

**PICO 1. Does a consultation supported by endoscopy provide greater reassurance than the consultation alone in a patient with refractory reflux-like symptoms?**

1 exp Endoscopy/	1003350
2 (endoscop* or gastroscop* or esophagogastroduodenoscop* or oesophagogastroduodenoscop* or EGD).tw,kw.	574837
3 or/1-2	1257391
4 (reassur* or satisf*).tw,kw.	838529
5 exp personal satisfaction/ or exp satisfaction/	266375
6 or/4-5	926854
7 3 and 6	38133
8 (reflux* or GERD or GORD).tw,kw.	148084
9 exp Gastroesophageal Reflux/	92008
10 or/8-9	174866
11 7 and 10	2379
12 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	3560512
13 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1016178
14 (guideline* or recommendation* or consensus).ti.	319070
15 or/12-14	4515591
16 11 and 15	395
17 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	4044624
18 16 not 17	355
19 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10559405
20 18 not 19	355
21 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	4320977
22 20 not 21	339
23 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	4798693
24 22 not 23	330
25 remove duplicates from 24	216

**PICO 1 extra search**

1 exp Endoscopy/	1004161
2 (endoscop* or gastroscop* or esophagogastroduodenoscop* or oesophagogastroduodenoscop* or EGD).tw,kw.	575483
3 or/1-2	1258587

4 (reassur* or satisf*).tw,kw.	839662
5 exp personal satisfaction/ or exp satisfaction/	266724
6 or/4-5	928083
7 3 and 6	38181
8 (reflux* or GERD or GORD).tw,kw.	148206
9 exp Gastroesophageal Reflux/	92081
10 or/8-9	175008
11 7 and 10	2382
12 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	3565066
13 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1018612
14 (guideline* or recommendation* or consensus).ti.	319630
15 or/12-14	4522293
16 11 and 15	395
17 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt. or "Journal: Conference Abstract".pt.	4047034
18 16 not 17	355
19 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10566206
20 18 not 19	355
21 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	4324885
22 20 not 21	339
23 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	4805490
24 22 not 23	330
25 remove duplicates from 24	216
26 endoscop*.ti.	225130
27 3 and 10 and 26 and 15	878
28 27 not (17 or 19 or 21 or 23)	624
29 28 not 24	583
30 remove duplicates from 29	364

**(UPDATED JULY 14, 2024) PICO 1. Does a consultation supported by endoscopy provide greater reassurance than the consultation alone in a patient with refractory reflux-like symptoms?**

1 exp Endoscopy/	1241387
2 (endoscop* or gastroscop* or esophagogastroduodenoscop* or oesophagogastroduodenoscop* or EGD).tw,kw.	719795
3 or/1-2	1563993
4 (reassur* or satisf*).tw,kw.	1087395
5 exp personal satisfaction/ or exp satisfaction/	338278
6 or/4-5	1193365
7 3 and 6	49522
8 (reflux* or GERD or GORD).tw,kw.	172174
9 exp Gastroesophageal Reflux/	111244
10 or/8-9	206532
11 7 and 10	2866
12 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	4498486
13 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1569224
14 (guideline* or recommendation* or consensus).ti.	408850
15 or/12-14	5904819
16 11 and 15	485
17 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346814
18 16 not 17	430
19 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	11736727
20 18 not 19	430
21 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	5032694
22 20 not 21	410
23 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	5647511
24 22 not 23	400
25 endoscop*.ti.	283810
26 3 and 10 and 15 and 25	1207
27 26 not (17 or 19 or 21 or 23)	834
28 24 or 27	1179
29 remove duplicates from 28	779
30 limit 29 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	4

31	limit 29 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	13
32	limit 29 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	13
33	limit 29 to dd=20210801-20240714 use oomezd [Limit not valid in Ovid MEDLINE(R); records were retained]	11
34	limit 29 to dc=20210801-20240714 use oomezd	153
35	29 and 2024*.ep.	1
36	or/30-35	166

**PICO 2. Does endoscopy in a patient with refractory reflux-like symptoms help guide therapy by identifying patients with erosive esophagitis?**

**PICO 3. Does endoscopy with esophageal biopsy in a patient with refractory reflux-like symptoms help guide therapy by identifying patients with eosinophilic esophagitis?**

1 exp Endoscopy/	1002217
2 (endoscop* or gastroscop* or esophagogastroduodenoscop* or oesophagogastroduodenoscop* or EGD).tw,kw.	574194
3 or/1-2	1255924
4 (reflux* or GERD or GORD).tw,kw.	147950
5 exp Gastroesophageal Reflux/	91920
6 or/4-5	174689
7 3 and 6	49763
8 (refractory or refractories or resistan*).tw,kw.	2630138
9 ((failed or failure or failing or no or non or "not") adj2 (response or respond*)).tw,kw.	299887
10 ((failed or failure or failing) adj2 (proton pump inhibitor* or PPI or PPIs)).tw,kw.	333
11 or/8-10	2886960
12 7 and 11	3448
13 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	4039903
14 12 not 13	2480
15 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10550166
16 14 not 15	2476
17 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	4316700
18 16 not 17	2179
19 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	4790121
20 18 not 19	2148
21 remove duplicates from 20	1383

**PICO 3 extra search: GERD+ EoE+SRs- [What is the prevalence of eosinophilic esophagitis or lymphocytic esophagitis overall and/or in patients with GERD or rGERD]**

1 (reflux* or GERD or GORD).tw,kw.	148488
2 exp Gastroesophageal Reflux/	92191
3 or/1-2	175251

4 (eosinophilic adj5 (esophagitis or oesophagitis)).tw,kw.	9116
5 exp Eosinophilic Esophagitis/	8446
6 or/4-5	10319
7 3 and 6	3014
8 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1023692
9 7 and 8	77
10 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	4074387
11 9 not 10	65
12 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10558298
13 11 not 12	65
14 remove duplicates from 13	47
15 limit 14 to english language	45

**(UPDATED JULY 14, 2024) PICO 2. Does endoscopy in a patient with refractory reflux-like symptoms help guide therapy by identifying patients with erosive esophagitis?**

**(UPDATED JULY 14, 2024) PICO 3. Does endoscopy with esophageal biopsy in a patient with refractory reflux-like symptoms help guide therapy by identifying patients with eosinophilic esophagitis?**

1 exp Endoscopy/	1241387
2 (endoscop* or gastroscop* or esophagogastroduodenoscop* or oesophagogastroduodenoscop* or EGD).tw,kw.	719795
3 or/1-2	1563993
4 (reflux* or GERD or GORD).tw,kw.	172174
5 exp Gastroesophageal Reflux/	111244
6 or/4-5	206532
7 3 and 6	60200
8 (refractory or refractories or resistan*).tw,kw.	3316207
9 ((failed or failure or failing or no or non or "not") adj2 (response or respond*)).tw,kw.	366535
10 ((failed or failure or failing) adj2 (proton pump inhibitor* or PPI or PPIs)).tw,kw.	402
11 or/8-10	3627728
12 7 and 11	4427
13 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346814
14 12 not 13	3091
15 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).tw.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	11940450
16 14 not 15	3085
17 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	5032694
18 16 not 17	2745
19 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	5647511
20 18 not 19	2705
21 remove duplicates from 20	1781
22 limit 20 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	141
23 limit 20 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	181
24 limit 20 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	181
25 limit 20 to dd=20210801-20240714 use oomezd [Limit not valid in Ovid MEDLINE(R); records were retained]	17
26 limit 20 to dc=20210801-20240714 use oomezd	315

27	20 and 2024*.ep.	35
28	or/22-27	524
29	remove duplicates from 28	359

**(UPDATED JULY 14, 2024) PICO 3 extra search: GERD+ EoE+SRs- [What is the prevalence of eosinophilic esophagitis or lymphocytic esophagitis overall and/or in patients with GERD or rGERD]**

1	(reflux* or GERD or GORD).tw,kw.	172174
2	exp Gastroesophageal Reflux/	111244
3	or/1-2	206532
4	(eosinophilic adj5 (esophagitis or oesophagitis)).tw,kw.	12828
5	exp Eosinophilic Esophagitis/	12591
6	or/4-5	14830
7	3 and 6	3877
8	Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1569224
9	7 and 8	112
10	conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346814
11	9 not 10	95
12	(exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).tw.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	11940450
13	11 not 12	95
14	remove duplicates from 13	68
15	limit 14 to english language	66
16	limit 13 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	8
17	limit 13 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	7
18	limit 13 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	7
19	limit 13 to dd=20210801-20240714 use oemezd [Limit not valid in Ovid MEDLINE(R); records were retained]	0
20	limit 13 to dc=20210801-20240714 use oemezd	20
21	13 and 2024*.ep.	2
22	or/16-21	29
23	remove duplicates from 22	21



**PICO 4. Does higher dose PPI therapy result in a higher proportion of patients with symptom resolution in those with histological features of reflux compared with those without histological features in patients with refractory reflux-like symptoms on BID PPI therapy?**

**PICO 5. Does treatment of confirmed H. pylori in a patient with refractory reflux-like symptoms lead to a greater proportion of patients reporting symptom relief than continued PPI (GERD) therapy?**

1 (reflux* or GERD or GORD).tw,kw.	147950
2 exp Gastroesophageal Reflux/	91920
3 or/1-2	174689
4 (refractory or refractories or resistan*).tw,kw.	2630138
5 ((failed or failure or failing or no or non or "not") adj2 (response or respond*)).tw,kw.	299887
6 ((failed or failure or failing) adj2 (proton pump inhibitor* or PPI or PPIs)).tw,kw.	333
7 or/4-6	2886960
8 3 and 7	9207
9 (histology or histological or biopsy or biopsies or microscopic finding* or hyperplasia or papillomatosis or (increased adj4 intraepithelial eosinophils)).tw,kw.	1995019
10 exp Histology/	1682424
11 exp Biopsy/	1046138
12 or/9-11	3636600
13 8 and 12	1153
14 (helicobacter or pylori or pyloridis or "H.pylori").tw,kw.	112397
15 8 and 14	493
16 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	3555265
17 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1013764
18 (guideline* or recommendation* or consensus).ti.	318576
19 or/16-18	4508304
20 15 and 19	138
21 13 or 20	1270
22 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	4039903
23 21 not 22	858
24 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10550166
25 23 not 24	831
26 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	4316700
27 25 not 26	740

28 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	4790121
29 27 not 28	735
30 remove duplicates from 29	498

#### PICO 4 extra search: NERD+ histology+ SR/RCT/GL

1 (reflux* or GERD or GORD).tw,kw.	148488
2 exp Gastroesophageal Reflux/	92191
3 or/1-2	175251
4 (non-erosive or nonerosive or NERD).tw,kw.	5029
5 3 and 4	3386
6 (histology or histological or biopsy or biopsies or microscopic finding* or hyperplasia or papillomatosis or (increased adj4 intraepithelial eosinophils)).tw,kw.	2002879
7 exp Histology/	1686331
8 exp Biopsy/	1048922
9 or/6-8	3647027
10 5 and 9	637
11 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	3570783
12 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1023692
13 (guideline* or recommendation* or consensus).ti.	320330
14 or/11-13	4532107
15 10 and 14	77
16 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	4074387
17 15 not 16	51
18 remove duplicates from 17	42

#### PICO 5 GERD+HP+SRs extra search- [What is the prevalence of Helicobacter pylori in patients with refractory reflux-like symptoms?]

