Medtronic

Global value dossier
for minimally invasive surgery

Nissen Fundoplication

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Date:	April 02, 2016
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Date updated:	April 8, 2021
Purpose for dossier:	This Global Value Dossier is intended to demonstrate the potential clinical and economic value of the Nissen fundoplication for patients, hospitals, and the health care system. The preferred procedure is that which, in the healthcare professional's judgement, addresses the need of the individual patient. Actual potential clinical and economic value may vary.

The original document was completed in April 2016, with literature review conducted in 2015. During the update in 2021, all originally included references were cross checked for accuracy and any claims supported only by publications pre-2010 were further examined for accuracy against more recent literature. No exhaustive literature review was performed during the update.

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1.1 Overview of procedure

Gastroesophageal reflux disease (GERD) is a common and costly chronic condition which has a high prevalence throughout the world.[1] Prevalence is estimated to range between 10% and 20% across Europe and North America, but estimates are restricted by the lack of consensus definition of GERD.[2] GERD can have a substantial impact on quality of life, as sufferers often experience sleep disturbance, lower levels of concentration, and difficulties with exercise.[3] If the condition is left untreated, persistent GERD can also lead to complications such as ulceration, erosive esophagitis, esophageal strictures, hemorrhage, and esophageal adenocarcinoma.[4]

Treatment of GERD typically depends on the severity of symptoms and can include both medical and surgical management. Individuals suffering from GERD typically use regular or continuous medication, particularly proton pump inhibitors (PPIs), to suppress acid production and control the condition.[5] Although these medicines are generally considered safe and effective, questions have been raised regarding the long-term side-effects of prolonged acid suppression.[5,6] Despite GERD's sizeable impact on patient morbidity, associated GERD-related mortality is rare.[7]

Since GERD is a chronic condition, medical therapy may be required for the rest of a patient's life. There is increasing interest in the use of surgery to improve the disease process for patients suffering GERD. Reasons for seeking surgical management of GERD include:[8]

- Failed medical management (inadequate symptom control, severe regurgitation not controlled with acid suppression, or medication side effects).
- Patients who opt for surgery despite successful medical management (due to quality-of-life considerations, life-long need for medication intake, expense of medication etc.).
- Complications of GERD (Barrett's esophagus, peptic stricture).
- Extraesophageal manifestations, e.g., the coexistence of Barrett's esophagus with reflux symptoms is considered by many as clear indication for antireflux surgery.

Although changing in the rate of utilization, different surgical procedures can be undertaken for the treatment of GERD. The two methods of fundoplication which may be used are:

- Classical open methods
- Laparoscopic techniques

Since the advent of laparoscopic surgery in the 1980s, minimally invasive, laparoscopic surgical techniques have progressively replaced open surgery techniques to become the standard of care for many procedures today; between 2003 and 2018, the proportion of Nissen fundoplication procedures performed laparoscopically (as opposed to using classical methods) has increased from 71% to 91%.[9]

Classical and laparoscopic Nissen fundoplication procedures differ in their exact process, however, the procedure itself can be divided into four typical stages of surgery: (1) access to the fundus, (2) dissection of the tissue for removal from the blood supply and other attached tissues, (3) identification of critical structures and fundus pull, where the fundus is wrapped around the esophagus and sutured to the stomach to keep in place, and (4) repair and closure. These techniques have the effect of creating a one-way valve in the esophagus to allow food to pass into the stomach but preventing stomach acid from flowing into the esophagus and thus preventing GERD.

Figure 1. Four typical stages of Nissen fundoplication showcasing instruments to assist in each phase

