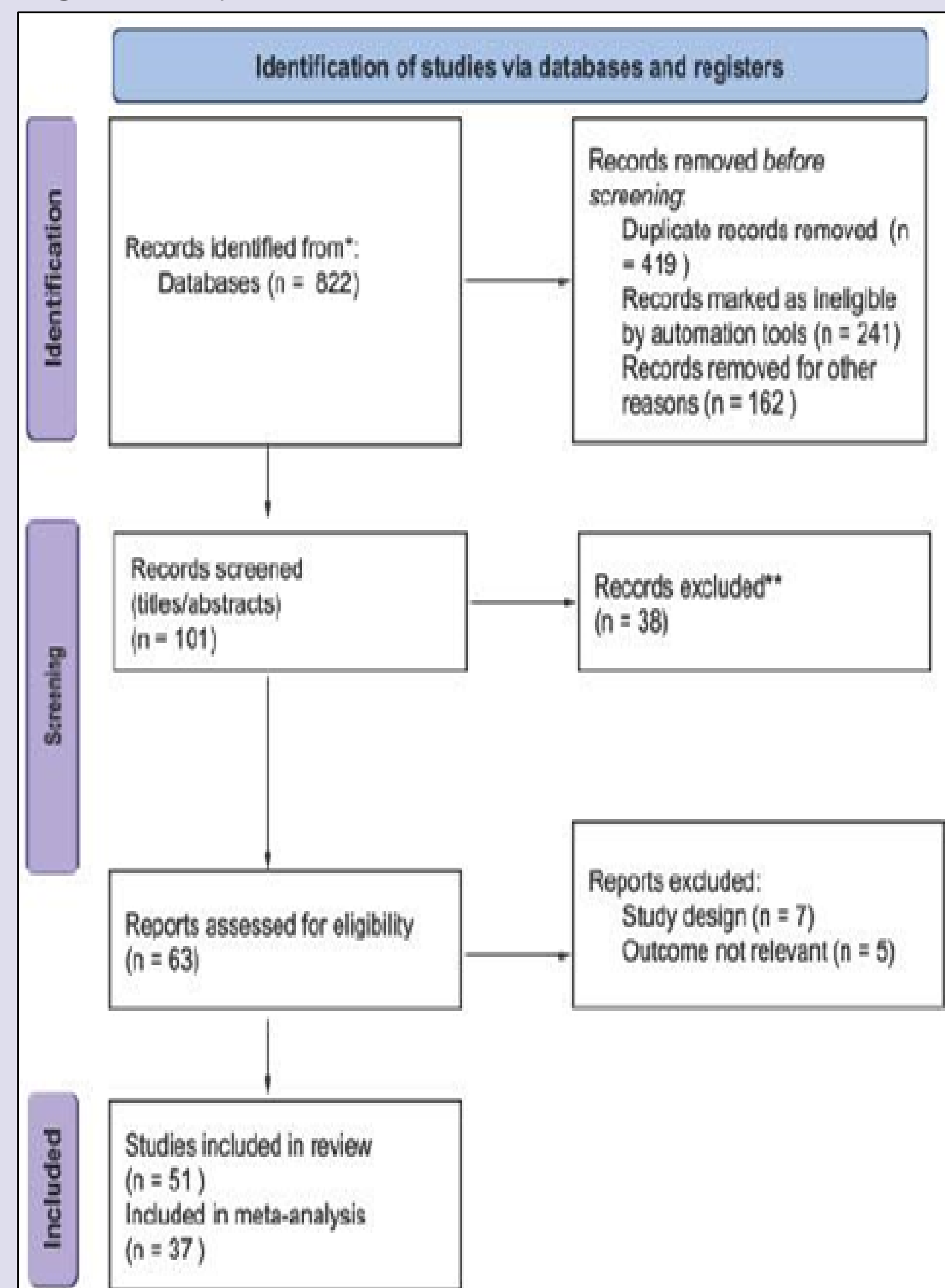
37 studies included Year range: 1991-2018
20,226 total participants
Mean Age (yr): 50.02, Range: 15.2
55.3% Male | 44.7% Female
27 Total Countries