1 (reflux* or GERD or GORD).tw,kw.	148488
2 exp *Gastroesophageal Reflux/	48089
3 or/1-2	154376
4 (helicobacter or pylori or pyloridis or "H.pylori").tw,kw.	112635
5 3 and 4	6176
6 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1023692
7 5 and 6	282
8 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	4074387
9 7 not 8	259
10 remove duplicates from 9	162

**(UPDATED JULY 14, 2024) PICO 4. Does higher dose PPI therapy result in a higher proportion of patients with symptom resolution in those with histological features of reflux compared with those without histological features in patients with refractory reflux-like symptoms on BID PPI therapy?**

**(UPDATED JULY 14, 2024) PICO 5. Does treatment of confirmed H. pylori in a patient with refractory reflux-like symptoms lead to a greater proportion of patients reporting symptom relief than continued PPI (GERD) therapy?**

1 (reflux* or GERD or GORD).tw,kw.	172174
2 exp Gastroesophageal Reflux/	111244
3 or/1-2	206532
4 (refractory or refractories or resistan*).tw,kw.	3316207
5 ((failed or failure or failing or no or non or "not") adj2 (response or respond*)).tw,kw.	366535
6 ((failed or failure or failing) adj2 (proton pump inhibitor* or PPI or PPIs)).tw,kw.	402
7 or/4-6	3627728
8 3 and 7	11596
9 (histology or histological or biopsy or biopsies or microscopic finding* or hyperplasia or papillomatosis or (increased adj4 intraepithelial eosinophils)).tw,kw.	2396603
10 exp Histology/	1981718
11 exp Biopsy/	1274485
12 or/9-11	4324486
13 8 and 12	1500
14 (helicobacter or pylori or pyloridis or "H.pylori").tw,kw.	129348
15 8 and 14	598
16 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	4498486
17 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1569224
18 (guideline* or recommendation* or consensus).ti.	408850
19 or/16-18	5904819
20 15 and 19	161
21 13 or 20	1633
22 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346814
23 21 not 22	1056
24 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	11736727
25 23 not 24	1023
26 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	5032694
27 25 not 26	924

28 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	5647511
29 27 not 28	919
30 remove duplicates from 29	658
31 limit 29 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	30
32 limit 29 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	34
33 limit 29 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	34
34 limit 29 to dd=20210801-20240714 use oomezd [Limit not valid in Ovid MEDLINE(R); records were retained]	1
35 limit 29 to dc=20210801-20240714 use oomezd	133
36 29 and 2024*.ep.	4
37 or/31-36	174
38 remove duplicates from 37	137

**(UPDATED JULY 14, 2024) PICO 4 extra search: NERD+ histology+ SR/RCT/GL**

1 (reflux* or GERD or GORD).tw,kw.	172174
2 exp Gastroesophageal Reflux/	111244
3 or/1-2	206532
4 (non-erosive or nonerosive or NERD).tw,kw.	5842
5 3 and 4	3800
6 (histology or histological or biopsy or biopsies or microscopic finding* or hyperplasia or papillomatosis or (increased adj4 intraepithelial eosinophils)).tw,kw.	2396603
7 exp Histology/	1981718
8 exp Biopsy/	1274485
9 or/6-8	4324486
10 5 and 9	722
11 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	4498486
12 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1569224
13 (guideline* or recommendation* or consensus).ti.	408850
14 or/11-13	5904819
15 10 and 14	88
16 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346814
17 15 not 16	57
18 remove duplicates from 17	38
19 limit 17 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	3
20 limit 17 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	3
21 limit 17 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	3

22 limit 17 to dd=20210801-20240714 use oomezd [Limit not valid in Ovid MEDLINE(R); records were retained]	0
23 limit 17 to dc=20210801-20240714 use oomezd	4
24 17 and 2024*.ep.	0
25 or/19-24	7
26 remove duplicates from 25	4

**(UPDATED JULY 14, 2024) PICO 5 GERD+HP+SRs extra search- [What is the prevalence of Helicobacter pylori in patients with refractory reflux-like symptoms?]**

1 (reflux* or GERD or GORD).tw,kw.	172174
2 exp *Gastroesophageal Reflux/	54649
3 or/1-2	178660
4 (helicobacter or pylori or pyloridis or "H.pylori").tw,kw.	129348
5 3 and 4	6846
6 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1569224
7 5 and 6	338
8 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346814
9 7 not 8	305
10 remove duplicates from 9	192
11 limit 9 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	13
12 limit 9 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	17
13 limit 9 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	17
14 limit 9 to dd=20210801-20240714 use oomezd [Limit not valid in Ovid MEDLINE(R); records were retained]	3
15 limit 9 to dc=20210801-20240714 use oomezd	26
16 9 and 2024*.ep.	3
17 or/11-16	47
18 remove duplicates from 17	28

**PICO 6. Does esophageal manometry in a patient with refractory reflux-like symptoms identify diagnoses that guide future therapy?**

**[What is the prevalence of achalasia or esophageal dysmotility in patients with refractory reflux-like symptoms?]**

1 (reflux* or GERD or GORD).tw,kw.	147950
2 exp Gastroesophageal Reflux/	91920
3 or/1-2	174689
4 (refractory or refractories or resistan*).tw,kw.	2630138
5 ((failed or failure or failing or no or non or "not") adj2 (response or respond*)).tw,kw.	299887
6 ((failed or failure or failing) adj2 (proton pump inhibitor* or PPI or PPIs)).tw,kw.	333
7 or/4-6	2886960
8 3 and 7	9207
9 exp Manometry/	39466
10 manometr*.tw,kw.	37615
11 or/9-10	55164
12 8 and 11	1011
13 (achalasia* or cardiospasm* or megaesophagus).tw,kw.	18235
14 Esophageal Achalasia/	14583
15 or/13-14	20989
16 3 and 15 and 11	2200
17 12 or 16	3029
18 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	4039903
19 17 not 18	2152
20 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).tw.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10550166
21 19 not 20	2138
22 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	4316700
23 21 not 22	2026
24 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	4790121
25 23 not 24	1988
26 remove duplicates from 25	1295

**(UPDATED JULY 14, 2024) PICO 6. Does esophageal manometry in a patient with refractory reflux-like symptoms identify diagnoses that guide future therapy? [What is the prevalence of achalasia or esophageal dysmotility in patients with refractory reflux-like symptoms?]**

1 (reflux* or GERD or GORD).tw,kw.	172174
2 exp Gastroesophageal Reflux/	111244
3 or/1-2	206532
4 (refractory or refractories or resistan*).tw,kw.	3316207
5 ((failed or failure or failing or no or non or "not") adj2 (response or respond*)).tw,kw.	366535
6 ((failed or failure or failing) adj2 (proton pump inhibitor* or PPI or PPIs)).tw,kw.	402
7 or/4-6	3627728
8 3 and 7	11596
9 exp Manometry/	43551
10 manometr*.tw,kw.	42651
11 or/9-10	61291
12 8 and 11	1283
13 (achalasia* or cardiospasm* or megaesophagus).tw,kw.	21687
14 Esophageal Achalasia/	18230
15 or/13-14	25144
16 3 and 15 and 11	2718
17 12 or 16	3765
18 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346814
19 17 not 18	2592
20 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).tw.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	11940450
21 19 not 20	2577
22 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	5032694
23 21 not 22	2445
24 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	5647511
25 23 not 24	2399
26 remove duplicates from 25	1617
27 limit 25 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	109
28 limit 25 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	101
29 limit 25 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	101

30	limit 25 to dd=20210801-20240714 use oomezd [Limit not valid in Ovid MEDLINE(R); records were retained]	12
31	limit 25 to dc=20210801-20240714 use oomezd	266
32	25 and 2024*.ep.	18
33	or/27-32	409
34	remove duplicates from 33	294



**PICO 7. Does esophageal pH testing on PPI therapy in a patient with refractory reflux-like symptoms lead to more diagnoses that guide future therapy than esophageal pH testing off PPI therapy?**

**PICO 8. Does esophageal pH-impedance testing on PPI therapy in a patient with refractory reflux-like symptoms lead to more diagnoses that guide future therapy than esophageal pH-impedance testing off PPI therapy?**

**PICO 9. Does esophageal pH-impedance testing on PPI therapy in a patient with troublesome refractory reflux-like symptoms lead to more diagnoses that guide future therapy than esophageal pH testing on PPI therapy?**

**PICO 10. Does wireless esophageal pH testing on PPI therapy in a patient with refractory reflux-like symptoms lead to more diagnoses that guide future therapy than catheter-based esophageal pH testing on PPI therapy?**

**PICO 11. Does esophageal pH testing with symptom-reflux event correlation evaluation on PPI therapy in a patient with refractory reflux-like symptoms lead to more diagnoses that guide future therapy than esophageal pH testing without symptom-reflux event correlation evaluation on PPI therapy?**

**PICO 12. Does esophageal pH-impedance testing with symptom-reflux event correlation evaluation on PPI therapy in a patient with refractory reflux-like symptoms lead more diagnoses that guide future therapy than esophageal pH-impedance testing without symptom-reflux event correlation evaluation on PPI therapy?**

1 (reflux* or GERD or GORD).tw,kw.	147950
2 exp Gastroesophageal Reflux/	91920
3 or/1-2	174689
4 exp Proton Pump Inhibitors/	99467
5 (proton pump inhibitor* or PPI or PPIs).tw,kw.	76992
6 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	33910
7 or/4-6	145994
8 3 and 7	27961
9 ((pH adj3 testing) or pH impedance).tw,kw.	3904
10 ((esophag* or oesphag*) adj3 pH).tw,kw.	6478
11 ((esophag* or oesphag*) adj3 acid* adj3 measure*).tw,kw.	172
12 or/9-11	9587
13 8 and 12	2526
14 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt. or "Journal: Conference Abstract".pt.	4039903
15 13 not 14	1705
16 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10550166
17 15 not 16	1699
18 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	4316700
19 17 not 18	1563
20 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	4790121
21 19 not 20	1535
22 remove duplicates from 21	930

