

Effectiveness of Nissen fundoplication versus anterior and posterior partial funduplications for treatment of gastro-esophageal reflux disease: a systematic review protocol

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Review question/objective: The objective of this review is to determine the relative effectiveness of Nissen fundoplication compared to anterior and posterior partial fundoplication in controlling the symptoms of gastro-esophageal reflux disease and reducing their side effect profile in adults.

The specific questions posed by this review are: what is the effectiveness of Nissen fundoplication in comparison to anterior partial fundoplication (90 degree, 120 degree and 180 degree) and posterior 270 degree fundoplication in terms of symptom control of gastro-esophageal reflux disease, and what are the side effects of these surgical interventions?

Keywords anterior partial fundoplication; gastro-esophageal reflux disease; Nissen fundoplication; posterior partial fundoplication; treatment

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Introduction

Gastro-esophageal reflux disease (GERD) is a very common gastrointestinal disease. A meta-analysis of the epidemiology of GERD suggested that the prevalence in Europe and the United States is between 10–20%.¹ The Gastroenterological Society of Australia states that 15–20% of adults experience symptoms of GERD once per week.² Gastro-esophageal reflux disease occurs when an incompetent lower esophageal sphincter allows acidic gastric contents to flow up into the esophagus (Figure 1). This can result in symptoms such as; heartburn, regurgitation, upper abdominal pain, dysphagia or odynophagia, as well as complications such as peptic strictures and Barrett's esophagus.³ Gastro-esophageal reflux disease is a known risk factor for developing Barrett's esophagus and esophageal adenocarcinoma.^{4,5}

Gastro-esophageal reflux disease is a significant public health problem which places a large burden of disease upon the community.^{6,7} Gastro-esophageal

reflux disease causes some of the most commonly seen symptoms in primary care.⁸ The majority of patients are managed with a combination of lifestyle modifications and medical treatments such as acid lowering medications, primarily proton pump inhibitors (PPIs).⁹ In the 2015–2016 financial year, the total cost (to the patient and government) of acid lowering medications, which are the primary management of GERD, in Australia was AUD374 million.¹⁰ This does not include the additional cost of consultations and endoscopies.

The pain and discomfort caused by GERD can adversely affect patients' lives in many ways, including decreased productivity at work secondary to sleep disturbance.¹¹ The health-related quality of life for patients with GERD has been shown to be significantly impaired compared to the general population and the chronic disease population (for conditions such as arthritis, diabetes and cardiovascular disease).^{11,12} The greatest differences were seen in areas of physical functioning, physical role limitations, pain, general health perceptions and vitality.^{6,12} A recent systematic review found that there was a linear association between increases in the frequency and severity of symptoms and decreases in mental health and psychological wellbeing.¹¹

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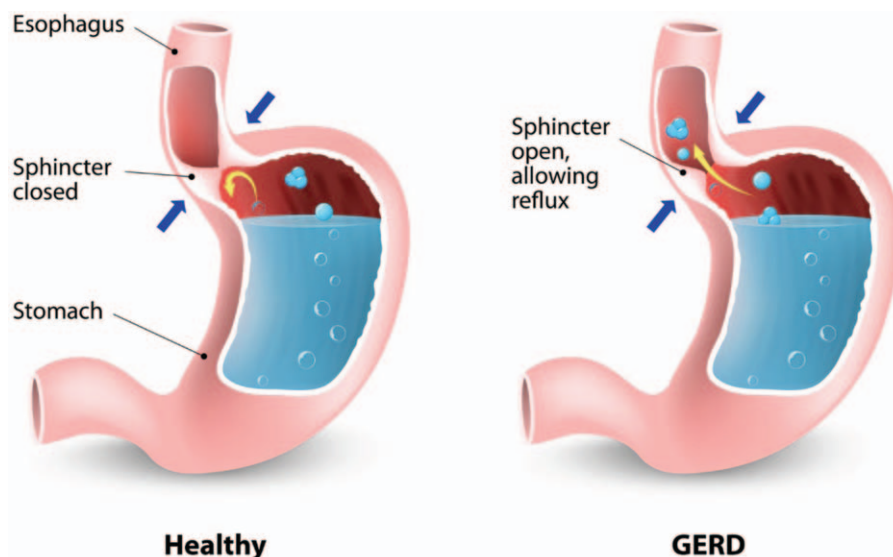


