

Gastroesophageal Reflux Disease: Omeprazole versus Lansoprazole – A Systematic Literature Review

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Abstract

Objective: The objective of the study was to evaluate the effectiveness and safety of omeprazole compared to lansoprazole in gastroesophageal reflux (GERD) disease patients. **Methods:** A systematic search of MEDLINE, EMBASE (inception to December 2019), and CENTRAL (January 2011–December 2019) was conducted to identify the relevant articles. A detailed inclusion-exclusion criterion was developed and implemented to screen the abstracts. Full texts of the selected abstracts were then assessed to establish their inclusion or exclusion in our review. Cochrane risk of bias criterion was used to assess the methodological quality of the included studies. All relevant data were extracted and the results were summarized narratively. **Results:** Nine studies met our inclusion-exclusion criteria and were included in this review. **Heartburn and Regurgitation:** In all three trials reporting on heartburn and regurgitation, both omeprazole and lansoprazole were found to be effective in relieving the symptoms of heartburn and regurgitation; however, there was no evidence that one is better than the other. **Intragastric pH:** Five out of six studies reporting on intragastric pH provided the evidence of omeprazole's superiority over lansoprazole in controlling gastric pH. Omeprazole lowered intragastric pH faster and the results lasted longer compared to lansoprazole. The results were statistically significant. **Conclusion:** There is no significant difference in the clinical effectiveness of omeprazole and lansoprazole in relieving symptoms of heartburn and regurgitation. However, omeprazole is more effective in reducing gastric acidity than lansoprazole.

Keywords: Gastroesophageal reflux disease, Heartburn, Intragastric pH, Lansoprazole, Omeprazole, Regurgitation

Introduction

Gastroesophageal reflux disease (GERD) is a digestive disorder. The condition results from the reflux of gastric contents into the esophagus.^[1] Gastroesophageal reflux (GER) is a common condition and is experienced occasionally by a large population. However, if GER occurs persistently more than twice a week, the condition is diagnosed as GERD.^[2] GERD is divided into two categories: Non-erosive esophageal reflux disease (NERD) and erosive reflux disease, also called erosive esophagitis (EE). Frequent flow back of stomach contents into esophagus can irritate the lining of the

esophagus.^[3] The prevalence of GERD varies remarkably throughout the world, with a pooled prevalence of 13.3% worldwide.^[4] However, the prevalence is significantly higher in western countries (20–30%) as compared to Asia (5%). Korea has seen a rise in GERD prevalence in recent year with the latest prevalence figure at 10%, probably attributed by Western diet styles.^[5] Heartburn and regurgitation are the main symptoms in GERD. The patients may also suffer from one or more of the following symptoms: Bad breath, feeling sick, bloating, chest pain, difficult swallowing, tooth decay, and sensation of a lump in



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the throat. Nighttime acid reflux may disrupt sleep, as well.^[6] GERD is caused by frequent acid reflux. The condition occurs because of the dysfunctioning of the lower esophageal sphincter (LES) (the ring of muscles at the bottom of the esophagus, between esophagus and stomach). LES plays a key role in the digestive system. Its opening and closing allow food to pass into the stomach and prevent backflow of stomach contents into the esophagus. GERD occurs when LES fails to function appropriately and allows stomach contents backflow into esophagus either by not closing fully or by opening at wrong times.^[7] Although the cause of weakening of this ring is not always clear, certain factors can increase the risk of this happening. These factors include eating unhealthy or fatty foods in large quantities, being overweight, smoking and alcohol, hiatus hernia, and certain medicines. In addition to these, stress and hormonal changes also increase the risk of developing GERD.^[6]

GERD is usually treated through self-help measures and acid suppressant medications. Self-help measures include changes in lifestyle. GERD patients can manage their condition significantly by adopting following style measures: Cutting down on eating fatty, sweet and spicy food, stop eating before being full, avoiding smoking and alcohol, and reducing coffee consumption. In addition to these, maintaining a correct posture and avoid wearing tight clothes helps to improve the symptoms. Losing weight helps to resolve GERD symptoms in addition to reducing the risk of several other medical conditions such as diabetes, hypertension, and cardiovascular diseases.^[8]