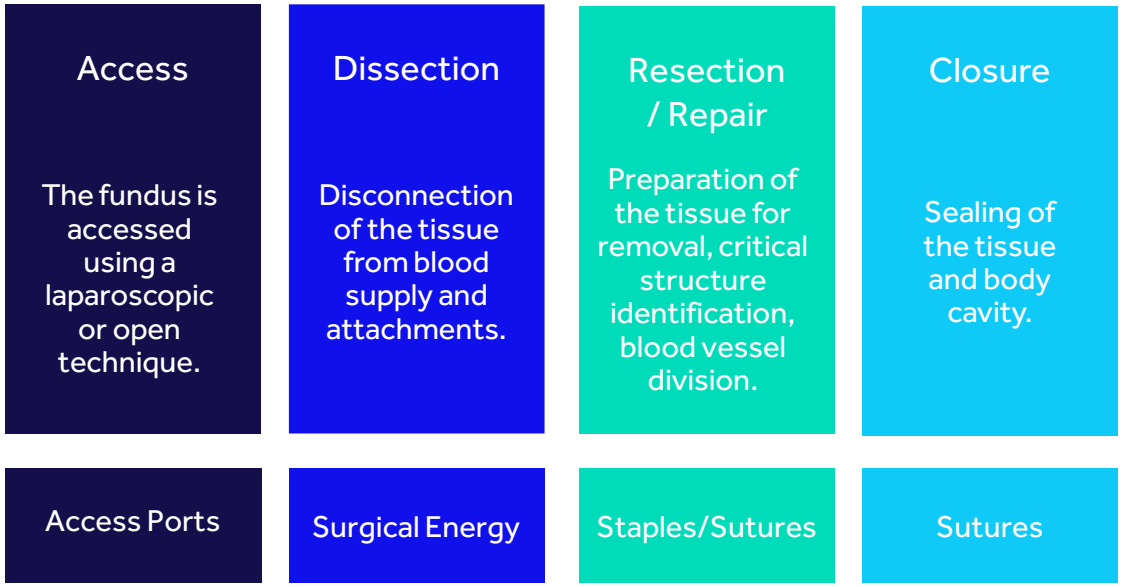


Image modified from a Medtronic internal file.

1.2 Clinical and economic outcomes associated with laparoscopic versus open fundoplication

Key findings

Clinical outcomes

- **Length of stay (LOS):** Laparoscopic fundoplication has been found to be associated with a significantly shorter LoS than open surgery (Figure 2.).[10-13]
- **Operating time:** Operating times were longer for laparoscopic fundoplication in studies in the US and UK,[12,14] but no significant differences were reported in other studies.[10,15]
- **GERD symptoms:** The resolution of reflux symptoms was comparable across open and laparoscopic surgeries in both short- and long-term.[12,16,17]}
- **Mortality:** Mortality rates appear low, and no significant differences between laparoscopic and open surgical procedures are observed.[14].
- **Pain and other post-operative outcomes:** Laparoscopic procedures are associated with reduced pain as well as postoperative wound infections.[18] Significantly less wound pain was reported following laparoscopic than open fundoplication.[12]
- **Re-intervention: A consensus is unclear.** Two studies reported no significance difference in re-intervention rates,[14,19] and a study also indicates that more patients underwent reoperation after open than laparoscopic fundoplication (however the mean interval between operation and re-intervention was longer after open surgery).[16]
- **Patient satisfaction:** Significantly more patients undergoing laparoscopic fundoplication gave a positive evaluation of their surgery than patients undergoing open surgery,[20] though no significant difference between surgical procedures was reported in other studies.[12,19,21]

Economic outcomes

- **Total costs:** Findings from studies reporting economic data are inconsistent.
    - **United States:** Data from the US has shown that total hospital costs may be lower with laparoscopic surgery,[11] but that surgical costs are likely to be higher than with open surgery.[14]
    - **Europe:** Laparoscopic fundoplication was found to have potential to be less cost in the Netherlands compared with open surgery.[13]