**(UPDATED JULY 14, 2024) PICO 7. Does esophageal pH testing on PPI therapy in a patient with refractory reflux-like symptoms lead to more diagnoses that guide future therapy than esophageal pH testing off PPI therapy?**

**(UPDATED JULY 14, 2024) PICO 8. Does esophageal pH-impedance testing on PPI therapy in a patient with refractory reflux-like symptoms lead to more diagnoses that guide future therapy than esophageal pH-impedance testing off PPI therapy?**

**(UPDATED JULY 14, 2024) PICO 9. Does esophageal pH-impedance testing on PPI therapy in a patient with troublesome refractory reflux-like symptoms lead to more diagnoses that guide future therapy than esophageal pH testing on PPI therapy?**

**(UPDATED JULY 14, 2024) PICO 10. Does wireless esophageal pH testing on PPI therapy in a patient with refractory reflux-like symptoms lead to more diagnoses that guide future therapy than catheter-based esophageal pH testing on PPI therapy?**

**(UPDATED JULY 14, 2024) PICO 11. Does esophageal pH testing with symptom-reflux event correlation evaluation on PPI therapy in a patient with refractory reflux-like symptoms lead to more diagnoses that guide future therapy than esophageal pH testing without symptom-reflux event correlation evaluation on PPI therapy?**

**(UPDATED JULY 14, 2024) PICO 12. Does esophageal pH-impedance testing with symptom-reflux event correlation evaluation on PPI therapy in a patient with refractory reflux-like symptoms lead more diagnoses that guide future therapy than esophageal pH-impedance testing without symptom-reflux event correlation evaluation on PPI therapy?**

1 (reflux* or GERD or GORD).tw,kw.	172174
2 exp Gastroesophageal Reflux/	111244
3 or/1-2	206532
4 exp Proton Pump Inhibitors/	126589
5 (proton pump inhibitor* or PPI or PPIs).tw,kw.	113384
6 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	39319
7 or/4-6	201154
8 3 and 7	33843
9 ((pH adj3 testing) or pH impedance).tw,kw.	4920
10 ((esophag* or oesphag*) adj3 pH).tw,kw.	6981
11 ((esophag* or oesphag*) adj3 acid* adj3 measure*).tw,kw.	184
12 or/9-11	10929
13 8 and 12	3014
14 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346814
15 13 not 14	1981
16 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).tw.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	11940450
17 15 not 16	1974
18 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	5032694
19 17 not 18	1819
20 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	5647511
21 19 not 20	1785
22 remove duplicates from 21	1097
23 limit 21 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	90
24 limit 21 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	97
25 limit 21 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	98
26 limit 21 to dd=20210801-20240714 use oemezd [Limit not valid in Ovid MEDLINE(R); records were retained]	11
27 limit 21 to dc=20210801-20240714 use oemezd	169
28 21 and 2024*.ep.	15
29 or/23-28	288
30 remove duplicates from 29	189

**PICO 13. Does higher dose PPI therapy in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy?**

**PICO 14. Does PCAB therapy in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy?**

**PICO 15. Does higher dose PPI therapy result in a higher proportion of patients with symptom resolution in those with erosive esophagitis compared with those without erosive esophagitis in patients with refractory reflux-like symptoms on BID PPI therapy?**

**PICO 16. Does PCAB therapy result in a higher proportion of patients with symptom resolution in those with erosive esophagitis compared with those without erosive esophagitis in patients with refractory reflux-like symptoms on BID PPI therapy?**

**PICO 17. Does the addition of a prokinetic in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

**PICO 18. Does the addition of a TLESR inhibitor in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

**PICO 19. Does the addition of an H2RA in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

**PICO 20. Does the addition of an alginate and/or antacid in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

#### **PICO 13-PPIs**

1 (reflux* or GERD or GORD).tw,kw.	147950
2 exp Gastroesophageal Reflux/	91920
3 or/1-2	174689
4 (refractory or refractories or resistan*).tw,kw.	2630138
5 ((failed or failure or failing or no or non or "not") adj2 (response or respond*)).tw,kw.	299887
6 ((failed or failure or failing) adj2 (proton pump inhibitor* or PPI or PPIs)).tw,kw.	333
7 or/4-6	2886960
8 3 and 7	9207
9 exp Proton Pump Inhibitors/	99467
10 (proton pump inhibitor* or PPI or PPIs).tw,kw.	76992
11 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	33910
12 or/9-11	145994
13 8 and 12	3552
14 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	3555265
15 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1013764
16 (guideline* or recommendation* or consensus).ti.	318576
17 or/14-16	4508304
18 13 and 17	665
19 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	4039903
20 18 not 19	538
21 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).tw.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10550166
22 20 not 21	537

23 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	4316700
24 22 not 23	514
25 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	4790121
26 24 not 25	506
27 remove duplicates from 26	346

#### PICO 14 and PICO 16 PCAB

1 (reflux* or GERD or GORD).tw,kw.	159714
2 exp Gastroesophageal Reflux/	96543
3 or/1-2	187570
4 vonoprazan.tw,kw.	1052
5 (PCAB or PCABs).tw,kw.	305
6 Potassium Competitive Acid Blocker*.tw,kw.	860
7 or/4-6	1658
8 3 and 7	456
9 exp Proton Pump Inhibitors/	107513
10 (proton pump inhibitor* or PPI or PPIs).tw,kw.	87450
11 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	42473
12 or/9-11	164625
13 8 and 12	430
14 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	5084587
15 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1129028
16 or/14-15	5817292
17 13 and 16	185
18 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	4442193
19 17 not 18	127
20 19 use ppez,oemezd	84
21 13 use coch,cctr	83
22 20 or 21	167
23 remove duplicates from 22	124
24 limit 23 to english language [Limit not valid in CDSR; records were retained]	82

#### PICO 17 Prokinetics

1 (reflux* or GERD or GORD).tw,kw.	159898
2 exp Gastroesophageal Reflux/	96663
3 or/1-2	187803
4 (prokinetic* or gastroprokinetic* or gastrokinetic* or gastro-kinetic*).tw,kw.	9715
5 (antiemetic* or anti-emetic or domperidon* or Metoclopramide or Cisapride or Itopride or ganaton or Mosapride or erythromycin).tw,kw.	100188
6 (Motilin adj (receptor* or agonist*)).tw,kw.	937
7 ((5HT3 or 5HT 3 or 5-HT3 or 5-HT 3) adj antagonist*).tw,kw.	3678
8 ((5HT or 5-HT or 5-hydroxytryptamine*) adj (agonist* or antagonist*)).tw,kw.	3689
9 ((5-HT1A or 5HT1A or 5-HT 1A or 5HT 1A) adj agonist*).tw,kw.	4081
10 exp Serotonin Antagonists/	306344
11 exp Serotonin 5-HT3 Receptor Antagonists/	7648
12 exp Serotonin 5-HT4 Receptor Agonists/	1263
13 exp Serotonin 5-HT1 Receptor Agonists/	8289
14 (serotonin adj3 receptor adj3 (agonist* or antagonist* or block*)).tw,kw.	6540
15 (tegaserod or Zelnorm or Zelnorm).tw,kw.	1410
16 ABT-229.tw,kw.	135
17 (Tandospirone or Sediell or metanopirone or buspirone).tw,kw.	7381
18 (alosetron or Lotronex).tw,kw.	982

19 (Acotiamide or YM-443 or Z-338D).tw,kw.	332
20 (acetylcholinesterase inhibitor* or cholinesterase Inhibitor* or anti-cholinesterase* or anticholinesterase*).tw,kw.	32316
21 ((5HT-4 or 5HT4 or 5-HT 4 or 5-HT4) adj agonist*).tw,kw.	789
22 or/4-21	448060
23 3 and 22	5267
24 exp Proton Pump Inhibitors/	107768
25 (proton pump inhibitor* or PPI or PPIs).tw,kw.	87790
26 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	42530
27 or/24-26	165125
28 23 and 27	2142
29 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	5100355
30 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1134665
31 or/29-30	5836864
32 28 and 31	772
33 conference abstract.pt.	4140837
34 32 not 33	724
35 34 use ppez,oomezd	508
36 28 use coch,cctr	254
37 35 or 36	762
38 remove duplicates from 37	532
39 limit 38 to english language [Limit not valid in CDSR; records were retained]	374
40 (Systematic review or meta-analysis).tw,kw.	698263
41 39 and 40	57
42 limit 41 to yr="2010 -Current"	35

#### PICO 17 Prokinetics extra search

1 (reflux* or GERD or GORD).tw,kw.	160157
2 exp Gastroesophageal Reflux/	96847
3 or/1-2	188134
4 (prokinetic* or gastroprokinetic* or gastrokinetic* or gastro-kinetic*).tw,kw.	9734
5 (antiemetic* or anti-emetic or domperidon* or Metoclopramide or Cisapride or Itopride or ganaton or Mosapride or erythromycin).tw,kw.	100340
6 (Motilin adj (receptor* or agonist*)).tw,kw.	937
7 ((5HT3 or 5HT 3 or 5-HT3 or 5-HT 3) adj antagonist*).tw,kw.	3684
8 ((5HT or 5-HT or 5-hydroxytryptamine*) adj (agonist* or antagonist*)).tw,kw.	3688
9 ((5-HT1A or 5HT1A or 5-HT 1A or 5HT 1A) adj agonist*).tw,kw.	4083
10 exp Serotonin Antagonists/	306869
11 exp Serotonin 5-HT3 Receptor Antagonists/	7665
12 exp Serotonin 5-HT4 Receptor Agonists/	1265
13 exp Serotonin 5-HT1 Receptor Agonists/	8302
14 (serotonin adj3 receptor adj3 (agonist* or antagonist* or block*)).tw,kw.	6545
15 (tegaserod or Zelnorm or Zelnorm).tw,kw.	1411
16 ABT-229.tw,kw.	135
17 (Tandospirone or Sediell or metanopirone or buspirone).tw,kw.	7389
18 (alosetron or Lotronex).tw,kw.	984
19 (Acotiamide or YM-443 or Z-338D).tw,kw.	333
20 (acetylcholinesterase inhibitor* or cholinesterase Inhibitor* or anti-cholinesterase* or anticholinesterase*).tw,kw.	32396
21 ((5HT-4 or 5HT4 or 5-HT 4 or 5-HT4) adj agonist*).tw,kw.	791
22 or/4-21	448819
23 3 and 22	5278
24 exp Proton Pump Inhibitors/	108127
25 (proton pump inhibitor* or PPI or PPIs).tw,kw.	88201
26 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	42597
27 or/24-26	165789
28 23 and 27	2150