Figure 1: Gastro-esophageal reflux disease (GERD)⁴³

The purpose of surgery in the management of GERD is for the management of patients who are nonresponsive or noncompliant with medical management. Laparoscopic fundoplication is the standard surgical treatment of GERD.¹³⁻¹⁵ A fundoplication is created by wrapping the fundus of the stomach around the lower esophagus. Nissen fundoplication is the most common surgical procedure used for the management of GERD.¹³⁻¹⁵ The Nissen fundoplication describes an operation where the fundus of the stomach is used to create a 360-degree wrap (Figure 2). This is a very effective operation for reducing symptoms relating to GERD, with up to 90% of patients experiencing resolution of

symptoms following laparoscopic fundoplication.¹⁶ But unfortunately fundoplication also has a significant association with postoperative dysphagia (8–12% of patients) and gas related symptoms; such as belching, gas bloating and flatulence (up to 19% of patients).¹⁷⁻²² These symptoms are commonly collectively referred to as post fundoplication syndrome.

Apart from Nissen fundoplication, other partial fundoplications (where the fundus of the stomach is only partially wrapped around the lower esophagus) have been developed with the goal of reducing the post fundoplication symptoms, without compromising anti reflux effectiveness. The most commonly used partial fundoplications in clinical practice today are: the 180-degree anterior fundoplication and the 270-degree posterior fundoplication (also known as the Toupet fundoplication).^{23,24} The 270-degree partial fundoplication has been suggested to reduce the postoperative prevalence of dysphagia and gas related symptoms.²⁵⁻²⁸ However, it has not been widely used because of the suggestion that it has inferior reflux control in comparison to a Nissen fundoplication.²⁹⁻³¹ The anterior 90-degree and 120-degree fundoplications have also been described.

A preliminary PubMed search for existing systematic reviews on this topic was conducted in April 2017. Several systematic reviews have already been

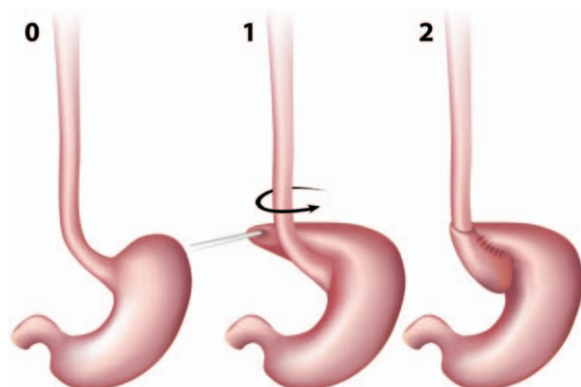


Figure 2: Nissen fundoplication⁴⁴

conducted in an effort to establish which is the best fundoplication. However, due to issues with methodological quality of the reviews, the results have not been able to influence clinical practice. Additionally, the choice of comparisons between surgical approaches may have influenced the results and failed to identify important differences. The two most recent systematic reviews by Memon *et al.* and Broeders *et al.* failed to account for the anatomical differences between these operations.^{32,33} Both reviews grouped 90-degree, 120-degree and 180-degree fundoplications into an “anterior” group and 270-degree and 360-degree wraps into a “posterior” group. These operations have differences in outcomes for both reflux control and side effects. The decision to categorize these operations into only two groups may have led to misleading outcomes. Randomized controlled trials (RCTs) have shown that 90-degree and 120-degree wraps have inferior reflux control compared to 180-degree and 360-degree wraps.³⁴⁻³⁶ Therefore by combining 90-degree, 120-degree and 180-degree wraps into the same group for meta-analysis, the result could be potentially biased towards poorer reflux control. Likewise posterior 270-degree wraps have been associated with fewer side effects compared to Nissen 360-degree wraps, so combining these two wraps into the same group could lead to an underestimation of the side effects for that group.¹⁹

Varin *et al.* and Cataric *et al.* completed a meta-analysis comparing partial and complete fundoplications.^{17,18} However in both of these reviews, anterior and posterior partial fundoplications were pooled and compared with total fundoplications. As described above, these operations have different outcomes and it is not appropriate to group the data in this way for a meaningful analysis.