Figure 2: Risk of bias among 37 included RCTs
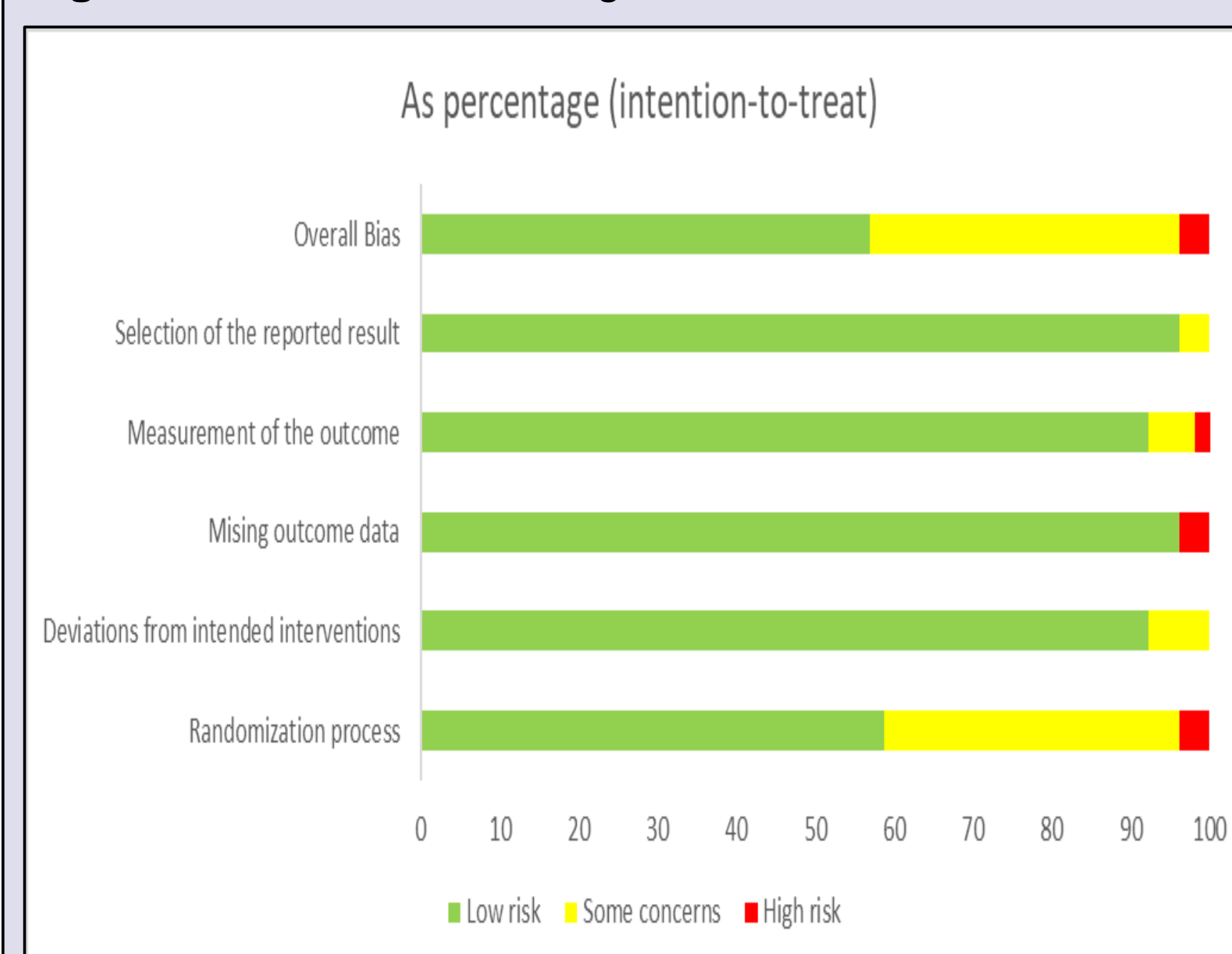
Results

- Most of these 37 trials included in the quantitative analysis compared double standard dose daily vs. standard dose daily or standard dose daily vs. half standard dose daily (**Table 1**).
- When compared to standard dose once-daily, double standard dose once-daily led to improved outcomes for GERD (OR 1.35, 95% CI 1.01-1.75) and esophageal healing (OR 1.62, 95% CI 1.27-2.07) but not heartburn (OR 1.08, 95% CI 0.94-1.24) (**Figure 3**).