29 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	5111594
30 28 and 29	711
31 30 use ppez,oomezd	495
32 28 use coch,cctr	254
33 31 or 32	749
34 remove duplicates from 33	504
35 limit 34 to yr="2019 -Current"	41

#### PICO 13 and PICO 15 searches for twice PPIs RCTs

1 (reflux* or GERD or GORD).tw,kw.	159524
2 exp *Gastroesophageal Reflux/	48982
3 or/1-2	16543
4 exp Proton Pump Inhibitors/	107694
5 (proton pump inhibitor* or PPI or PPIs).tw,kw.	87542
6 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	42439
7 or/4-6	164796
8 3 and 7	26954
9 (twice daily or bid or "b.i.d.").tw.	211873
10 8 and 9	1095
11 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	5081100
12 10 and 11	991
13 remove duplicates from 12	505
14 limit 13 to yr="2016 -Current"	10
15 conference abstract.pt.	4137525
16 14 not 15	66

#### PICO 13 and PICO 15 extra search three times four times PPIs

1 (reflux* or GERD or GORD).tw,kw. (152527)	
2 exp *Gastroesophageal Reflux/ (49213)	
3 or/1-2 (158491)	
4 ((high dose or three times or four times or 3 times or 4 times or tid or "t.i.d." or qid or "q.i.d." or "every 8hr*" or "every 8 hr*" or "every 8 hour*" or "every 6hr" or "every 6 hr*" or "every 6 hour*") adj5 (proton pump inhibitor* or PPI or PPIs or omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole)).tw. (2343)	
5 3 and 4 (622)	
6 (twice daily or bid or "b.i.d." or two times or 2 times or "every 12hr*" or "every 12 hr*" or "every 12 hour*").tw. (235292)	
7 5 and 6 (137)	
8 remove duplicates from 7 (88)	
9 conference abstract.pt. (4160546)	
10 8 not 9 (54)	

#### PICO 13 and PICO 15 high dose PPIs SRsMAs

(reflux\* or GERD or GORD).tw,kw. (151996)  
exp \*Gastroesophageal Reflux/ (48938)  
or/1-2 (157948)  
exp Proton Pump Inhibitors/ (103355)  
(proton pump inhibitor\* or PPI or PPIs).tw,kw. (82508)  
(omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw. (34819)  
or/4-6 (154003)

3 and 7 (24391)

((high or higher or double) adj5 dose\*).tw. (550057)

8 and 9 (1325)

Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab. (1096184)

10 and 11 (75)

remove duplicates from 12 (52)

limit 13 to yr="2010 -Current" (32)

<b>PICO 13 and PICO 15 twice dose PPIs SRsMAs</b>	1013764
1 (reflux* or GERD or GORD).tw,kw.	152114
2 exp *Gastroesophageal Reflux/	48978
3 or/1-2	158070
4 exp Proton Pump Inhibitors/	103536
5 (proton pump inhibitor* or PPI or PPIs).tw,kw.	82702
6 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	34852
7 or/4-6	154315
8 3 and 7	24410
9 (twice daily or bid or "b.i.d.").tw.	164341
10 8 and 9	1527
11 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1099294
12 10 and 11	37
13 remove duplicates from 12 (27)	27
<b>PICO 18 TLESR</b>	
1 (reflux* or GERD or GORD).tw,kw.	159898
2 exp Gastroesophageal Reflux/	96663
3 or/1-2	187803
4 ((TLESR or TLESRs or transient lower esophageal sphincter relaxation* or transient lower oesophageal sphincter relaxation* or TLES relaxation* or transient LES relaxation*) adj5 (antagonist* or inhibit* or block* or reducer*)).tw,kw.	9715
5 (((metabotropic glutamate receptor* or mGluR*) adj5 (antagonist* or inhibit* or block*)) or AZD2066).tw,kw.	100188
6 (Cannabinoid receptor agonist*).tw,kw.	937
7 ((GABA* adj3 receptor* adj3 agonis*) or lesogaberan or AZD3355).tw,kw.	3678
8 (Baclofen or Lioresal or arbaclofen placarbil).tw,kw.	3689
9 exp Baclofen/	4081
10 exp Muscle Relaxation/ or exp GABA Agonists/	306344
11 or/4-10	448060
12 3 and 11	5267
13 exp Proton Pump Inhibitors/	107768
14 (proton pump inhibitor* or PPI or PPIs).tw,kw.	87790
15 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	42530
16 or/13-15	165125
17 12 and 16	2142
18 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	5100355
19 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1134665
20 or/18-19	5836864
21 17 and 20	772

22	21 use ppez,oemez	4140837
23	17 use coch,cctr	724
24	22 or 23	508
25	remove duplicates from 24	254
26	limit 25 to english language	762
27	19 and 26	532
28	limit 27 to yr="2010 -Current"	374

#### PICO 18 RCTs

1	(reflux* or GERD or GORD).tw,kw.	160059
2	exp *Gastroesophageal Reflux/	49135
3	or/1-2	166022
4	((TLESR or TLESRs or transient lower esophageal sphincter relaxation* or transient lower oesophageal sphincter relaxation* or TLES relaxation* or transient LES relaxation*) adj5 (antagonist* or inhibit* or block* or reducer*)).tw,kw.	243
5	((metabotropic glutamate receptor* or mGluR*) adj5 (antagonist* or inhibit* or block*)) or AZD2066).tw,kw.	7021
6	Cannabinoid receptor agonist*.tw,kw.	2666
7	((GABA* adj3 receptor* adj3 agonis*) or lesogaberan or AZD3355).tw,kw.	8277
8	(Baclofen or Lioresal or arbaclofen placarbil).tw,kw.	19021
9	exp Baclofen/	24917
10	exp Muscle Relaxation/ or exp GABA Agonists/	476084
11	or/4-10	490137
12	3 and 11	3098
13	exp Proton Pump Inhibitors/	108377
14	(proton pump inhibitor* or PPI or PPIs).tw,kw.	88358
15	(omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	42605
16	or/13-15	166110
17	12 and 16	907
18	randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	5119498
19	17 and 18	297
20	19 use ppez,oemez	246
21	17 use cctr	62
22	20 or 21	308
23	remove duplicates from 22	250
24	limit 23 to yr="2014 -Current"	77

#### PICO 19 H2RAs-2021-08-10

1	(reflux* or GERD or GORD).tw,kw.
2	exp Gastroesophageal Reflux/
3	or/1-2
4	exp Histamine H2 Antagonists/
5	((histamine or H2 or H-2 or H2R or H 2 R) adj3 (antagonist* or blocker* or blockage* or blockader*)).tw,kw.
6	(H2RA or H2RAs or H2-RA or H2-RAs).tw,kw.



7 (antihistaminic\* adj2 (H2 or H-2)).tw,kw.  
8 (Cimetidine or Tagamet or altramet or biomet or biomet400 or eureceptor or histodil or skf 92334 or skf92334).tw,kw.  
9 (ranitidine or zantac or ah 19065 or ah19065 or biotidin or ranisen or ranitidine or sostril or zantic).tw,kw.  
10 (Famotidine or Pepcid or mk 208 or mk208 or ym 11170 or ym11170).tw,kw.  
11 (Nizatidine or Axid or axid or ly 139037 or ly139037).tw,kw.  
12 (Roxatidine or Rotane or Zorpe).tw,kw.  
13 or/4-12  
14 3 and 13  
15 exp Proton Pump Inhibitors/  
  
16 (proton pump inhibitor\* or PPI or PPIs).tw,kw.  
17 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.  
18 or/15-17  
19 14 and 18  
  
20 randomized controlled trial.pt. or (random\* or placebo\* or double-blind\*).mp.  
21 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.  
22 or/20-21  
23 19 and 22  
24 23 use ppez,oomezd  
25 19 use coch,cctr  
26 24 or 25  
27 remove duplicates from 26  
28 19 use coch  
29 (19 and 21) use ppez,oomezd  
30 28 or 29  
31 ((histamine or H2 or H-2 or H2R or H 2 R) adj3 (antagonist\* or blocker\* or blockage\* or blockader\*)).ti.  
32 (H2RA or H2RAs or H2-RA or H2-RAs).ti.  
33 (antihistaminic\* adj2 (H2 or H-2)).ti.  
34 (Cimetidine or Tagamet or altramet or biomet or biomet400 or eureceptor or histodil or skf 92334 or skf92334).ti.  
35 (ranitidine or zantac or ah 19065 or ah19065 or biotidin or ranisen or ranitidine or sostril or zantic).ti.  
36 (Famotidine or Pepcid or mk 208 or mk208 or ym 11170 or ym11170).ti.  
37 (Nizatidine or Axid or axid or ly 139037 or ly139037).ti.  
38 (Roxatidine or Rotane or Zorpe).ti.  
39 or/31-38  
40 30 and 39  
41 remove duplicates from 40

18

#### PICO 20 alginate antacid

1 (reflux* or GERD or GORD).tw,kw.	160656
2 exp Gastroesophageal Reflux/ 3 or/1-2	97240 188777
4 exp Alginates/ 5 (alginate or alginates).tw,kw.	37207 46920
6 exp Antacids/ 7 (antacid or antacids).tw,kw.	145374 12663
8 Gaviscon.tw,kw.	821
9 (magnesium carbonate or Magnesium hydroxide or aluminum hydroxide or Calcium carbonate).tw,kw.	23626
10 (Gelusil or Maalox or Mylanta or Roloids or Alternagel or Amphojel or Alka-Seltzer or Tums or Pepto-Bismol).tw,kw.	3393
11 or/4-10 12 3 and 11	211924 6881
13 exp Proton Pump Inhibitors/	108773

14 (proton pump inhibitor* or PPI or PPIs).tw,kw.	88966
15 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	42733
16 or/13-15	167013
17 12 and 16	3589
18 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	5144197
19 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1154037
20 or/18-19	5893686
21 17 and 20	1069
22 21 use ppez,oomezd	863
23 17 use coch,cctr	220
24 22 or 23	1083
25 remove duplicates from 24	820
26 conference abstract.pt.	4177561
27 25 not 26	756
28 limit 27 to english language [Limit not valid in CDSR; records were retained]	645

(UPDATED JULY 14, 2024) PICO 13. Does higher dose PPI therapy in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy?

