Guidelines for the Surgical Treatment of Gastroesophageal Reflux (GERD)
Appendices

Appendix 1 (KQ1) Medical (PPI) management versus Surgical (fundoplication) in adult and pediatric patients with GERD

Note: The systematic review originally addressed medical management versus fundoplication. Given their interest specifically in surgical management, the ssspanel decided to address fundoplication versus medication management in the guideline. The EtD below reflects the original systematic review data for reference.

QUESTION 1

Should medical management (PPI) vs. fundoplication be used for adult and pediatric patients with chronic GERD?	
POPULATION:	GERD: chronic, chronic refractory, or both; children and adults
INTERVENTION:	proton pump inhibitors (PPI)
COMPARISON:	Fundoplication
MAIN OUTCOMES:	Complications; pH normalization; Failure of surgery or therapy; Gas/bloat; Post intervention PPI use; quality of life; Symptom control
SETTING:	International
PERSPECTIVE:	Patient-surgeon

ASSESSMENT

Desirable Effects for medical management
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence from a separately published systematic review, including 15 RCTs, addressed this guideline question.	The panel felt it was important to note that 2.6% of patients in the medical arm ended up receiving surgery as well.

Outcomes	**Relative effect (95% CI)**	**Anticipated absolute effects* (95% CI)**			**Certainty of the evidence (GRADE)**	**Importance**
		With PPI	**With Surgery**	**Difference (PPI – surgery)**		
		Study population				CRITICAL

Complications (Clavien-Dindo >=3 *) № of participants: 1129 (5 RCTs [1-5])	**RR 0.72** (0.47 to 1.09)	**7.5%** (4.9 to 11.4)	10.5%	**2.9% fewer** (5.6 fewer to 0.9 more)	⊕⊕◯◯ LOW [a (1,2,3),b]	
Failure (reoperation or operation for symptom recurrence) № of participants: 485 (2 RCTs [7,10])	**RR 0.52** (0.22 to 1.25)	Study population			⊕◯◯◯ VERY LOW [b,c]	CRITICAL
		2.6% (1.1 to 6.4)	5.1%	**2.4% fewer** (4 fewer to 1.3 more)		
Gas/bloat (> 5 year follow-up) № of participants: 554 (1 RCT [9])	**RR 0.70** (0.55 to 0.89)	Study population			⊕⊕◯◯ LOW [c]	IMPORTANT
		28.0% (22 to 35.5)	39.9%	**12.0% fewer** (18 fewer to 4.4 fewer)		

a. A large portion of the studies were high risk of bias, with details in separate systematic review.
b. Wide confidence interval suggests potential for both harm and benefit.
c. All studies were high risk of bias with details in separate systematic review.

*When "Clavien Dindo classification" was not specifically used in a study, serious adverse events and interventions, e.g. endoscopy, were included for analysis.

Undesirable Effects for medical management

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ● Moderate ○ Small ○ Trivial ○ Varies ○ Don't know	Evidence from a separately published systematic review, including 15 RCTs, addressed this guideline question.	The panel felt it was important to note that over 25% of patients in the operative arm still needed PPI during long term follow-up (>5-year follow-up).

Outcomes	**Relative effect (95% CI)**	**Anticipated absolute effects* (95% CI)**			**Certainty of the evidence (GRADE)**	**What happens**
		With PPI	**With surgery**	**Difference (PPI – Surgery)**		
%time with abnormal pH № of participants: 572 (4 RCTs [3,6,7-8])	-	-	The mean normalization without PPI was **0**	MD **2.11 higher** (1.83 higher to 2.38 higher)	⊕⊕◯◯ LOW [c]	IMPORTANT
Post intervention PPI use № of participants:	**RR 2.57** (1.31 to 5.02)	Study population			⊕◯◯◯ VERY LOW [c, d]	IMPORTANT
		71.8% (36.6 to 100)	27.9%	**43.8% more** (8.7 more		