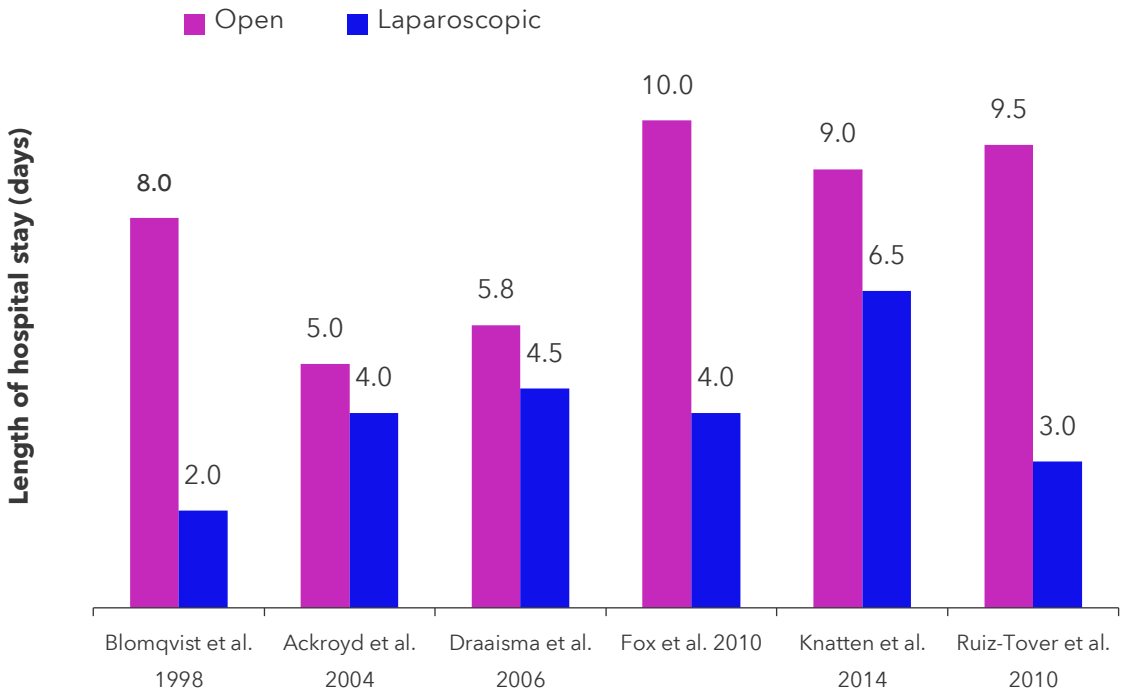
- **Savings due to clinical benefits:** Clinical benefits of laparoscopic Nissen fundoplication, including shorter length of hospital stay have been shown to translate into economic benefits (cost savings from the payer perspective) in the US).[11]

Other findings

Long-term outcomes: Significantly more patients remain symptomatic after open surgery than after laparoscopic surgery.[22] Long-term symptomatic outcomes of both procedures appear to remain unchanged following the first 10 years following surgery.[20]