Our proposed review will compare the benefits and risks of a complete 360-degree Nissen fundoplication to both a partial anterior fundoplication (90 degree, 120-degree and 180-degree) and a partial posterior 270-degree fundoplication. By defining these operations as separate groups we hope to both minimize the potential for bias and produce a result that will guide clinical practice.

Inclusion criteria

Participants

The review will consider studies that include patients:

- Diagnosed with gastro-esophageal reflux disease (GERD). The diagnosis of GERD is made based on evidence from 24-hour esophageal pH monitoring investigations or endoscopically proven esophagitis. For pH monitoring investigations the patient is required to have a probe inserted into the esophagus which measures the pH over a period of time, typically 24 hours. The data collected is then analyzed by an expert clinician who interprets the results in terms of peak acid exposure, total acid time and the patient’s symptoms. Endoscopic esophagitis is the appearance of the esophageal mucosa on direct visualization during endoscopy.
- 18 years of age or over.
- Undergoing laparoscopic and open operations will be included in this review, but these may be analyzed separately in the meta-analysis.

Only patients undergoing primary anti reflux surgery with no concurrent esophageal or gastric motility disorders will be included.

Patients who are undergoing revision anti reflux surgery will be excluded. This is a specialized and complex patient group, the results from these patients cannot be generalized with the rest of the patient population.

Intervention

This review will consider studies that evaluate the Nissen fundoplication (also known as a complete or 360-degree fundoplication/wrap).

Comparator

The comparators of interest in this review are the anterior partial fundoplication (90-degree, 120-degree and 180-degree) and posterior partial 270-degree fundoplication (also known as Toupet fundoplication).

Outcomes

This review will consider studies that include the following outcomes: dysphagia, gas bloating, recurrent reflux symptoms, need for revision surgery and mortality.

These outcomes will be measured by the following:

- Dysphagia
 - Measured with a validated scoring system (eg. modified Dakkak dysphagia score).

- Recurrent reflux symptoms
 - Measured with subjective measures of the presence and severity of reflux symptoms will be considered.
 - Measured with objective measures such as pH studies and endoscopy will be included where the information is presented using a validated scoring system (e.g. DeMeester score).
- Gas bloating
 - Measured by the presence of gas bloating, flatulence, inability to belch.
- Re-operation rate.
- Mortality rate.

Types of studies

This review will consider English language studies with both experimental and quasi-experimental study designs including RCTs, non-RCTs, before and after studies and interrupted time-series studies. In addition, analytical observational studies including prospective and retrospective cohort studies, case-control studies and analytical cross-sectional studies will be considered for inclusion. This review will also consider descriptive observational study designs including case series, individual case reports and descriptive cross-sectional studies for inclusion.

Due to the existence of a relatively large number of RCTs available for inclusion for this topic, a hierarchical approach for evidence inclusion will be used in order to base the results and any corresponding recommendations for practice on the best available evidence. After the initial search, the results will be ordered according to study design/level of evidence and the review team will meet to discuss the results. Preference for inclusion will be given to higher levels of evidence. The review group will be required to come to a consensus regarding the inclusion of studies. If there are sufficient high quality studies available lower levels of evidence will be excluded from the analysis, but listed in an appendix of the final review report.