(UPDATED JULY 14, 2024) PICO 14. Does PCAB therapy in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy?

(UPDATED JULY 14, 2024) PICO 15. Does higher dose PPI therapy result in a higher proportion of patients with symptom resolution in those with erosive esophagitis compared with those without erosive esophagitis in patients with refractory reflux-like symptoms on BID PPI therapy?

(UPDATED JULY 14, 2024) PICO 16. Does PCAB therapy result in a higher proportion of patients with symptom resolution in those with erosive esophagitis compared with those without erosive esophagitis in patients with refractory reflux-like symptoms on BID PPI therapy?

(UPDATED JULY 14, 2024) PICO 17. Does the addition of a prokinetic in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?

(UPDATED JULY 14, 2024) PICO 18. Does the addition of a TLESR inhibitor in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?

(UPDATED JULY 14, 2024) PICO 19. Does the addition of an H2RA in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?

(UPDATED JULY 14, 2024) PICO 20. Does the addition of an alginate and/or antacid in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?

**(UPDATED JULY 14, 2024) PICO 13-PPIs**

1 (reflux* or GERD or GORD).tw,kw.	172174
2 exp Gastroesophageal Reflux/	111244
3 or/1-2	206532
4 (refractory or refractories or resistan*).tw,kw.	3316207
5 ((failed or failure or failing or no or non or "not") adj2 (response or respond*)).tw,kw.	366535
6 ((failed or failure or failing) adj2 (proton pump inhibitor* or PPI or PPIs)).tw,kw.	402
7 or/4-6	3627728
8 3 and 7	11596
9 exp Proton Pump Inhibitors/	126589
10 (proton pump inhibitor* or PPI or PPIs).tw,kw.	113384
11 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	39319
12 or/9-11	201154
13 8 and 12	4432
14 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	4498486
15 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1569224
16 (guideline* or recommendation* or consensus).ti.	408850
17 or/14-16	5904819
18 13 and 17	839
19 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346814
20 18 not 19	666
21 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).tw.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	11940450
22 20 not 21	664
23 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	5032694

25 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	5647511
26 24 not 25	629
27 remove duplicates from 26	438
28 limit 26 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	35
29 limit 26 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	36
30 limit 26 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	37
31 limit 26 to dd=20210801-20240714 use oemezd [Limit not valid in Ovid MEDLINE(R); records were retained]	3
32 limit 26 to dc=20210801-20240714 use oemezd	78
33 26 and 2024*.ep.	7
34 or/28-33	126
35 remove duplicates from 34	90

**(UPDATED JULY 14, 2024) PICO 14 and PICO 16 PCAB**

1 (reflux* or GERD or GORD).tw,kw.	181128
2 exp Gastroesophageal Reflux/	113799
3 or/1-2	215766
4 vonoprazan.tw,kw.	1968
5 (PCAB or PCABs).tw,kw.	413
6 Potassium Competitive Acid Blocker*.tw,kw.	1500
7 or/4-6	2976
8 3 and 7	812
9 exp Proton Pump Inhibitors/	131860
10 (proton pump inhibitor* or PPI or PPIs).tw,kw.	119186
11 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	47734
12 or/9-11	213286
13 8 and 12	759
14 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	6060877
15 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1595298
16 or/14-15	7117392
17 13 and 16	360
18 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346890
19 17 not 18	282
20 19 use medall,oemezd	172
21 13 use coch,cctr	129
22 20 or 21	301
23 remove duplicates from 22	210
24 limit 23 to english language [Limit not valid in CDSR; records were retained]	200
25 limit 23 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
26 limit 23 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	3
27 limit 23 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	3
28 limit 23 to dd=20210801-20240714 use oemezd [Limit not valid in Ovid MEDLINE(R); records were retained]	3
29 limit 23 to dc=20210801-20240714 use oemezd [Limit not valid in CCTR,CDSR; records were retained]	61
30 23 and 2024*.ep.	1
31 limit 23 to yr="2021 -Current" use coch,cctr	28
32 or/25-31	92
33 remove duplicates from 32	92
34 limit 33 to english language [Limit not valid in CDSR; records were retained]	89

**(UPDATED JULY 14, 2024) PICO 17 Prokinetics**

1 (reflux* or GERD or GORD).tw,kw.	181128
2 exp Gastroesophageal Reflux/	113799
3 or/1-2	215766

4 (prokinetic* or gastroprokinetic* or gastrokinetic* or gastro-kinetic*).tw,kw.	10815
5 (antiemetic* or anti-emetic or domperidon* or Metoclopramide or Cisapride or Itopride or ganaton or Mosapride or erythromycin).tw,kw.	110272
6 (Motilin adj (receptor* or agonist*)).tw,kw.	980
7 ((5HT3 or 5HT 3 or 5-HT3 or 5-HT 3) adj antagonist*).tw,kw.	3759
8 ((5HT or 5-HT or 5-hydroxytryptamine*) adj (agonist* or antagonist*)).tw,kw.	3719
9 ((5-HT1A or 5HT1A or 5-HT 1A or 5HT 1A) adj agonist*).tw,kw.	4177
10 exp Serotonin Antagonists/	376251
11 exp Serotonin 5-HT3 Receptor Antagonists/	13240
12 exp Serotonin 5-HT4 Receptor Agonists/	1370
13 exp Serotonin 5-HT1 Receptor Agonists/	11203
14 (serotonin adj3 receptor adj3 (agonist* or antagonist* or block*)).tw,kw.	6965
15 (tegaserod or Zelnorm or Zelnorm).tw,kw.	1457
16 ABT-229.tw,kw.	137
17 (Tandospirone or Sediel or metanopirone or buspirone).tw,kw.	7837
18 (alosetron or Lotronex).tw,kw.	1020
19 (Acotiamide or YM-443 or Z-338D).tw,kw.	366
20 (acetylcholinesterase inhibitor* or cholinesterase Inhibitor* or anti-cholinesterase* or anticholinesterase*).tw,kw.	36251
21 ((5HT-4 or 5HT4 or 5-HT 4 or 5-HT4) adj agonist*).tw,kw.	832
22 or/4-21	525599
23 3 and 22	7086
24 exp Proton Pump Inhibitors/	131860
25 (proton pump inhibitor* or PPI or PPIs).tw,kw.	119186
26 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	47734
27 or/24-26	213286
28 23 and 27	3116
29 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	6060877
30 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1595298
31 or/29-30	7117392
32 28 and 31	923
33 conference abstract.pt.	5203382
34 32 not 33	871
35 34 use medall,oemezd	657
36 28 use coch,cctr	262
37 35 or 36	919
38 remove duplicates from 37	682
39 limit 38 to english language [Limit not valid in CDSR; records were retained]	573
40 (Systematic review or meta-analysis).tw,kw.	1012640
41 39 and 40	83
42 limit 41 to yr="2010 -Current"	55
43 limit 42 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
44 limit 42 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
45 limit 42 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
46 limit 42 to dd=20210801-20240714 use oemezd [Limit not valid in Ovid MEDLINE(R); records were retained]	0
47 limit 42 to dc=20210801-20240714 use oemezd [Limit not valid in CCTR,CDSR; records were retained]	11
48 42 and 2024*.ep.	0
49 limit 42 to yr="2021 -Current" use coch,cctr	0
50 or/43-49	11
51 remove duplicates from 50	11

**(UPDATED JULY 14, 2024) PICO 17 Prokinetics extra search**

1 (reflux* or GERD or GORD).tw,kw.	181128
2 exp Gastroesophageal Reflux/	113799
3 or/1-2	215766
4 (prokinetic* or gastroprokinetic* or gastrokinetic* or gastro-kinetic*).tw,kw.	10815

5 (antiemetic* or anti-emetic or domperidon* or Metoclopramide or Cisapride or Itopride or ganaton or Mosapride or erythromycin).tw,kw.	110272
6 (Motilin adj (receptor* or agonist*)).tw,kw.	980
7 ((5HT3 or 5HT 3 or 5-HT3 or 5-HT 3) adj antagonist*).tw,kw.	3759
8 ((5HT or 5-HT or 5-hydroxytryptamine*) adj (agonist* or antagonist*)).tw,kw.	3719
9 ((5-HT1A or 5HT1A or 5-HT 1A or 5HT 1A) adj agonist*).tw,kw.	4177
10 exp Serotonin Antagonists/	376251
11 exp Serotonin 5-HT3 Receptor Antagonists/	13240
12 exp Serotonin 5-HT4 Receptor Agonists/	1370
13 exp Serotonin 5-HT1 Receptor Agonists/	11203
14 (serotonin adj3 receptor adj3 (agonist* or antagonist* or block*)).tw,kw.	6965
15 (tegaserod or Zelnorm or Zelnorm).tw,kw.	1457
16 ABT-229.tw,kw.	137
17 (Tandospirone or Sediol or metanopirone or buspirone).tw,kw.	7837
18 (alosestron or Lotronex).tw,kw.	1020
19 (Acotiamide or YM-443 or Z-338D).tw,kw.	366
20 (acetylcholinesterase inhibitor* or cholinesterase Inhibitor* or anti-cholinesterase* or anticholinesterase*).tw,kw.	36251
21 ((5HT-4 or 5HT4 or 5-HT 4 or 5-HT4) adj agonist*).tw,kw.	832
22 or/4-21	525599
23 3 and 22	7086
24 exp Proton Pump Inhibitors/	131860
25 (proton pump inhibitor* or PPI or PPIs).tw,kw.	119186
26 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	47734
27 or/24-26	213286
28 23 and 27	3116
29 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	6060877
30 28 and 29	823
31 30 use medall,oemezd	609
32 28 use coch,cctr	262
33 31 or 32	871
34 remove duplicates from 33	619
35 limit 34 to yr="2019 -Current"	82
36 limit 35 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
37 limit 35 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
38 limit 35 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
39 limit 35 to dd=20210801-20240714 use oemezd [Limit not valid in Ovid MEDLINE(R); records were retained]	5
40 limit 35 to dc=20210801-20240714 use oemezd [Limit not valid in CCTR,CDSR; records were retained]	33
41 35 and 2024*.ep.	0
42 limit 35 to yr="2021 -Current" use coch,cctr	8
43 or/36-42	41
44 remove duplicates from 43	41