Lifestyle interventions are highly effective for improving reflux symptoms in GERD patients. However, they may not resolve all the symptoms of GERD, and the patients may need pharmacological interventions to solve this medical problem. The most commonly prescribed medication for GERD is proton-pump inhibitors (PPIs). PPI is a group of medication that reduces the secretion of stomach acid. PPIs are among the most widely used GERD medications in the world and are considered the most effective treatment of GERD.^[9] The first one, omeprazole, is on the WHO Model List of Essential Medicines.^[10] There are several PPIs available. Omeprazole and lansoprazole have been available the longest and are among the most commonly used medicines. Although they are structurally and chemically similar, there are relatively few comparisons of these drugs with

each other.^[11] Moreover, they respond differently in different patients and may not be suitable for every patient. The side effects of both of these drugs also vary from patient to patient. There is no systematic review to compare the safety and effectiveness of omeprazole and lansoprazole. We are, therefore, conducting this systematic review to identify the studies comparing the effectiveness and safety of omeprazole and lansoprazole.

Objective

There were two objectives of this systematic review:

- To evaluate the effectiveness and safety of omeprazole compared to lansoprazole in GERD patients.
- To highlight the gap in the evidence.

Methods

This systematic review was conducted to identify evidence comparing the efficacy and safety of omeprazole and lansoprazole. We followed PRISMA reporting guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) for this systematic literature review.^[12] We aimed to apply a rigorous and transparent methodology to reduce bias in the selection of relevant studies.

Criteria for considering studies for this review

Eligibility criteria

Eligibility criteria for including studies for this systematic literature review were as follows:

Type of studies

All published randomized controlled trials, including cluster and cross-over trials, were eligible for inclusion in this systematic review. In addition to this, non-randomized clinical trials, cohort, case-control, cross-sectional studies and systematic reviews were also eligible for inclusion. Systematic reviews were included for cross-referencing. We, however, excluded letters to the editor, narrative reviews, editorials, expert opinions, case studies, and case series.

Types of participants

Adult patients (over 18 years) with NERD were included in this systematic review. We excluded studies investigating patients with other conditions,



including EE. Studies on adolescents and children under the age of 18 years, including neonates and infants with NERD, were excluded. We also excluded the studies focusing on treating NERD symptoms in patients with other diseases.

Types of interventions

Studies comparing omeprazole and lansoprazole were included in this systematic review.

Outcomes

The primary outcomes were heartburn and regurgitation. The secondary outcomes were intragastric pH and treatment-emergent adverse effects.

Data sources and search strategy

We systematically searched three databases; Medline, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) for this review. Medline and Embase were searched through ProQuest from inception to December 2019 while CENTRAL was searched to retrieve the relevant literature of the past 9 years (January 2011–December 2019). The search strategy used for Medline and Embase is reported in the Supplementary Materials and was constructed from search terms relating to GERD, to omeprazole and lansoprazole. The search was narrowed by applying filters to limit the studies only to abstracts, English language, and human. The search was not limited by age group at this stage. The reference lists of relevant studies were also screened to identify other relevant studies. The search results were downloaded and imported in reference management software “Zotero.”

Study selection

The studies were screened in abstract screening software “Rayyan”^[13] by two researchers by title and abstracts and discrepancies were resolved through discussion. Primary research studies and systematic reviews relevant to patients with GERD, reporting intervention effectiveness and safety outcomes and published in English, were included in our research. We excluded all children and infants studies. The inclusion and exclusion criteria are reported in full in Table 1 in Supplementary Materials. The full texts were retrieved for all studies that met the inclusion criteria for the title and abstract

screening. Full texts were screened using the same inclusion criteria as abstract screening but focused on identifying studies with clinically relevant outcomes. Two researchers independently conducted full-text screening and resolved the disagreements through discussion.

Data extraction

A pre-agreed MS Excel template was used to extract the relevant data. The data from the included studies were extracted by one reviewer, and all data extraction tables were checked by a second reviewer. All included studies were assessed for methodological quality using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions.^[14] The results were synthesized narratively to identify common themes and gaps in the evidence.

Results

The database search of MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL) identified 2161 citations, of which 635 were duplicates, leaving 1526 unique citations for screening [Table 2]. We identified many studies that compared omeprazole or lansoprazole with other interventions, but the evidence based on the direct comparative effectiveness of omeprazole and lansoprazole was limited. Twenty-one articles were identified as potentially meeting the inclusion criteria and were retrieved as full texts, and nine of these were subsequently included in the review [Figures 1-3].