Methods

Search strategy

The search strategy will aim to find both published and unpublished studies. An initial limited search of MEDLINE (PubMed) has been undertaken, followed by analysis of the text words contained in the titles and abstracts, and of the index terms used to describe the articles. This informed the development of a search

strategy which will be tailored for each information source. The reference lists of all studies selected for critical appraisal will be screened for additional studies. Studies published from 1955, when the Nissen fundoplication was first described, until the date of the search will be included in this review.³⁷

Information sources

The databases to be searched will include: MEDLINE (PubMed), Embase and CINAHL

The trial registers to be searched will include: Cochrane Central Register of Controlled Trials (CENTRAL), ISRCTN Registry and ClinicalTrials.gov

The search for unpublished studies will include: MedNar and ProQuest Dissertations and Theses.

The initial search strategy that will be used when searching the MEDLINE (PubMed) database is shown in Appendix I.

Study selection

Following the search, all identified citations will be collated and uploaded into EndNote (Clarivate Analytics, PA, USA) and duplicates removed. Titles and abstracts will then be screened by one reviewer for assessment against the inclusion criteria for the review. Studies that meet or could potentially meet the inclusion criteria will be retrieved in full and their details imported into Joanna Briggs Institute System for the Unified Management, Assessment and Review of Information (JBI SUMARI). The full text of selected studies will be retrieved and assessed in detail against the inclusion criteria. Full text studies that do not meet the inclusion criteria will be excluded and reasons for exclusion will be provided in an appendix in the final systematic review report. Included studies will undergo a process of critical appraisal. The results of the search will be reported in full in the final report and presented in a PRISMA flow diagram.³⁸

Assessment of methodological quality

Selected studies will be critically appraised by two independent reviewers at the study level for methodological quality in the review using the appropriate standardized critical appraisal instruments from the Joanna Briggs Institute.³⁹ Any disagreements that arise will be resolved through discussion, or with a third reviewer.

Prior to undertaking the critical appraisal process the reviewers will come to a consensus as to which

questions in the various appraisal tools are mandatory for inclusion; this process will be clearly reported in the final review. Following critical appraisal, studies that do not meet a specified quality threshold will be excluded.

Authors will also be contacted for clarification regarding issues of methodological quality.

The results of critical appraisal will also influence the decision to include/exclude studies of lower level study designs in the event that higher level studies are deemed to have methodological deficiencies. In this case, lower level studies may be included in the review if deemed of greater methodological quality than higher level studies.

Data extraction

Data will be extracted from papers included in the review using the standardized data extraction tool available in JBI SUMARI by one reviewer.⁴⁰ Ideally two reviewers would extract the data independently from the relevant sources. However, as this review is being completed as part of a Masters of Clinical Science which must be completed within a two-year timeframe, time constraints will not allow for this process. The data extracted will include specific details about the interventions, populations, study methods and outcomes of significance to the review questions and specific objective. Authors of papers will be contacted to request missing or additional data, where required.

Data synthesis

Papers will, where possible, be pooled in statistical meta-analysis using JBI SUMARI. Decisions to undertake meta-analyses of the included studies will be based upon an assessment of statistical and clinical homogeneity. Heterogeneity will be assessed statistically using the standard chi-squared and I squared tests. Where appropriate, data will be pooled in statistical meta-analysis using JBI SUMARI and the results presented in one of more forest plots. Effect sizes will be expressed as either odds ratios (for dichotomous data) and weighted (or standardized) mean differences (for continuous data), and their 95% confidence intervals will be calculated for analysis. Heterogeneity will be assessed statistically using the standard chi-squared and I squared tests. The choice of model (random or fixed effects) and method for meta-analysis will be based on the guidance by Tufunaru *et al.*⁴¹

Studies will be grouped into patients with anterior 90-degree fundoplication, anterior 120-degree fundoplication, anterior 180-degree fundoplication, posterior 270-degree fundoplication and Nissen 360-degree fundoplication. The combined results of each fundoplication will be compared with one another as five separate groups. Studies may also be grouped into patients with anterior fundoplications, posterior fundoplications and Nissen fundoplications. Laparoscopic and open operations may be analyzed separately in the meta-analysis.

Where statistical pooling is not possible, the findings will be presented in narrative form including tables and figures to aid in data presentation where appropriate.