**(UPDATED JULY 14, 2024) PICO 13 and PICO 15 extra search PPI twice dose or high dose PPIs RCTs or SRs MAs**

1 (reflux* or GERD or GORD).tw,kw.	181128
2 exp *Gastroesophageal Reflux/	54653
3 or/1-2	187618
4 ((twice daily or bid or "b.i.d." or two times or 2 times or "every 12hr*" or "every 12 hr*" or "every 12 hour*") adj5 (proton pump inhibitor* or PPI or PPIs or omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole)).tw.	5526
5 ((three times or four times or 3 times or 4 times or tid or "t.i.d." or qid or "q.i.d." or "every 8hr*" or "every 8 hr*" or "every 8 hour*" or "every 6hr" or "every 6 hr*" or "every 6 hour*") adj5 (proton pump inhibitor* or PPI or PPIs or omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole)).tw.	879

6 ((high or higher or double) adj5 dose* adj5 (proton pump inhibitor* or PPI or PPIs or omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole)).tw.	3881
7 or/4-6	9170
8 3 and 7	2579
9 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	6060877
10 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1595298
11 or/9-10	7117392
12 8 and 11	1035
13 limit 12 to yr="2016 -Current"	291
14 conference abstract.pt.	5203382
15 13 not 14	226
16 limit 15 to english language [Limit not valid in CDSR; records were retained]	217
17 remove duplicates from 16	130
18 limit 17 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	2
19 limit 17 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	1
20 limit 17 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	1
21 limit 17 to dd=20210801-20240714 use oemezd [Limit not valid in Ovid MEDLINE(R); records were retained]	2
22 limit 17 to dc=20210801-20240714 use oemezd [Limit not valid in CCTR,CDSR; records were retained]	15
23 17 and 2024*.ep.	0
24 limit 8 to yr="2021 -Current" use coch,cctr	28
25 or/18-24	45
26 remove duplicates from 25	39

#### (UPDATED JULY 14, 2024) PICO 18 TLESR

1 (reflux* or GERD or GORD).tw,kw.	181128
2 exp Gastroesophageal Reflux/	113799
3 or/1-2	215766
4 ((TLESR or TLESRs or transient lower esophageal sphincter relaxation* or transient lower oesophageal sphincter relaxation* or TLES relaxation* or transient LES relaxation*) adj5 (antagonist* or inhibit* or block* or reducer*)).tw,kw.	229
5 (((metabotropic glutamate receptor* or mGluR*) adj5 (antagonist* or inhibit* or block*)) or AZD2066).tw,kw.	7367
6 Cannabinoid receptor agonist*.tw,kw.	3026
7 ((GABA* adj3 receptor* adj3 agonis*) or lesogaberan or AZD3355).tw,kw.	8725
8 (Baclofen or Lioresal or arbaclofen placarbil).tw,kw.	20666
9 exp Baclofen/	27819
10 exp Muscle Relaxation/ or exp GABA Agonists/	718429
11 or/4-10	733301
12 3 and 11	5430
13 exp Proton Pump Inhibitors/	131860
14 (proton pump inhibitor* or PPI or PPIs).tw,kw.	119186
15 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	47734
16 or/13-15	213286
17 12 and 16	1706
18 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	6060877
19 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1595298
20 or/18-19	7117392
21 17 and 20	458
22 21 use medall,oemezd	408
23 17 use coch,cctr	63
24 22 or 23	471

25 remove duplicates from 24	409
26 limit 25 to english language [Limit not valid in CDSR; records were retained]	401
27 19 and 26	91
28 limit 27 to yr="2010 -Current"	60
29 limit 27 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
30 limit 27 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
31 limit 27 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
32 limit 27 to dd=20210801-20240714 use oemezd [Limit not valid in Ovid MEDLINE(R); records were retained]	2
33 limit 27 to dc=20210801-20240714 use oemezd [Limit not valid in CCTR,CDSR; records were retained]	19
34 27 and 2024*.ep.	0
35 limit 17 to yr="2021 -Current" use coch,cctr	3
36 or/29-35	22
37 remove duplicates from 36	22

#### (UPDATED JULY 14, 2024) PICO 18 RCTs SRs

1 (reflux* or GERD or GORD).tw,kw.	181128
2 exp *Gastroesophageal Reflux/	54653
3 or/1-2	187618
4 ((TLESR or TLESRs or transient lower esophageal sphincter relaxation* or transient lower oesophageal sphincter relaxation* or TLES relaxation* or transient LES relaxation*) adj5 (antagonist* or inhibit* or block* or reducer*)).tw,kw.	229
5 (((metabotropic glutamate receptor* or mGluR*) adj5 (antagonist* or inhibit* or block*)) or AZD2066).tw,kw.	7367
6 Cannabinoid receptor agonist*.tw,kw.	3026
7 ((GABA* adj3 receptor* adj3 agonis*) or lesogaberan or AZD3355).tw,kw.	8725
8 (Baclofen or Lioresal or arbaclofen placarbil).tw,kw.	20666
9 exp Baclofen/	27819
10 exp Muscle Relaxation/ or exp GABA Agonists/	718429
11 or/4-10	733301
12 3 and 11	4075
13 exp Proton Pump Inhibitors/	131860
14 (proton pump inhibitor* or PPI or PPIs).tw,kw.	119186
15 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	47734
16 or/13-15	213286
17 12 and 16	1261
18 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	6060877
19 17 and 18	359
20 19 use medall,oemezd	310
21 17 use cctr,coch	62
22 20 or 21	372
23 remove duplicates from 22	316
24 limit 23 to yr="2014 -Current"	101
25 limit 23 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
26 limit 23 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
27 limit 23 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
28 limit 23 to dd=20210801-20240714 use oemezd [Limit not valid in Ovid MEDLINE(R); records were retained]	1
29 limit 23 to dc=20210801-20240714 use oemezd [Limit not valid in CCTR,CDSR; records were retained]	20
30 23 and 2024*.ep.	0
31 limit 17 to yr="2021 -Current" use coch,cctr	3
32 or/25-31	23
33 remove duplicates from 32	22

#### (UPDATED JULY 14, 2024) PICO 19 H2RAs-2021-08-10

1 (reflux* or GERD or GORD).tw,kw.	181128
2 exp Gastroesophageal Reflux/	113799
3 or/1-2	215766
4 exp Histamine H2 Antagonists/	103734
5 ((histamine or H2 or H-2 or H2R or H 2 R) adj3 (antagonist* or blocker* or blockage* or blockader*)).tw,kw.	33832
6 (H2RA or H2RAs or H2-RA or H2-RAs).tw,kw.	2445
7 (antihistaminic* adj2 (H2 or H-2)).tw,kw.	143
8 (Cimetidine or Tagamet or altramet or biomet or biomet400 or eureceptor or histodil or skf 92334 or skf92334).tw,kw.	30734



9 (ranitidine or zantac or ah 19065 or ah19065 or biotidin or ranisen or ranitidine or sostril or zantic).tw,kw.	20118
10 (Famotidine or Pepcid or mk 208 or mk208 or ym 11170 or ym11170).tw,kw.	7486
11 (Nizatidine or Axid or axid or ly 139037 or ly139037).tw,kw.	1562
12 (Roxatidine or Rotane or Zorpe).tw,kw.	558
13 or/4-12	127292
14 3 and 13	11289
15 exp Proton Pump Inhibitors/	131860
16 (proton pump inhibitor* or PPI or PPIs).tw,kw.	119186
17 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	47734
18 or/15-17	213286
19 14 and 18	7802
20 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	6060877
21 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1595298
22 or/20-21	7117392
23 19 and 22	2011
24 23 use medall,oemezd	1686
25 19 use coch,cctr	405
26 24 or 25	2091
27 remove duplicates from 26	1534
28 19 use coch	28
29 (19 and 21) use medall,oemezd	559
30 28 or 29	587
31 ((histamine or H2 or H-2 or H2R or H 2 R) adj3 (antagonist* or blocker* or blockage* or blockader*)).ti.	8579
32 (H2RA or H2RAs or H2-RA or H2-RAs).ti.	106
33 (antihistaminic* adj2 (H2 or H-2)).ti.	97
34 (Cimetidine or Tagamet or altramet or biomet or biomet400 or eureceptor or histodil or skf 92334 or skf92334).ti.	13565
35 (ranitidine or zantac or ah 19065 or ah19065 or biotidin or ranisen or ranitidine or sostril or zantic).ti.	8834
36 (Famotidine or Pepcid or mk 208 or mk208 or ym 11170 or ym11170).ti.	3141
37 (Nizatidine or Axid or axid or ly 139037 or ly139037).ti.	800
38 (Roxatidine or Rotane or Zorpe).ti.	371
39 or/31-38	32247
40 30 and 39	38
41 remove duplicates from 40	23
42 limit 41 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
43 limit 41 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
44 limit 41 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
45 limit 41 to dd=20210801-20240714 use oemezd [Limit not valid in Ovid MEDLINE(R); records were retained]	0
46 limit 41 to dc=20210801-20240714 use oemezd [Limit not valid in CCTR,CDSR; records were retained]	1
47 41 and 2024*.ep.	0
48 limit 19 to yr="2021 -Current" use coch,cctr	13
49 or/42-48	14
50 remove duplicates from 49	14

**(UPDATED JULY 14, 2024) PICO 20 alginate antacid**

1 (reflux* or GERD or GORD).tw,kw.	181128
2 exp Gastroesophageal Reflux/	113799
3 or/1-2	215766
4 exp Alginates/	48177
5 (alginate or alginates).tw,kw.	61508
6 exp Antacids/	170145
7 (antacid or antacids).tw,kw.	13439
8 Gaviscon.tw,kw.	869
9 (magnesium carbonate or Magnesium hydroxide or aluminum hydroxide or Calcium carbonate).tw,kw.	28000
10 (Gelusil or Maalox or Mylanta or Roloids or Alternagel or Amphojel or Alka-Seltzer or Tums or Pepto-Bismol).tw,kw.	3546
11 or/4-10	255103
12 3 and 11	7643
13 exp Proton Pump Inhibitors/	131860

14 (proton pump inhibitor* or PPI or PPIs).tw,kw.	119186
15 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	47734
16 or/13-15	213286
17 12 and 16	4062
18 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	6060877
19 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1595298
20 or/18-19	7117392
21 17 and 20	1188
22 21 use medall,oemezd	958
23 17 use coch,cctr	251
24 22 or 23	1209
25 remove duplicates from 24	923
26 conference abstract.pt.	5203382
27 25 not 26	842
28 limit 27 to english language [Limit not valid in CDSR; records were retained]	781
29 limit 28 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
30 limit 28 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	2
31 limit 28 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	2
32 limit 28 to dd=20210801-20240714 use oemezd [Limit not valid in Ovid MEDLINE(R); records were retained]	0
33 limit 28 to dc=20210801-20240714 use oemezd [Limit not valid in CCTR,CDSR; records were retained]	60
34 28 and 2024*.ep.	0
35 limit 17 to yr="2021 -Current" use coch,cctr	33
36 or/29-35	95
37 remove duplicates from 36	91