Participants and study designs

Nine studies included in the systematic review all described primary research on GERD symptoms. Two of these studies were conducted on healthy volunteers^[15,16] while all others were conducted on GERD patients. Six studies included in this review were the primary reports of the randomized cross-over studies;^[15,17-21] of these, one study was randomized double-blinded clinical trial;^[16] one was randomized, parallel-group comparative study;^[22] one was randomized, open-label trial^[21] and one was randomized clinical study.^[23] All subjects were adults (over 18 years) males and females. All included studies reported our outcomes of interest. The study characteristics of included studies are reported in Table 3. Nine studies



Table 1: Inclusion and exclusion criteria

Category	Inclusion criteria	Exclusion criteria
Population	Adult patients (older than 18 years of age) with non-erosive esophageal reflux disease (NERD).	<ul style="list-style-type: none"> • Studies investigating patients without NERD • Studies on patients younger than 18 years of age with NERD • Studies treating NERD symptoms in patients with other diseases
Outcomes	<ul style="list-style-type: none"> • Primary symptoms included heartburn and regurgitation. • Intragastric pH • Adverse effects 	<ul style="list-style-type: none"> • Articles without relevant data on any of the outcomes of interest • Genetic profiling studies • Phenotype-guided dosing studies • Prevalence studies • Studies assessing our interventions' effect for <i>Helicobacter pylori</i> gastritis or eradication. • Studies coadministering omeprazole or lansoprazole with other drugs (PPI or other) • Studies comparing our PPI with Chinese traditional medicine/herbal drug • Studies assessing the effect of combination therapies. • Studies comparing our interventions with surgical treatments.
Study design	<ul style="list-style-type: none"> • Cohort studies • Case-control studies • Cross-sectional studies • Randomized controlled trials • Database studies • Systematic reviews • Cross-over studies 	<ul style="list-style-type: none"> • Letters to the editor • Narrative reviews • Editorials • Expert opinions • Case studies • Case series
Year of Publication	From inception to December 30, 2019, for Medline and Embase January 2011 to December 2019 for CENTRAL	Studies before January 1, 2011, and after December 13, 2019 (for CENTRAL only)
Language	English language	Non-English language
Filter applied	Human, abstracts	

Table 2: Total number of studies identified from database searches

Source	Number of hits	Total after deduplication
PubMed	576	1526
Embase	1419	
Central	166	

reporting on our outcomes of interest enrolled a total of 418 participants, undergoing omeprazole and lansoprazole treatment at 1:1 ratio in parallel studies. In all studies, baseline characteristics were comparable between the two interventions.

Interventions

Patients were treated with 20 mg omeprazole and 30 mg lansoprazole in cross-over trials in

Funaki *et al.* (2013),^[17] Katz *et al.* (2000),^[15] and Janczewska *et al.* (1998).^[20]

In Katz *et al.* (2001), the subjects were divided into two separate trials; study 1 and study 2. In study 1, the subjects were assigned 20 mg omeprazole and 30 m lansoprazole while in study 2, the subjects were offered 40 mg omeprazole and 30 mg lansoprazole. An equal number of subjects were treated first with omeprazole or lansoprazole in this cross-over trial. The drugs were administered openly but in random order in each trial.^[19]

Miner *et al.* (2010) administered 20.6 mg omeprazole and 15 mg lansoprazole in healthy volunteers in a randomized double-blind trial to establish the superiority of one drug over the other one.^[16]

Vivian *et al.* (1999) randomized the patients into two groups using a random number chart in this cross-over study. One group received omeprazole 20 mg once daily for 2 weeks then omeprazole



Table 3: Characteristics of studies included in this review

Reference	Country	Participants (n)	Male n (%)	Focus of the study
Arezoomandi <i>et al.</i> [23]	Iran	120	NR	Heartburn and regurgitation
Funaki <i>et al.</i> [17]	Japan	10	NR	Gastric pH
Miner <i>et al.</i> [16]	USA	40	28 (70%)	Gastric pH
Fass <i>et al.</i> [22]	USA	95	NR	Heartburn and regurgitation
Vivian <i>et al.</i> [18]	USA	27	26 (96%)	Heartburn and regurgitation
Katz <i>et al.</i> [19]	USA	36	6 (17%)	Gastric pH
Katz <i>et al.</i> [15]	USA	20	10 (50%)	Gastric pH
Howden <i>et al.</i> [21]	USA	55	NR	Gastric pH
Janczewska <i>et al.</i> [20]	Sweden	14	NR	Gastric pH