A funnel plot will be generated to assess publication bias if there are 10 or more studies included in a meta-analysis. Statistical tests for funnel plot asymmetry (Egger test, Begg test, Harbord test) will be performed where appropriate.

Assessing certainty in the findings

A Summary of Findings will be created using GRADEPro GDT software.⁴² The GRADE approach for grading the quality of evidence will be followed. The Summary of Findings will present the following information where appropriate: absolute risks for treatment and control, estimates of relative risk, and a ranking of the quality of the evidence based on study limitations (risk of bias), indirectness, inconsistency, imprecision and publication bias.

The following outcomes will be included in the Summary of Findings:

- Dysphagia
- Recurrent reflux symptoms
- Gas bloating
- Reoperation rate
- Mortality.

References

1. Dent J, El-Serag H, Wallander MA, Johansson S. Epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut* 2005;54(5):710–7.
2. Gastroenterological Society of Australia. Gastro-oesophageal Reflux Disease in Adults [Internet]. Melbourne 2011 [cited 2017 May]. Available from: www.cart.gesa.org.au/membes/files/Clinical%20Guidelines%20and%20Updates/Reflux_Disease.pdf.

3. Vakil N, Van Zanten SV, Kahrilas P, Dent J, Jones R. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol* 2006;101(8):1900–20.
4. Dent J. Barrett's esophagus: A historical perspective, an update on core practicalities and predictions on future evolutions of management. *J Gastroenterol Hepatol* 2011; 26(S1):11–30.
5. Sikkema M, de Jonge P, Steyerberg E, Kuipers E. Risk of Esophageal Adenocarcinoma and Mortality in Patients With Barrett's Esophagus: A Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol* 2010;8(3):235–44.
6. Darbà J, Kaskens L, Plans P, Elizalde J, Coma M, Cuomo R, et al. Epidemiology and societal costs of gastroesophageal reflux disease and Barrett's syndrome in Germany, Italy and Spain. *Expert review of pharmacoeconomics & outcomes research* 2011;11(2):225–32.
7. El-Serag H, Sweet S, Winchester C, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut* 2014;63(6):871–80.
8. Grant A, Wileman S, Ramsay C, Mowat N, Krukowski Z, Heading R, et al. Minimal access surgery compared with medical management for chronic gastro-oesophageal reflux disease: UK collaborative randomised trial. *BMJ* 2008;337:a2664.
9. Spechler SJ. Group* tDoVAGRDS. Comparison of Medical and Surgical Therapy for Complicated Gastroesophageal Reflux Disease in Veterans. *NEJM* 1992;326(12): 786–92.
10. Australian Government Department of Health. Expenditure and Prescriptions Twelve Months to 30 June 2016. [internet] 2016. [cited 28/08/2017] Available from; <http://www.pbs.gov.au/info/statistics/pbs-expenditure-prescriptions-30-june-2016>.
11. Tack J, Becher A, Mulligan C, Johnson D. Systematic review: the burden of disruptive gastro-oesophageal reflux disease on health-related quality of life. *Alimen Pharmacol Ther* 2012;35(11):1257–66.
12. Farup C, Kleinman L, Sloan S, Ganoczy D, Chee E, Lee C, et al. The impact of nocturnal symptoms associated with gastro-oesophageal reflux disease on health-related quality of life. *Arch Intern Med* 2001;161(1):45–52.
13. Salminen P, Hiekkanen H, Rantala A, Ovaska J. Comparison of long-term outcome of laparoscopic and conventional nissen fundoplication: a prospective randomized study with an 11-year follow-up. *Ann Surg* 2007;246(2):201–6.