**PICO 21. Does the addition of a bile acid sequestrant in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

1 (reflux* or GERD or GORD).tw,kw.	151657
2 exp *Gastroesophageal Reflux/	49163
3 or/1-2	157593
4 (Bile Acid Sequestrant*).tw,kw.	173156
5 exp Hypolipidemic Agents/	72280
6 exp bile acid sequestrant/	51728
7 (cholestyramine or Questran or Prevalite or colestipol or Colestid or colestipid or colestilan or colesevelam or cholestagel or Lodlis or Welchol).tw,kw.	12701
8 or/4-7	253298
9 3 and 8	622
10 (random* or placebo* or double-blind*).tw.	3113988
11 (Systematic review or meta-analysis).tw. or (Medline or Embase or Pubmed or Cochrane).ab.	874003
12 (guideline* or recommendation* or consensus).ti.	330058
13 or/10-12	3981292
14 9 and 13	116
15 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	4208606
16 14 not 15	96
17 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10696306
18 16 not 17	91
19 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	4405965
20 18 not 19	89
21 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	4939739
22 20 not 21	88
23 limit 22 to english language	62
24 remove duplicates from 23	48

**Extra search removed gastritis**

1 (reflux* or GERD or GORD).tw,kw.	160047
2 exp *Gastroesophageal Reflux/	49188
3 or/1-2	166016
4 (Bile Acid and Sequestrant*).tw,kw.	1985
5 exp bile acid sequestrant/	13977
6 (cholestyramine or Questran or Prevalite or colestipol or Colestid or colestipid or colestilan or colesevelam or cholestagel or Lodlis or Welchol or IW-3718).tw,kw.	8388
7 or/4-6	18951
8 3 and 7	161
9 reflux gastritis.ti.	561
10 8 not 9	132
11 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt. or "Journal: Conference Abstract".pt.	4404957
12 10 not 11	111
13 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10732072
14 12 not 13	101
15 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	4967514
16 14 not 15	98
17 limit 16 to english language [Limit not valid in CDSR; records were retained]	67

18 remove duplicates from 17	53
19 case report/ or case report.ti.	4879216
20 18 not 19	47

#### supplement search including conference

1 (reflux* or GERD or GORD).tw.	157729
2 Bile Acid Sequestrant*.tw.	1827
3 Hypolipidemic Agent*.tw.	1657
4 (cholestyramine or Questran or Prevalite or colestipol or Colestid or colestipid or colestilan or colesevelam or cholestigel or Lodlis or Welchol).tw.	8272
5 IW-3718.tw.	20
6 or/2-5	10923
7 1 and 6	92
8 (random* or RCT*).tw.	3969333
9 (Systematic review or meta-analysis).tw. or (Medline or Embase or Pubmed or Cochrane).ab.	913482
10 or/8-9	4546632
11 7 and 10	24
12 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10731188
13 11 not 12	24
14 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	4554059
15 13 not 14	24
16 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	4966742
17 15 not 16	24
18 limit 17 to english language [Limit not valid in CDSR; records were retained]	22
19 remove duplicates from 18	12

**(UPDATED JULY 14, 2024) PICO 21. Does the addition of a bile acid sequestrant in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

1 (reflux* or GERD or GORD).tw,kw.	181128
2 exp *Gastroesophageal Reflux/	54653
3 or/1-2	187618
4 Bile Acid Sequestrant*.tw,kw.	2153
5 exp Hypolipidemic Agents/	573949
6 exp bile acid sequestrant/	15085
7 (cholestyramine or Questran or Prevalite or colestipol or Colestid or colestipid or colestilan or colesevelam or cholestagel or Lodlis or Welchol or IW-3718).tw,kw.	8933
8 or/4-7	575953
9 3 and 8	913
10 reflux gastritis.ti.	583
11 9 not 10	879
12 (random* or placebo* or double-blind*).tw.	5282744
13 meta-analysis/ or (Systematic review or meta-analysis).tw. or (Medline or Embase or Pubmed or Cochrane).ab.	1387051
14 (guideline* or recommendation* or consensus).ti.	413921
15 or/12-14	6561477
16 11 and 15	114
17 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	11741347
18 16 not 17	113
19 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	5188975
20 18 not 19	111
21 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	5669558
22 20 not 21	109
23 limit 22 to english language [Limit not valid in CDSR; records were retained]	108
24 11 use coch,cctr	18
25 23 use medall,oomezd	96
26 24 or 25	114
27 remove duplicates from 26	94
28 limit 27 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
29 limit 27 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
30 limit 27 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
31 limit 27 to dd=20210801-20240714 use oomezd [Limit not valid in Ovid MEDLINE(R); records were retained]	8
32 limit 27 to dc=20210801-20240714 use oomezd [Limit not valid in CCTR,CDSR; records were retained]	18
33 27 and 2024*.ep.	0
34 limit 24 to yr="2021 -Current" use coch,cctr	1
35 or/28-34	19
36 remove duplicates from 35	19

**PICO 22. Does the addition of a (tricyclic) antidepressant in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

1 (reflux* or GERD or GORD).tw,kw.	151657
2 exp Gastroesophageal Reflux/	93787
3 or/1-2	178352
4 exp antidepressant agent/	484803
5 (antidepress* or anti-depress*).tw,kw.	178149
6 (TCA* or tricyclic*).tw,kw.	73608
7 (Amitriptyline or Amoxapine or Desipramine or Norpramin or Doxepin or Imipramine or Tofranil or Nortriptyline or Pamelor or Protriptyline or Trimipramine).tw,kw.	52377
8 (Amineptine or Clomipramine or Lofepramine or Butriptyline or Dibenzepin or Dosulepin or Iprindole or Lofepramine or Maprotiline or Norclomipramine or Northiaden or Opipramol or Protriptyline or Tianeptine).tw,kw.	12837
9 or/4-8	635337
10 3 and 9	2755
11 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	3665953
12 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1074561
13 (guideline* or recommendation* or consensus).ti.	330058
14 or/11-13	4670504
15 10 and 14	638
16 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	4208606
17 15 not 16	580
18 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10696306
19 17 not 18	575
20 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	4405965
21 19 not 20	541
22 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	4939739
23 21 not 22	525
24 remove duplicates from 23	462

**(UPDATED JULY 14, 2024) PICO 22. Does the addition of a (tricyclic) antidepressant in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

1 (reflux* or GERD or GORD).tw,kw.	181128
2 exp Gastroesophageal Reflux/	113799
3 or/1-2	215766
4 exp antidepressant agent/	593510
5 (antidepress* or anti-depress*).tw,kw.	223561
6 (TCA* or tricyclic*).tw,kw.	90794
7 (Amitriptyline or Amoxapine or Desipramine or Norpramin or Doxepin or Imipramine or Tofranil or Nortriptyline or Pamelor or Protriptyline or Trimipramine).tw,kw.	61051
8 (Amineptine or Clomipramine or Lofepamine or Butriptyline or Dibenzepin or Dosulepin or Iprindole or Lofepamine or Maprotiline or Norclomipramine or Northiaden or Opipramol or Protriptyline or Tianeptine).tw,kw.	14977
9 or/4-8	795756
10 3 and 9	3677
11 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	6060877
12 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1595298
13 (guideline* or recommendation* or consensus).ti.	413921
14 or/11-13	7469911
15 10 and 14	846
16 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346890
17 15 not 16	770
18 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).tw.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	11946922
19 17 not 18	765
20 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	5188975
21 19 not 20	719
22 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	5669558
23 21 not 22	701
24 10 use coch,cctr	72
25 23 use medall,oemzd	633
26 24 or 25	705
27 remove duplicates from 26	641
28 limit 27 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
29 limit 27 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
30 limit 27 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	0
31 limit 27 to dd=20210801-20240714 use oemzd [Limit not valid in Ovid MEDLINE(R); records were retained]	1
32 limit 27 to dc=20210801-20240714 use oemzd [Limit not valid in CCTR,CDSR; records were retained]	96
33 27 and 2024*.ep.	0
34 limit 24 to yr="2021 -Current" use coch,cctr	6
35 or/28-34	102

**PICO 23. Is an abnormal pH or pH-impedance study result in patients with refractory reflux-like symptoms associated with a greater proportion of patients achieving symptom relief after an anti-reflux procedure than a normal pH or pH-impedance study result? [includes endoscopic, surgical & fundoplication procedures]**

1 (reflux* or GERD or GORD).tw,kw.	147998
2 exp Gastroesophageal Reflux/	91977
3 or/1-2	174774
4 ((anti-reflux or antireflux) adj5 (procedure* or endoscop* or technique* or device)).tw,kw.	4041
5 (surger* or surgical or operat*).tw,kw.	6004402
6 (fundoplication or Linx).tw,kw.	15219
7 exp Fundoplication/	15820
8 laparoscopy/	166203
9 (laparoscop* or LARS).tw,kw.	345773
10 (endoscop* adj5 (Thermal or Inject* or Implantation or sutur* or Plicating or plication* or Stapl*)).tw,kw.	13407
11 (Enteryx or Gatekeeper or Durasphere or EndoCinch or NDO Plicator or EsophyX).tw,kw.	8407
12 (Radiofrequency ablation or radiofrequency energy or RF ablation or RFA or stretta).tw,kw.	53751
13 (Syntheon or His-Wiz or Medigus or Full-Thickness Plication*).tw,kw.	140
14 (transmural suture or transmural plication* or Nissen or Toupet).tw,kw.	8175
15 (gastroplication or Magnetic Sphincter Augmentation or magnetic sphincter implant* or Endostapler).tw,kw.	1047
16 (MUSE system or LES-stim or Lower Esophageal Sphincter Stimulation System or LES pacemaker*).tw,kw.	23
17 or/4-16	6160801
18 3 and 17	54478
19 ((pH adj3 testing) or pH impedance).tw,kw.	3904
20 ((esophag* or oesphag*) adj3 pH).tw,kw.	6479
21 ((esophag* or oesphag*) adj3 acid* adj3 measure*).tw,kw.	172
22 or/19-21	9588
23 18 and 22	2610
24 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	4039899
25 23 not 24	1986
26 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10554793
27 25 not 26	1949
28 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	4318235
29 27 not 28	1656
30 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	4793797
31 29 not 30	1647
32 remove duplicates from 31	962