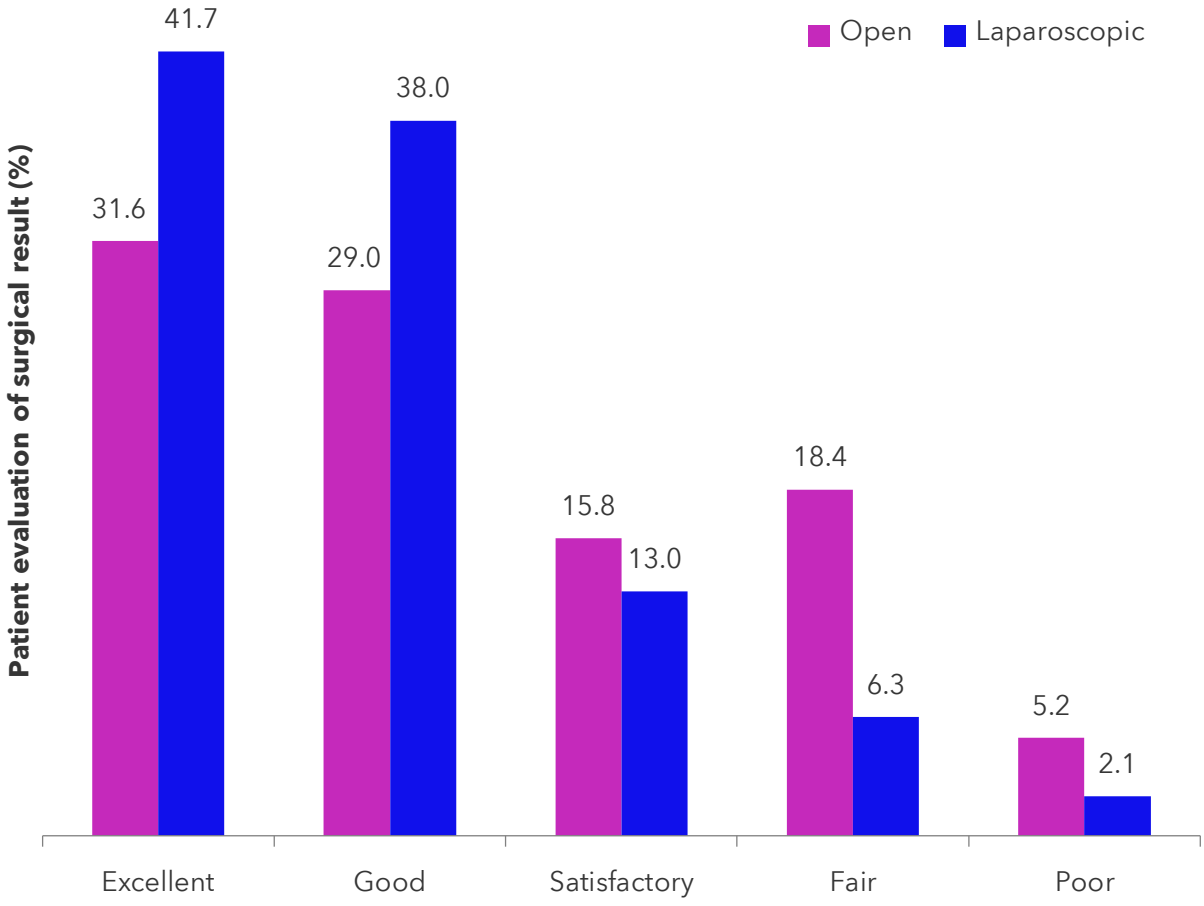
Surgeon volume: Laparoscopic fundoplication operating time decreased as surgeons performed more procedure. This may have benefits in terms of health-economic and, potentially, clinical outcomes.[12]

Figure 2. Length of hospital stay with open versus laparoscopic fundoplication



NR, not reported. Blomqvist[17] p=NR, Ackroyd[12] p=<0.001, Draaisma[13] p=0.029, Fox[11] p=<0.01, Ruiz-Tover[22] p=<0.001.

Figure 3. Patient evaluation of surgical result for laparoscopic versus open Nissen fundoplication



p=0.0484 for difference between groups on total excellent, good, or satisfactory evaluations.

Source: Salminen et al. 2012[20]

1.3 Clinical and economic evidence tables for fundoplication

Table 1-1 Summary of key meta-analyses studies comparing open versus laparoscopic fundoplication

Authors	Details	Procedures	Outcome	Standardized mean differences (95% CI)	P value
Siddiqui et al. 2011[10]	6 studies of which 4 were retrospective studies and two were prospective trials (466 patients in the laparoscopic group and 255 in the open group)	Open versus laparoscopic Nissen fundoplication for GERD in children	Operative time (hours)	−0.55 (−1.69, 0.60), no significant difference	0.35
			Hospital stay (days)	0.93 (0.41, 1.44) shorter with laparoscopy	p<0.01
			Start of feeding (hours)	4.13 (1.00, 7.27) sooner with laparoscopy	<0.01
			30-day morbidity	Relative risk 3.22 (1.98,5.25) higher with open	<0.01
			12-month recurrence	Relative risk 2.49 (0.50, 12.37), no significant difference	0.26

CI: confidence interval; GERD: gastro-esophageal reflux disease.

Table 1-2 Summary of key clinical studies comparing open versus laparoscopic fundoplication

Study	Setting	Study details	Procedure (year performed)	Endpoint	Summary of clinical findings		
					Open	Laparoscopic	P value
Fyhn et al. 2015[19]	Norway	RCT in children, n=43 open, n=44 laparoscopic	Laparoscopic versus open Nissen fundoplication (2003–2009)	**Post-operative outcomes after 4 years of follow up**			
				Recurrence of GERD, %	7	37	0.001
				Repeat fundoplication, %	5	16	0.16
				Able to burp, %	71%	92	<0.05
				Increased flatulence, %	67	57	NS
				Retching (4-7 days/week), %	11	0	NS
				Meal-related discomfort, %	25	29	NS
				Improved well-being, %	97	100	NS
Papandria et al. 2015[14]	United States	Randomized, prospective study in children <2 years	Laparoscopic versus open Nissen fundoplication (2005–2012)	**Operative and peri-operative outcomes**			
				Median operating room time (mins)	165	209	0.002