14. Draaisma W, Rijnhart-de Jong H, Broeders I, Smout A, Furnee E, Gooszen H. Five-year subjective and objective results of laparoscopic and conventional Nissen fundoplication: a randomized trial. *Ann Surg* 2006;244(1):34–41.
15. Broeders J, Rijnhart-de Jong H, Draaisma W, Bredenoord A, Smout A, Gooszen H. Ten-year outcome of laparoscopic and conventional nissen fundoplication: randomized clinical trial. *Ann Surg* 2009;250(5):698–706.
16. Zacharoulis D, O'Boyle C, Sedman P, Brough W, Royston C. Laparoscopic fundoplication: A 10-year learning curve. *Surg Endosc* 2006;20(11):1662–70.
17. Varin O, Velstra B, De Sutter S, Ceelen W. Total vs partial fundoplication in the treatment of gastroesophageal reflux disease: A meta-analysis. *Arch Surg* 2009;144(3):273–8.
18. Catarci M, Gentileschi P, Papi C, Carrara A, Marrese R, Gaspari AL, et al. Evidence-Based Appraisal of Antireflux Fundoplication. *Ann Surg* 2004;239(3):325–37.
19. Broeders J, Mauritz F, Ahmed Ali U, Draaisma W, Ruurda J, Gooszen H, et al. Systematic review and meta-analysis of laparoscopic Nissen (posterior total) versus Toupet (posterior partial) fundoplication for gastro-oesophageal reflux disease. *BJS* 2010;97(9):1318–30.
20. Nadorp J, Smout M, van der Graaf Y, Gooszen H. Laparoscopic or conventional Nissen fundoplication for gastro-oesophageal reflux disease: randomised clinical trial. *Lancet* 2000;355(9199):170–4.
21. Klaus A, Hinder R, DeVault K, Achem S. Bowel dysfunction after laparoscopic antireflux surgery: incidence, severity, and clinical course. *Am J Med* 2003;114(1):6–9.
22. McKenzie D, Grayson T, Polk H. The impact of omeprazole and laparoscopy upon hiatal hernia and reflux esophagitis. *J Am Coll Surg* 1996;183(4):413–8.
23. Stefanidis D, Hope W, Kohn G, Reardon P, Richardson W, Fanelli R. Guidelines for surgical treatment of gastroesophageal reflux disease. *Surg Endosc* 2010;24(11):2647–69.
24. Broeders J, Roks D, Ali U, Watson D, Baigrie R, Cao Z, et al. Laparoscopic anterior 180-degree versus nissen fundoplication for gastroesophageal reflux disease: systematic review and meta-analysis of randomized clinical trials. *Ann Surg* 2013;257(5):850–9.
25. Granderath F, Kamolz T, Granderath U, Pointner R. Gas-related symptoms after laparoscopic 360° Nissen or 270° Toupet fundoplication in gastrooesophageal reflux disease patients with aerophagia as comorbidity. *Dig Liver Dis* 2007;39(4):312–8.
26. Rydberg L, Ruth M, Lundell L. Mechanism of action of antireflux procedures. *BJS* 1999;86(3):405–10.
27. Lundell L, Abrahamsson H, Ruth M, Rydberg L, Lönroth H, Olbe L. Long-term results of a prospective randomized comparison of total fundic wrap (Nissen-Rossetti) or semi-fundoplication (Toupet) for gastro-oesophageal reflux. *BJS* 1996;83(6):830–5.
28. Thor K, Silander T. A long-term randomized prospective trial of the Nissen procedure versus a modified Toupet technique. *Ann Surg* 1989;210(6):719–24.
29. Dallemagne B, Weerts J, Markiewicz S, Dewandre J-M, Wahlen C, Monami B, et al. Clinical results of laparoscopic fundoplication at ten years after surgery. *Surg Endosc* 2006;20(1):159–65.
30. Fein M, Bueter M, Thalheimer A, Pachmayr V, Heimbucher J, Freys SM, et al. Ten-year Outcome of Laparoscopic Antireflux Surgery. *J Gastrointest Surg* 2008;12(11):1893–9.