**(UPDATED JULY 14, 2024) PICO 23. Is an abnormal pH or pH-impedance study result in patients with refractory reflux-like symptoms associated with a greater proportion of patients achieving symptom relief after an anti-reflux procedure than a normal pH or pH-impedance study result? [includes endoscopic, surgical & fundoplication procedures]**

1 (reflux* or GERD or GORD).tw,kw.	172174
2 exp Gastroesophageal Reflux/	111244
3 or/1-2	206532
4 ((anti-reflux or antireflux) adj5 (procedure* or endoscop* or technique* or device)).tw,kw.	4535
5 (surger* or surgical or operat*).tw,kw.	7468370
6 (fundoplication or Linx).tw,kw.	17806
7 exp Fundoplication/	18821
8 laparoscopy/	207427
9 (laparoscop* or LARS).tw,kw.	426790
10 (endoscop* adj5 (Thermal or Inject* or Implantation or sutur* or Plicating or plication* or Stapl*)).tw,kw.	16537
11 (Enteryx or Gatekeeper or Durasphere or EndoCinch or NDO Plicator or EsophyX).tw,kw.	11181
12 (Radiofrequency ablation or radiofrequency energy or RF ablation or RFA or stretta).tw,kw.	67614
13 (Syntheon or His-Wiz or Medigus or Full-Thickness Plication*).tw,kw.	189
14 (transmural suture or transmural plication* or Nissen or Toupet).tw,kw.	9171
15 (gastroplication or Magnetic Sphincter Augmentation or magnetic sphincter implant* or Endostapler).tw,kw.	1419
16 (MUSE system or LES-stim or Lower Esophageal Sphincter Stimulation System or LES pacemaker*).tw,kw.	36
17 or/4-16	7659949
18 3 and 17	65550
19 ((pH adj3 testing) or pH impedance).tw,kw.	4920
20 ((esophag* or oesphag*) adj3 pH).tw,kw.	6981
21 ((esophag* or oesphag*) adj3 acid* adj3 measure*).tw,kw.	184
22 or/19-21	10929
23 18 and 22	3031
24 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346814
25 23 not 24	2191
26 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1.ti.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	11736727
27 25 not 26	2141
28 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	5032694
29 27 not 28	1841
30 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	5647511
31 29 not 30	1832
32 limit 31 to english language [Limit not valid in CDSR; records were retained]	1653
33 remove duplicates from 32	972
34 limit 33 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	5
35 limit 33 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	7
36 limit 33 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	7
37 limit 33 to dd=20210801-20240714 use oomezd [Limit not valid in Ovid MEDLINE(R); records were retained]	6
38 limit 33 to dc=20210801-20240714 use oomezd [Limit not valid in CCTR,CDSR; records were retained]	107
39 33 and 2024*.ep.	2
40 or/34-39	115

**PICO 24. Does an endoscopic anti-reflux procedure in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

**PICO 25. Does a surgical anti-reflux procedure (e.g. Linx) in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

**PICO 26. Does a surgical fundoplication procedure in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

1 (reflux* or GERD or GORD).tw,kw.	152184
2 exp Gastroesophageal Reflux/	95031
3 or/1-2	179935
4 ((anti-reflux or antireflux) adj3 (procedure* or endoscop* or technique* or device*)).tw,kw.	3757
5 (surger* or surgical or operat*).tw,kw.	6212139
6 (fundoplication or Linx).tw,kw.	15595
7 exp Fundoplication/	16213
8 laparoscopy/	171504
9 (laparoscop* or LARS).tw,kw.	356820
10 (endoscop* adj5 (Thermal or Inject* or Implantation or sutur* or Plicating or plication* or Stapl*)).tw,kw.	13935
11 (Enteryx or Gatekeeper or Durasphere or EndoCinch or NDO Plicator or EsophyX).tw,kw.	8805
12 (Radiofrequency ablation or radiofrequency energy or RF ablation or RFA or stretta).tw,kw.	55721
13 (Syntheon or His-Wiz or Medigus or Full-Thickness Plication*).tw,kw.	147
14 (transmural suture or transmural plication* or Nissen or Toupet).tw,kw.	8325
15 (gastropliation or Magnetic Sphincter Augmentation or magnetic sphincter implant* or Endostapler).tw,kw.	1093
16 (MUSE system or LES-stim or Lower Esophageal Sphincter Stimulation System or LES pacemaker*).tw,kw.	23
17 or/4-16	6373188
18 3 and 17	56024
19 exp Proton Pump Inhibitors/	104160
20 (proton pump inhibitor* or PPI or PPIs).tw,kw.	81839
21 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	35107
22 or/19-21	153947
23 18 and 22	7444
24 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	3693244
25 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1083349
26 (guideline* or recommendation* or consensus).ti.	331716
27 or/24-26	4703855
28 23 and 27	1388
29 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	4220700
30 28 not 29	1223
31 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).tw.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	10919287
32 30 not 31	1208
33 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	4425828
34 32 not 33	1139
35 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	4963295
36 34 not 35	1089
37 remove duplicates from 36	759

**Extra search for PICO 26**

1 (reflux* or GERD or GORD).ti.	62819
2 *Gastroesophageal Reflux/	43599
3 or/1-2	74468
4 ((anti-reflux or antireflux) and (procedure* or technique* or device* or surg* or operat* or laparoscop* or LARS)).ti.	3287
5 Fundoplication/	15966
6 fundoplication.ti.	6774
7 (surgical or surger* or operat*).ti.	1708557
8 or/4-7	1722142
9 3 and 8	11967
10 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	5074907
11 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1123506
12 (guideline* or recommendation* or consensus).ti.	336799
13 or/10-12	6093494
14 9 and 13	1729
15 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt. or "Journal: Conference Abstract".pt.	4432102
16 14 not 15	1589
17 remove duplicates from 16	972
18 limit 17 to yr="2020 -Current"	50
19 limit 18 to english language [Limit not valid in CDSR; records were retained]	46
20 10 and 19	27

**(UPDATED JULY 14, 2024) PICO 24. Does an endoscopic anti-reflux procedure in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

**(UPDATED JULY 14, 2024) PICO 25. Does a surgical anti-reflux procedure (e.g. Linx) in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

**(UPDATED JULY 14, 2024) PICO 26. Does a surgical fundoplication procedure in a patient with refractory reflux-like symptoms after 8 weeks of therapy with a BID PPI lead to a greater proportion of patients reporting symptom relief than continuing with BID PPI therapy alone?**

1 (reflux* or GERD or GORD).tw,kw.	172174
2 exp Gastroesophageal Reflux/	111244
3 or/1-2	206532
4 ((anti-reflux or antireflux) adj3 (procedure* or endoscop* or technique* or device*)).tw,kw.	4137
5 (surger* or surgical or operat*).tw,kw.	7468370
6 (fundoplication or Linx).tw,kw.	17806
7 exp Fundoplication/	18821
8 laparoscopy/	207427
9 (laparoscop* or LARS).tw,kw.	426790
10 (endoscop* adj5 (Thermal or Inject* or Implantation or sutur* or Plicating or plication* or Stapl*)).tw,kw.	16537
11 (Enteryx or Gatekeeper or Durasphere or EndoCinch or NDO Plicator or EsophyX).tw,kw.	11181
12 (Radiofrequency ablation or radiofrequency energy or RF ablation or RFA or stretta).tw,kw.	67614
13 (Syntheon or His-Wiz or Medigus or Full-Thickness Plication*).tw,kw.	189
14 (transmural suture or transmural plication* or Nissen or Toupet).tw,kw.	9171
15 (gastropliation or Magnetic Sphincter Augmentation or magnetic sphincter implant* or Endostapler).tw,kw.	1419
16 (MUSE system or LES-stim or Lower Esophageal Sphincter Stimulation System or LES pacemaker*).tw,kw.	36
17 or/4-16	7659902
18 3 and 17	65515
19 exp Proton Pump Inhibitors/	126589
20 (proton pump inhibitor* or PPI or PPIs).tw,kw.	113384
21 (omeprazole or lansoprazole or pantoprazole or rabeprazole or esomeprazole or dexlansoprazole or dexrabeprazole or tenatoprazole).tw,kw.	39319
22 or/19-21	201154
23 18 and 22	8993
24 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	4498486
25 Meta-Analysis/ or (Systematic review or meta-analysis).tw,kw. or (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab.	1569224
26 (guideline* or recommendation* or consensus).ti.	408850
27 or/24-26	5904819
28 23 and 27	1614
29 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346814
30 28 not 29	1376
31 (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).tw.) not (humans/ or human/ or human experiment/ or (human* or men or women or patients or subjects).tw.)	11940450
32 30 not 31	1360
33 (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or kid or kids or adolescen* or preschool or pre-school or toddler*).tw.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).tw.)	5032694
34 32 not 33	1278
35 note/ or editorial/ or letter/ or Comment/ or news/ or (note or editorial or letter or Comment or news).pt.	5647511
36 34 not 35	1227
37 remove duplicates from 36	880
38 limit 37 to english language	803
39 limit 38 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	4
40 limit 38 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	4
41 limit 38 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	4
42 limit 38 to dd=20210801-20240714 use oemezd [Limit not valid in Ovid MEDLINE(R); records were retained]	4
43 limit 38 to dc=20210801-20240714 use oemezd [Limit not valid in CCTR,CDSR; records were retained]	106
44 38 and 2024*.ep.	1

**Extra search for PICO 26**

1 (reflux* or GERD or GORD).ti.	65496
2 *Gastroesophageal Reflux/	48699
3 or/1-2	78532
4 ((anti-reflux or antireflux) and (procedure* or technique* or device* or surg* or operat* or laparoscop* or LARS)).ti.	3524
5 Fundoplication/	17482
6 fundoplication.ti.	7193
7 (surgical or surger* or operat*).ti.	1907783
8 or/4-7	1922578
9 3 and 8	12908
10 randomized controlled trial.pt. or (random* or placebo* or double-blind*).mp.	4498486
11 9 and 10	1340
12 conference abstract.pt. or Congresses as Topic/ or Conference Review.pt.	5346814
13 11 not 12	1226
14 limit 13 to yr="2020 -Current"	161
15 limit 14 to english language	157
16 remove duplicates from 15	102
17 limit 16 to ed=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	18
18 limit 16 to ez=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	15
19 limit 16 to dt=20210801-20240714 use medall [Limit not valid in Embase; records were retained]	15
20 limit 16 to dd=20210801-20240714 use oemezd [Limit not valid in Ovid MEDLINE(R); records were retained]	7
21 limit 16 to dc=20210801-20240714 use oemezd [Limit not valid in CCTR,CDSR; records were retained]	61
22 16 and 2024*.ep.	1
23 or/17-22	80