	old, n=21 open, n=18 laparoscopic	Median surgery length (mins)	91	173	<0.001
		Median duration of epidural catheter (days)	2	2	0.78
		Median duration of narcotic use (days)	3	4	0.26
		Median time to full enteral feeds (days)	3	4	0.91
		Median LoS (days)	4	6	0.08
		Median operating room charges (USD)	2,722	4,450	0.002
		Median total hospital charges (USD)	13,906	26,445	0.18
		30-day re-admissions, %	13.6	29.4	0.26
		Post-operative outcomes (median 42 months follow up)	14	18	0.99
		Mortality, %	4	12	0.57
		Re-operation, %	4	6	0.99
		Continued symptomatic reflux, %	68	76	0.72
		Antacid use, %			

Fox et al. 2011[11]	United States	Retrospective database analysis in children (aged <19 years), n=3,105 open, n=3,978 laparoscopic	Laparoscopic versus open fundoplication (2005–2008)	**Unadjusted operative outcomes**			
				Infection, %	27.6	15.7	<0.01
				Surgical complications, %	25.5	12.0	<0.01
				Post-procedure length of stay (days)	6	3	<0.01
				Total LoS (days)	10	4	<0.01
				Total costs (2008 USD)	22,487	13,003	<0.01

Ruiz-Tover et al. 2010[22]	Spain	Retrospective database analysis, n=88 open, n=78 laparoscopic	Laparoscopic versus open Nissen fundoplication (1996–1998)	**Operative and peri-operative outcomes**			
				Mean surgical time (minutes)	151	142	NS
				Complication rate, %	5	5	NR
				Median post-operative stay (days)	9.5	3	<0.001
				Post-operative outcomes (10 years follow up)			
				Occasional symptoms (e.g. heartburn or regurgitation), %	24	11	<0.05
				PPI use, %	16	7	<0.05
				Satisfaction rate, %	96	97	NS

Thatch et al. 2010[15]	United States	Retrospective medical records review, n=32 open, n=25 laparoscopic	Laparoscopic versus open Nissen fundoplication and gastrotomy placement in neonatal intensive care unit (2002–2008)	**Operative and post-operative outcomes**			
				Time to goal feed (days)	6.1	4.3	0.04
				24-hour post-operative narcotic requirement (mg/kg)	0.55	0.24	0.007
				Blood loss (mL)	13	11	0.33
				Operation time (minutes)	111	113	0.76

Knatten et al. 2014[23]	Norway	RCT in children, n=13 open, n=16 laparoscopic	Laparoscopic versus open Nissen fundoplication (2003–2007)	**Post-operative complications occurring in the first three days after surgery**			
				Pulmonary complications (Grade II), %	46	6	NR
				Gastrostomy infection (Grade II), %	0	6	NR
				Blood transfusion (Grade II), %	15	13	NR
				Repeat gastrostomy (Grade IIIb), %	0	6	NR
				Total post-operative infection complications			
				Infection, %	46	13	0.09

Pacilli et al. 2014[21]	United Kingdom	RCT in children, n=20 open, n=19 laparoscopic	Laparoscopic versus open Nissen fundoplication (2006)	**Post-operative findings at follow-up in 31 surviving patients (n=16 open, n=15 laparoscopic**			
				Retching, %	50	7	0.01
				Gas bloat syndrome, %	31	13	NS
				Dumping syndrome, %	6	7	NS
				Any of the above, %	56	27	NS
				Child's and parental overall quality of life (1=excellent, 2=good, 3=average, 4=poor, 5=terrible), mean (SD)			
				6 months before surgery	4.1 (0.6)	4.1 (0.7)	NR
				6 months after surgery (vs 6 months before surgery)	2.3 (0.8)	1.9 (1.0)	p<0.001
				At follow up (4.1 years) (vs 6 months before surgery)	1.7 (0.7)	1.5 (0.6)	p<0.001