31. Fernando H, Luketich J, Christie N, Ikramuddin S, Schauer P. Outcomes of laparoscopic Toupet compared to laparoscopic Nissen fundoplication. *Surg Endosc* 2002;16(6): 905–8.
32. Memon M, Subramanya M, Hossain M, Yunus R, Khan S, Memon B. Laparoscopic anterior versus posterior fundoplication for gastro-esophageal reflux disease: a meta-analysis and systematic review. *World J Surg* 2015;39(4):981–96.
33. Broeders J, Roks D, Ahmed Ali U, Draaisma W, Smout A, Hazebroek E. Laparoscopic anterior versus posterior fundoplication for gastroesophageal reflux disease: systematic review and meta-analysis of randomized clinical trials. *Ann Surg* 2011;254(1):39–47.
34. Yau P, Watson D, Ascott N, Lafullarde T, Jamieson G. Efficacy of a 90° anterior fundoplication vs a total fundoplication in an experimental model. *Surgical Endosc* 2000;14(9):830–3.
35. Watson D, Jamieson G, Lally C, Archer S, Bessell J, Booth M, et al. Multicenter, prospective, double-blind, randomized trial of laparoscopic nissen vs anterior 90° partial fundoplication. *Archives of Surgery* 2004;139(11):1160–7.
36. Watson D, Jamieson G, Pike G, Davies N, Richardson M, Devitt P. Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *BJS* 1999;86(1):123–30.
37. Stylopoulos N, Rattner DW. The History of Hiatal Hernia Surgery: From Bowditch to Laparoscopy. *Ann Surg* 2005; 241(1):185–93.
38. Moher D, Liberati A, Tetzlaff J, Altman D. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLOS Medicine* 2009;6(7):e1000097.
39. The Joanna Briggs Institute. Critical Appraisal Tools [Internet]. Adelaide: The Joanna Briggs Institute, The University of Adelaide; 2017 [updated 2017; cited 2017 May]. Available from: <http://joannabriggs.org/research/critical-appraisal-tools.html>.
40. The Joanna Briggs Institute. Joanna Briggs Institute Reviewers' Manual: 2014 edition Australia: The Joanna Briggs Institute; 2014.
41. Tufanaru C, Munn Z, Stephenson M, Aromataris E. Fixed or random effects meta-analysis? Common methodological issues in systematic reviews of effectiveness. *International Journal of Evidence-Based Healthcare* 2015;13(3): 196–207.
42. McMaster University (developed by Evidence Prime I. GRADEpro GDT: GRADEpro Guideline Development Tool [Software]. 2015.
43. Dreamstime. Gastroesophageal Reflux Disease. [Cited 2017 Aug 16]. Available from: <https://www.dreamstime.com/stock-illustration-gastroesophageal-reflux-disease-heartburn-gerd-stomach-releases-strong-acids-to-help-break-down-food-if-esophageal-image52387976>.
44. Dreamstime. Nissen Fundoplication Surgery. [Cited 2017 Aug 16]. Available from: <https://www.dreamstime.com/stock-photography-nissen-fundoplication-surgery-image22192922>.

Appendix I: Search strategy

The initial search strategy to be used in MEDLINE (PubMed) is as follows:

gastroesophageal reflux[mh] OR gastroesophageal reflux [tw] OR gastro esophageal reflux[tw] OR gastro oesophageal reflux[tw] OR gastric acid reflux[tw] OR oesophageal reflux[tw] OR esophageal reflux[tw] OR GERD[tw] OR GORD[tw] OR

laryngopharyngeal reflux[mh] OR laryngopharyngeal reflux[tw] OR acid reflux[tw] OR heartburn[tw]

AND

Nissen Operation[mh] OR Nissen[tw]

AND

Anterior Fundoplication*[tw] OR Anterior Partial Fundoplication*[tw] OR Watson Fundoplication*[tw] OR Dor Fundoplication*[tw] OR 180 degree Fundoplication*[tw] OR 120 degree Fundoplication*[tw] OR 90 degree Fundoplication*[tw] OR Posterior Fundoplication*[tw] OR Posterior Partial Fundoplication*[tw] OR Toupet Fundoplication*[tw] OR 270 degree Fundoplication*[tw]