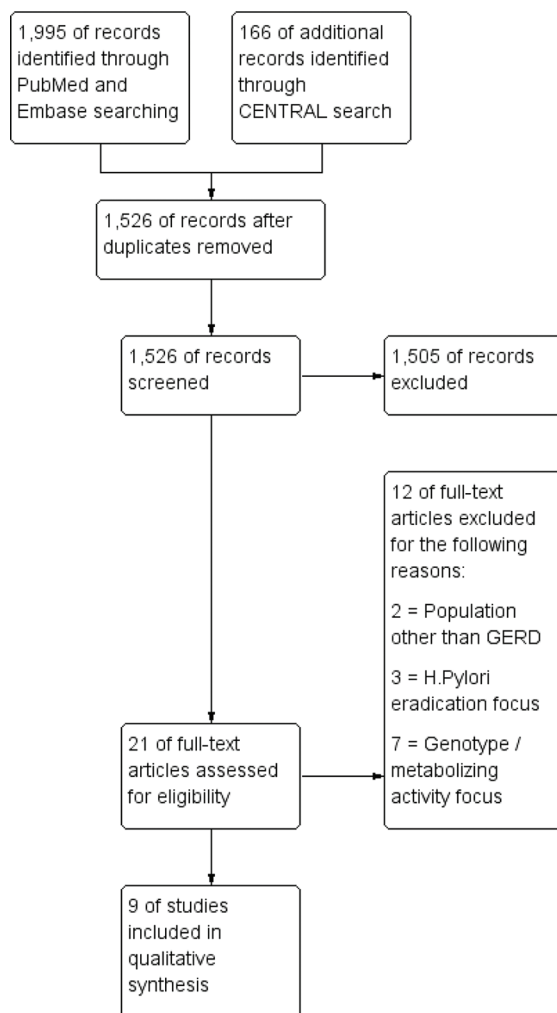


Figure 1: PRISMA flow diagram

40 mg once daily for an additional 2 weeks while the other group received lansoprazole 15 mg once daily

for 2 weeks then lansoprazole 30 mg once daily for an additional 2 weeks. Both groups switched over the medication after 1-week washout.^[18]

Fass *et al.* (2000) administered 40 mg omeprazole and 30 mg lansoprazole in severe symptomatic GERD patients for 6 weeks to determine the clinical effectiveness of these interventions.^[22]

Arezoomandi *et al.* (2019) administered 40 mg omeprazole and 30 mg lansoprazole for 8 weeks to evaluate the effects of omeprazole and lansoprazole on the symptoms of GERD.^[23]

Howden *et al.* (2009) conducted a 3-period cross over study to compare the effects of 40 mg omeprazole, 30 mg lansoprazole, and 40 mg pantoprazole on intragastric acidity.^[21]

Outcomes

Heartburn and regurgitation

Three studies reported on heartburn and regurgitation.^[18,22,23] Arezoomandi *et al.* (2019) reported a significant reduction in heartburn and regurgitation between 0 and 8 weeks of treatment ($P < 0.001$). However, there was not a significant difference between the interventions in reducing GERD symptoms. Fass *et al.* (2000) reported equal effectiveness and tolerance for omeprazole and lansoprazole in symptom control of patients with GERD. Although both interventions were successful in improving the symptoms, there was no significant evidence that one is better than the other. The outcomes from Vivian *et al.* (1999) study were similar to the above studies, and the authors were not able to conclude the clinical effectiveness superiority of one intervention over the other.



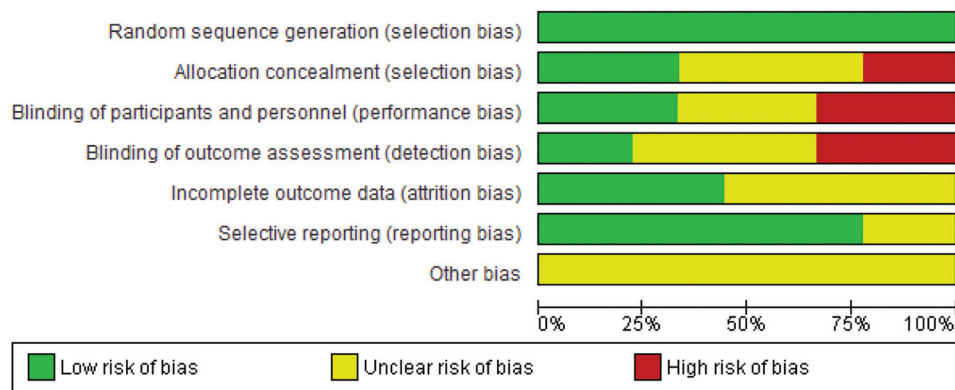


Figure 2: Risk of bias graph. Review authors' judgments about each risk of bias item presented as percentages across all included studies

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Arezoomandi 2019	+	?	?	+	?	?	?
Fass 2000	+	?	?	?	+	+	?
Funaki 2013	+	+	+	+	+	?	?
Howden 2009	+	?	-	-	+	+	?
Janczewska 1998	+	+	+	?	+	+	?
Katz 2000	+	-	-	-	?	+	?
Katz 2001	+	-	-	-	?	+	?
Miner 2010	+	+	+	?	?	+	?
Vivian 1999	+	?	?	?	?	+	?