671 (3 RCTs [7,11-12])				to 112.2 more)		
Short term quality of life (<5-year follow-up) № of participants: 1169 (4 RCTs [1,3,8,13])	-	-	The mean short-term quality of life (<5 year) without PPI was **0**	SMD **0.51 lower** (0.63 lower to 0.4 lower)	⊕⊕⊕◯ MODERATE [a (1,3,14)]	IMPORTANT
Long-term Symptom Control (> 5-year follow-up) № of participants: 748 (5 RCTs [2,4,6,14-15])	**RR 0.79** (0.63 to 0.99)	Study population			⊕◯◯◯ VERY LOW [a (2,6,15-16), e, f]	CRITICAL
		62.6% (49.9 to 78.4)	79.2%	**16.6% fewer** (29.3 fewer to 0.8 fewer)		

a. A large portion of the studies were high risk of bias, with details in separate systematic review.
b. Wide confidence interval suggests potential for both harm and benefit.
c. All studies were high risk of bias with details in separate systematic review.
d. There was statistically significant heterogeneity (p< 0.00001, I2 = 92%). The source of heterogeneity was not due to quality (all high risk of bias) nor wrap type (there were two similar clusters, each including a study with Nissen and a study with mixed wraps). All four were from different countries (UK, USA, Sweden, Canada).
e. Wide confidence interval suggests potential for both harm and no difference.
f. There is statistically significant heterogeneity (p <0.00001, I2 = 87%). The only low risk of bias study (Parrilla 2003), demonstrates no difference (RR 0.99), but there is still significant heterogeneity even when this study is removed (p < 0.0001, I2 = 87%) to suggest heterogeneity is not entirely due to study quality.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies		

Outcomes	Importance	Certainty of the evidence (GRADE)
Complications (Clavien dindo ≥ 3)	CRITICAL	⊕⊕◯◯ LOW
pH Normalization	IMPORTANT	⊕⊕◯◯ LOW
Failure	CRITICAL	⊕◯◯◯ VERY LOW

Gas/bloat (> 5-year follow-up)	IMPORTANT	⨁⨁◯◯ LOW
Post intervention PPI use	IMPORTANT	⨁◯◯◯ VERY LOW
Short term quality of life (< 5-year follow-up)	IMPORTANT	⨁⨁⨁◯ MODERATE
Long-term Symptom CONTROL (> 5-year follow-up)	CRITICAL	⨁◯◯◯ VERY LOW

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability		

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors Surgery ● Probably favors Surgery ○ Does not favor either the intervention or the comparison ○ Probably favors PPI ○ Favors PPI ○ Varies ○ Don't know		No comparative studies in the pediatric population evaluated medical versus surgical management for GERD, precluding analysis. However, there is a growing body of literature that demonstrates PPI use may have additional drawbacks in the pediatric population, including increased risk of fracture. A recent and large single arm study [16], demonstrates the risk of fracture at least is a significant risk in pediatric patients. This could in part support a recommendation for pediatric recommendations. Additionally, a long-term study of 36 patients with over ten years of follow-up demonstrated that laparoscopic fundoplication produced a good clinical result and a good quality of life [17].

Acceptability

Is the option above (probably surgery) acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know		

Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know		

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	**Moderate**	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	**Probably favors the comparison**	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention (against medical management)	**Conditional recommendation against the intervention (against medical management)**	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention (for medical management)	Strong recommendation for the intervention (for medical management)
○	●	○	○	○

CONCLUSIONS

Recommendation

We suggest that adult patients with confirmed chronic, chronic refractory, or both, gastroesophageal reflux may benefit from surgical fundoplication over medical management only (conditional recommendation based on very low certainty of the evidence about effects).

Justification

The panel judged there are moderate desirable effects of surgery over medical management which outweighed small undesirable effects. This balance favoring surgery would likely apply to most adult patients with GERD. However, due to very low certainty evidence, only a conditional recommendation could be made.

Subgroup considerations

The available comparative evidence does not address pediatric patients. There is a growing body of literature that demonstrates PPI use may have additional drawbacks in the pediatric population, including increased risk of fracture. Although there is no comparative data on this risk explicitly against fundoplication, recent and large single arm evidence [16], demonstrates the risk of fracture at least is a significant risk in pediatric patients. This could further support a recommendation for pediatric recommendations.

Implementation considerations

Monitoring and evaluation

Research priorities

More recent, well-designed RCT comparing medical treatment to surgical therapy, especially with large sample size sufficient to create precise estimates, are needed. Comparative evidence on medical versus surgical therapy for pediatric patients is needed.