Figure 3: Forest plot comparison for Standard dose, QD vs. Double Standard dose, QD in resolution of GERD symptoms (3A) and Heartburn (3B)
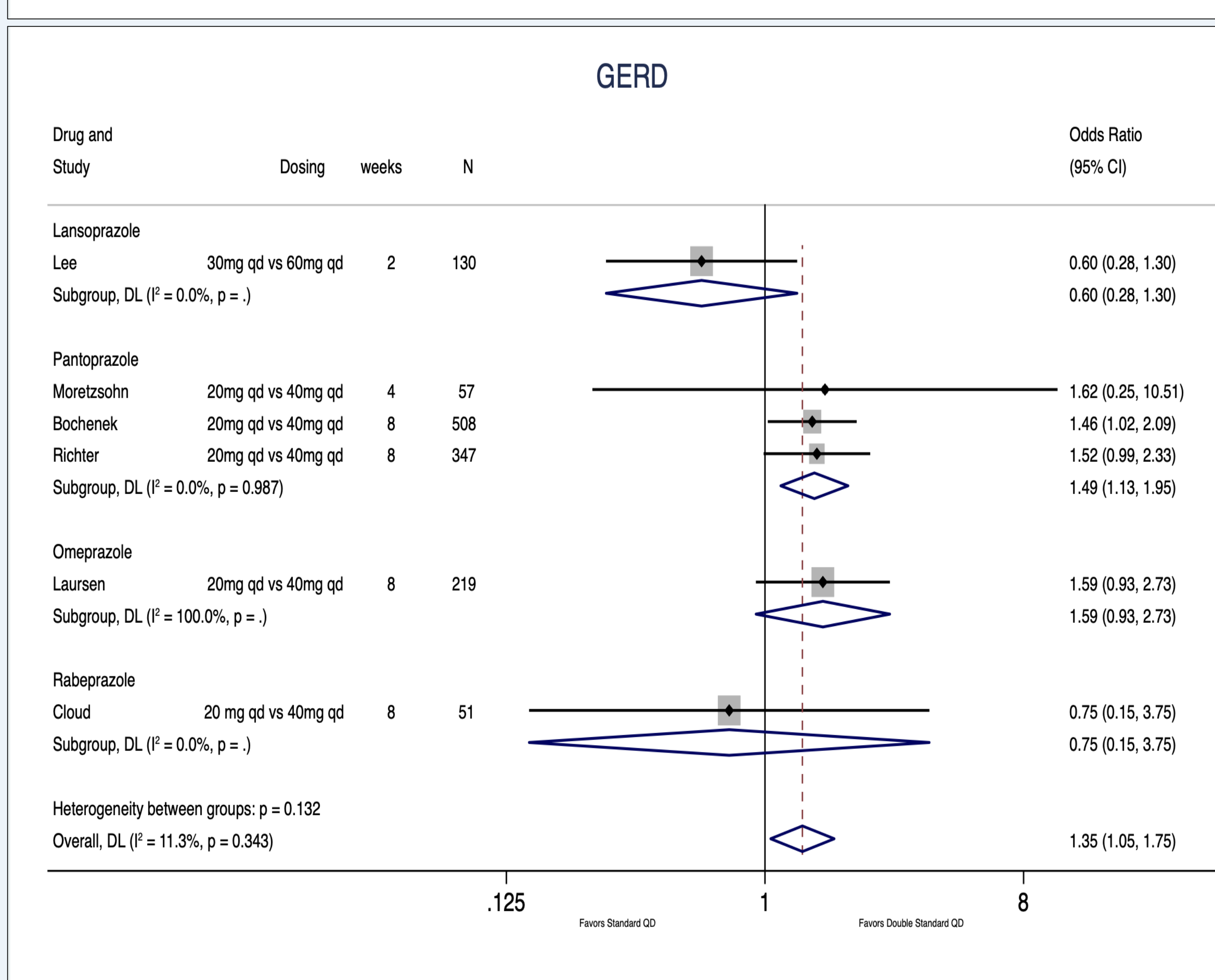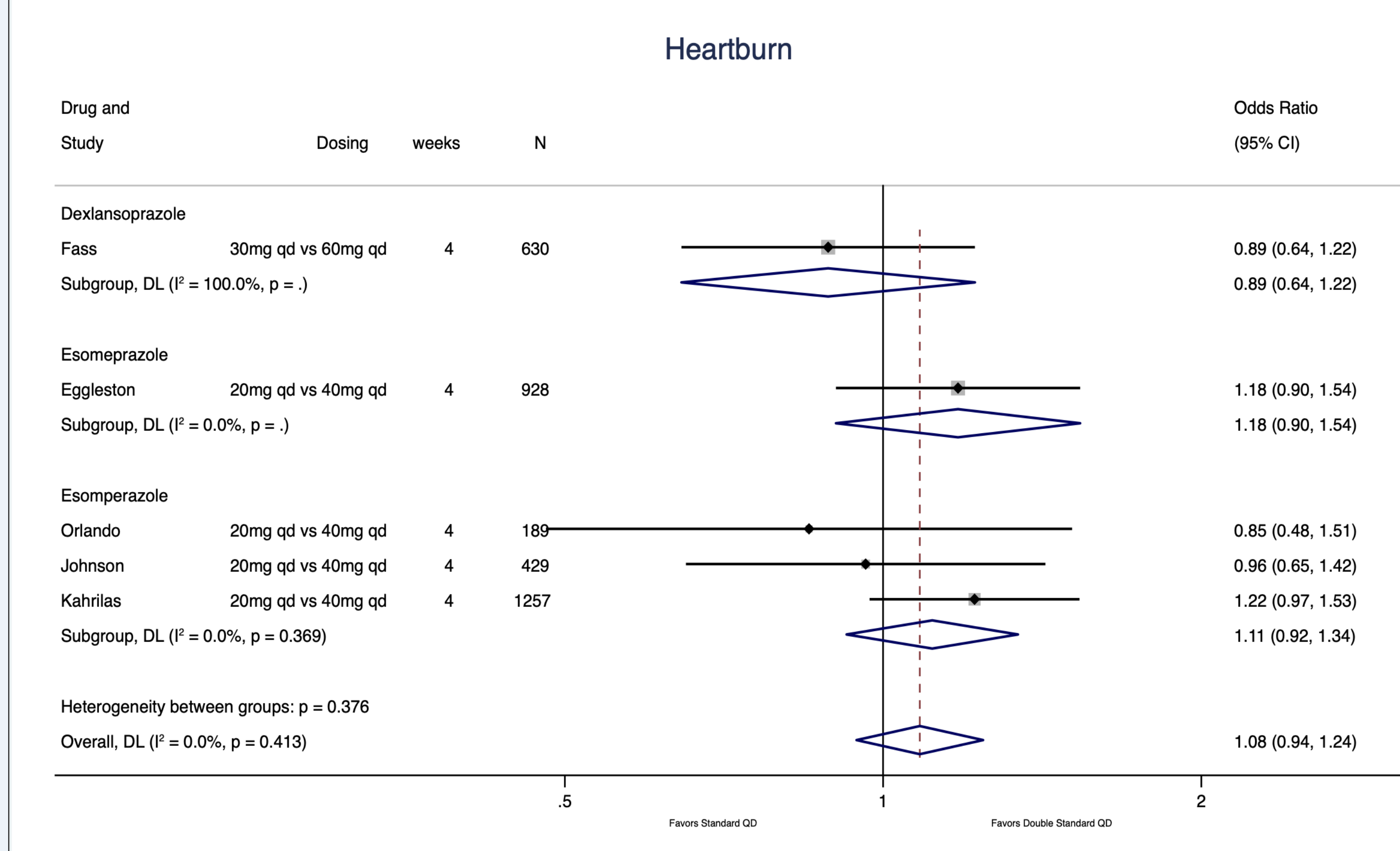