Figure 3: Risk of bias summary. Review authors' judgments about each risk of bias item for each included study

Gastric pH

Six studies reported on intragastric pH;^[15-17,19-21] four of these studies were conducted on GERD patient^[17,19-21] while two were conducted on healthy volunteers.^[15,16] Omeprazole showed a significant increase in pH, compared with lansoprazole ($P < 0.05$) in Funaki *et al.* (2013). The patients in Katz *et al.* (2001) study were divided into two groups. Group 1 was given 30 mg lansoprazole and 20 mg omeprazole while Group 2 was given 30 mg lansoprazole and 40 mg omeprazole. The authors found no significant difference in intragastric pH in Group 1 patients who were treated with either 30 mg lansoprazole or 20 mg omeprazole. However, in Group 2 patients, omeprazole 40 mg provided statistically significantly higher increase in intragastric pH than with lansoprazole 30 mg. Similar results were found in Howden *et al.* (2009). The authors observed an extended period of high gastric pH ($pH > 4$) with omeprazole than with lansoprazole ($P = 0.005$). Although both drugs were well tolerated, median intragastric pH was significantly higher with omeprazole than with lansoprazole ($P = 0.003$). In contrast to the above three, Janczewska *et al.* (1998) found lansoprazole 30 mg more effective than omeprazole 20 mg in reducing gastric acidity.

In both studies conducted on healthy volunteers, omeprazole appears to be more effective than lansoprazole in gastric acid control. In healthy volunteers, twice-daily dosing of omeprazole 20 mg appears to be significantly more effective than lansoprazole 30 mg in controlling gastric acidity. The clinical importance of such a difference remains to be defined in GERD patients.^[15] Omeprazole-Mg



20.6 mg provided a statistically significantly ($P < 0.0001$) greater acid control than lansoprazole 15 mg.^[16] The authors reported that there were no serious adverse effects.

Discussion

Rapid acid suppression is vital to control unpleasant reflux symptoms in the treatment of GERD.^[17] Omeprazole and lansoprazole are the most commonly used PPIs to treat GERD symptoms. Although there is a risk of increased bacterial growth and spontaneous bacterial peritonitis with PPI therapy,^[24] they have been proven safe and effective to treat non-erosive reflux disease (NERD). None of the studies in our systematic review reported any serious adverse effects, which also provides evidence that omeprazole and lansoprazole are safe and effective to use at least for a short period. However, this review only focused on NERD, and the implications may be different for erosive reflux disease.

Although no studies in our systematic review have provided any evidence of the superiority of omeprazole and lansoprazole in terms of clinical effectiveness, both interventions were successful in providing heartburn and regurgitation symptoms relief. The effect of these interventions is, however, limited.^[5] There is significant evidence that change in lifestyle can improve GERD symptoms^[25] and that combining lifestyle interventions with PPIs provide better results.^[8] In addition to this, combining omeprazole with other drugs like baclofen is a more effective treatment for heartburn and regurgitation than omeprazole alone.^[26] Increasing the dose may also be an option to increase gastric pH and improve reflux symptoms. However, this, in turn, may change the absorption of trace elements. A study conducted in Iran found significantly lower levels of zinc (Zn) in males after omeprazole consumption.^[27] Omeprazole is also effective in controlling nocturnal acid in patients who suffer from nighttime heartburn. A study conducted in the USA concluded that bedtime immediate relief omeprazole (IR-OME) provided more rapid control of nighttime gastric pH and decreased nocturnal acid breakthrough (NAB) compared with lansoprazole.^[28]

All the studies in this review favored omeprazole in increasing gastric pH and reducing GERD symptoms except one conducted in Sweden by Janczewska *et al.*, however, the small sample size ($n = 14$) in this trial makes the results less generalizable. We had not found any other study concluding lansoprazole

superiority over omeprazole. This does not mean that omeprazole always performs better than lansoprazole. There are several case studies which demonstrate non-tolerability of omeprazole and excellent tolerability and effectiveness of lansoprazole. However, case studies were excluded to meet inclusion and exclusion criteria of this research. There is a significant evidence base on the superiority of lansoprazole when compared with other interventions or placebo but this review only included the studies which were comparing omeprazole and lansoprazole.