Salminen et al. 2012[20]	Finland	RCT, n=38 open, n=48 laparoscopic	Laparoscopic versus open Nissen fundoplication (1992–1995)	**Post-operative (15-year)**			
				Positive evaluation of surgical result, %	76.3	91.7	0.0484
				Barrett's esophagus, %	7.1	19.4	0.2778
				Hiatal hernia, %	57.1	30.6	0.0326
				Partial plication disruption, %	32.1	8.3	0.0035
				Total plication disruption, %	14.3	2.8	0.0035
				Would choose surgery again, %	65.8	77.1	0.1384
Broeders et al. 2009[16]	Netherlands	RCT, n=69 open, n=79 laparoscopic	Laparoscopic versus open Nissen fundoplication (1997–1999)	**Post-operative**			
				GERD symptoms relieved, %	91	92	NS
				Relief of regurgitation, %	91	99	0.030
				Quality of life (VAS)	61	65	NS
				Would choose surgery again, %	73	79	NS
				Re-operation, %	35	15	0.006
				Mean interval between surgery and reintervention (months)	50.6	22.9	0.047

Ackroyd et al. 2004[12]	United Kingdom	RCT, n=47 open, n=52 laparoscopic	Laparoscopic versus open Nissen fundoplication (1993–2000)	**Peri-operative**			
				Median operating time, mins	46	82	0.001
				Time to oral fluid intake (days)	1	1	0.084
				Time to solid food intake (days)	2	2	0.004
				LoS (days)	5	4	<0.001
				Median time to return to work (weeks)	7	4	0.002
				Post-operative			
				Median acid exposure times (pH<4), %	0.4	0.1	0.250
				Median reflux episodes	3	1	0.169
				Amplitude distal esophageal motility, mmHg	80	70.5	0.038

GERD, gastro-esophageal reflux disease; kg, kilogram; LoS, length of stay; PPI, proton pump inhibitor; mg, milligram; mL, milliliter; NA, not applicable; NS, not significant; pH, potential of hydrogen; RCT, randomized controlled trial; SD, standard deviation; USD, United States Dollar; VAS, Visual Analogue Scale.

Table 1-3 Summary of key studies comparing economic outcomes of open versus laparoscopic fundoplication

Study	Setting	Study details	Procedures	Currency (Cost year)	Outcome	Cost	
						Open	Laparoscopic
Draaisma et al. 2006[13]	Netherlands	Cost-effectiveness analysis based on RCT and cohort study data n=46 open, n=57 laparoscopic, plus n=121 laparoscopic from the cohort study	Laparoscopic versus open Nissen fundoplication (1997–1999)	EUR (2004)	**Open versus laparoscopic Nissen fundoplication,**		
					RCT mean hospital costs	6,989	9,126
					Cohort mean hospital costs	6,951	7,782
					RCT mean sick leave costs	13,940	6,351
					Cohort mean hospital costs	0.59	6,560
					RCT mean total costs		15,477
					Cohort mean total costs		14,342

RCT mean QALYs in one year (VAS)	0.63
Cohort mean QALYs in one year	0.66
RCT ICER (cost per QALY gained)	38,425
Cohort ICER (cost per QALY gained)	5,743

Blomqvist et al. 1998[17]	Sweden	Prospective observational study, n=28 open, n=28 laparoscopic	Laparoscopic versus open fundoplication (1991–1993)	SEK (1995)	**Direct costs**		
					Laboratory tests	664	157
					Blood transfusions	189	12
					Post-operative recovery unit	3,677	1,481
					Operating theatre	12,856	18,363
					Disposables (operating theatre)	0	5,850
					Hospital stay	18,102	5,558
					Doctors' visits	1,929	1,993
					Endoscopies	65	129
					Total direct costs	37,482	27,693
					Indirect costs		
					Lost productivity due to surgery, doctors' visits and endoscopies	37,126	12,596
					Total costs	**74,608**	**40,289**

EUR, Euros; ICER, incremental cost-effectiveness ratio; RCT, randomized controlled trial; QALY, quality-adjusted life year; SEK, Swedish Kronor; VAS, Visual Analogue Scale.

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