Table 1: Dosing Comparisons across RCTs (≤12 weeks)

Dosing Comparison	RCTs (N)	Patients (n)	Outcome	OR (95% CI)
Standard dose BID vs. Standard dose QD (ref)	1	202	Esophageal Healing	2.34 (1.27, 4.31) *
	1	202	Heartburn	3.03 (1.62, 5.68) *
Double standard dose QD vs. Standard dose QD (ref)	7	2408	Esophageal Healing	1.62 (1.27, 2.07) *
	6	1312	GERD	1.35 (1.05, 1.75) *
	5	3433	Heartburn	1.08 (0.94, 1.24)
Double standard dose, BID vs. Standard dose QD (ref)	1	197	Heartburn	0.77 (0.44, 1.35)
Standard dose QD vs. Half standard dose QD (ref)	9	1762	Esophageal Healing	1.79 (1.44, 2.22) *
	8	1718	GERD	1.42 (1.15, 1.76) *
	14	3327	Heartburn	1.41 (1.17, 1.69) *
Standard dose QD vs. Half standard dose BID (ref)	2	411	Esophageal Healing	1.94 (1.15, 3.26) *
	1	205	Heartburn	2.14 (1.19, 3.85) *
Double standard dose BID vs. Double standard dose QD (ref)	1	190	Heartburn	0.90 (0.51, 1.60)
	1	200	GERD	2.63 (1.30, 5.35) *
Standard dose BID vs. Half standard dose BID (ref)	1	202	Esophageal Healing	0.92 (0.47, 1.79)
	1	203	Heartburn	1.42 (0.74, 2.74)
Half Standard dose, BID vs. Half standard dose QD (ref)	1	324	Esophageal Healing	7.43 (3.81, 14.49) *

*p<0.05

Conclusions

- <u>**Increasing daily PPI dosing was generally associated with improved outcomes in the treatment of GERD symptoms.**</u>
- Further studies are needed to determine whether twice-daily dosing, a common practice used in clinical practice, improves clinical outcomes.