Two-third of the studies in our review were cross-over trials. More double-blinded RCTs are needed to establish a true superiority of our interventions. We did not find any observational studies which met our inclusion criterion. Although RCTs are considered as gold standard, additional evidence from observational studies would not only improve the strength of our evidence but also enhance our understanding regarding long-term use of omeprazole and lansoprazole. Hence, there is a need to design and conduct high-quality observational studies.

Conclusion

There is no significant difference in the clinical effectiveness of omeprazole and lansoprazole in relieving symptoms of heartburn and regurgitation. However, omeprazole is more effective in increasing intragastric pH than lansoprazole. Both interventions are safe to use with only mild side effects which disappear when discontinued.

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Supplementary material

Search strategy for Medline and Embase			
Set#	Searched for	Databases	Results
S1	(MJMESH.EXACT.EXPLODE("Gastroesophageal Reflux"))	MEDLINE®	19260*
S2	(ti,ab(GER OR GERD OR GORD))	MEDLINE®	11945*
S3	(ti,ab("acid reflux" or "chronic acid reflux"))	MEDLINE®	2366°
S4	(ti,ab("heart burn and acid reflux"))	MEDLINE®	0°
S5	(ti,ab("gastroesophageal reflux disease" or "gastro esophageal reflux disease"))	MEDLINE®	11142*
S6	(ti,ab("gastroesophageal reflux" or "gastro esophageal reflux"))	MEDLINE®	19159*
S7	(ti,ab("gastro-oesophageal reflux disease" or "gastro oesophageal reflux disease"))	MEDLINE®	2125°
S8	S7 OR S6 OR S5 OR S4 OR S3 OR S2 OR S1	MEDLINE®	30922*
S9	MJMESH.EXACT("Lansoprazole")	MEDLINE®	168°
S10	(ti,ab(prevacid or lansoprazole))	MEDLINE®	2315°
S11	S10 OR S9	MEDLINE®	2337°
S12	MJMESH.EXACT("Omeprazole")	MEDLINE®	5012*
S13	(ti,ab(omeprazole or Prilosec or "Prilosec OTC" or Zegerid))	MEDLINE®	8080*
S14	S13 OR S12	MEDLINE®	9482*
S15	(s8 and (s11 or s14))	MEDLINE®	1367°
S16	(s15) and (human(yes) AND abany(yes) AND (la.exact("English"))	MEDLINE®	576°
S17	(MJEMB.EXACT.EXPLODE("gastroesophageal reflux"))	Embase®	29433*
S18	((ti,ab(GER OR GERD OR GORD)))	Embase®	22079*
S19	((ti,ab("acid reflux" or "chronic acid reflux")))	Embase®	4001°
S20	((ti,ab("heart burn and acid reflux")))	Embase®	2°
S21	((ti,ab("gastroesophageal reflux disease" or "gastro esophageal reflux disease")))	Embase®	17584*
S22	((ti,ab("gastroesophageal reflux" or "gastro esophageal reflux")))	Embase®	29521*
S23	((ti,ab("gastro-oesophageal reflux disease" or "gastro oesophageal reflux disease")))	Embase®	2785°
S24	S23 OR S22 OR S21 OR S20 OR S19 OR S18 OR S17	Embase®	50860*
S25	MJEMB.EXACT("lansoprazole")	Embase®	3242°
S26	((ti,ab(prevacid or lansoprazole)))	Embase®	3626°
S27	S26 OR S25	Embase®	4872°
S28	MJEMB.EXACT("omeprazole")	Embase®	11106*
S29	((ti,ab(omeprazole or Prilosec or "Prilosec OTC" or Zegerid)))	Embase®	11958*
S30	S29 OR S28	Embase®	16314*
S31	(S24 and (S27 or S30))	Embase®	3012°
S32	(S31) and (human(yes) AND abany(yes) AND (la.exact("English"))	Embase®	1419°
S33	(S16 or S32)	Embase®, MEDLINE®	1499°

Medline was searched from 1946 to December 2019, Embase from 1947 to December 2019 and CENTRAL was searched from January 2010 to December 2019