Selected Studies

1. Lundell, Lars, et al. "Comparing laparoscopic antireflux surgery with esomeprazole in the management of patients with chronic gastro-oesophageal reflux disease: a 3-year interim analysis of the LOTUS trial." *Gut* 57.9 (2008): 1207-1213.
2. Grant AM, Cotton SC, Boachie C, Ramsay CR, Krukowski ZH, Heading RC, Campbell MK (2013) Minimal access surgery compared with medical management for gastro-oesophageal reflux disease: five year follow-up of a randomised controlled trial (REFLUX). BMJ 346**:**f1908
3. Anvari, Mehran, et al. "A randomized controlled trial of laparoscopic Nissen fundoplication versus proton pump inhibitors for the treatment of patients with chronic gastroesophageal reflux disease (GERD): 3-year outcomes." *Surgical endoscopy* 25.8 (2011): 2547-2554.
4. Parrilla, Pascual, et al. "Long-term results of a randomized prospective study comparing medical and surgical treatment of Barrett's esophagus." *Annals of surgery* 237.3 (2003): 291.
5. Spechler, Stuart J., et al. "Randomized trial of medical versus surgical treatment for refractory heartburn." *New England Journal of Medicine* 381.16 (2019): 1513-1523.
6. Hatlebakk, Jan G., et al. "Gastroesophageal acid reflux control 5 years after antireflux surgery, compared with long-term esomeprazole therapy." *Clinical Gastroenterology and Hepatology* 14.5 (2016): 678-685.
7. Spechler, Stuart Jon, et al. "Long-term outcome of medical and surgical therapies for gastroesophageal reflux disease: follow-up of a randomized controlled trial." *Jama* 285.18 (2001): 2331-2338.
8. Mahon, D., et al. "Randomized clinical trial of laparoscopic Nissen fundoplication compared with proton-pump inhibitors for treatment of chronic gastro-oesophageal reflux." *British Journal of Surgery: Incorporating European Journal of Surgery and Swiss Surgery* 92.6 (2005): 695-699.
9. Galmiche, Jean-Paul, et al. "Laparoscopic antireflux surgery vs esomeprazole treatment for chronic GERD: the LOTUS randomized clinical trial." *Jama* 305.19 (2011): 1969-1977.
10. Grant, Adrian M., et al. "Minimal access surgery compared with medical management for chronic gastro-oesophageal reflux disease: UK collaborative randomised trial." *Bmj* 337 (2008): a2664.
11. Lundell, L., et al. "Continued (5-year) followup of a randomized clinical study comparing antireflux surgery and omeprazole in gastroesophageal reflux disease." *Journal of the American College of Surgeons* 192.2 (2001): 172-179.
12. Grant, A. M., et al. "Minimal access surgery compared with medical management for gastro-oesophageal reflux disease: five year follow-up of a randomised controlled trial (REFLUX)." *Bmj* 346 (2013): f1908.
13. Grant, Adrian Maxwell, et al. "The effectiveness and cost-effectiveness of minimal access surgery amongst people with gastro-oesophageal reflux disease–a UK collaborative study." (2008).
14. Mehta, Samir, et al. "Prospective trial of laparoscopic Nissen fundoplication versus proton pump inhibitor therapy for gastroesophageal reflux disease: seven-year follow-up." *Journal of Gastrointestinal Surgery* 10.9 (2006): 1312-1317.
15. Lundell, Lars, et al. "Comparison of outcomes twelve years after antireflux surgery or omeprazole maintenance therapy for reflux esophagitis." *Clinical Gastroenterology and Hepatology* 7.12 (2009): 1292-1298
16. Wang YH, Wintzell V, Ludvigsson JF, Svanstrom H, Pasternak B (2020) Association Between Proton Pump Inhibitor Use and Risk of Fracture in Children. JAMA Pediatr 174**:**543-551
17. Esposito C, De Luca C, Alicchio F, Giurin I, Miele E, Staiano AM, Settimi A (2012) Long-term outcome of laparoscopic Nissen procedure in pediatric patients with gastroesophageal reflux disease measured using the modified QPSG Roma III European Society for Pediatric Gastroenterology Hepatology and Nutrition's questionnaire. J Laparoendosc Adv Surg Tech A;22:937-940.

Appendix 2 (KQ2) Should Robotic or laparoscopic fundoplication be used in adult and pediatric patients with GERD?

QUESTION 2A: Adults

Should robotic approach vs. laparoscopic approach be used for fundoplication in adults with GERD?	
POPULATION:	fundoplication in adults with GERD
INTERVENTION:	robotic approach
COMPARISON:	laparoscopic approach
MAIN OUTCOMES:	Symptomatic reflux control; Re-operation for wrap failure; PPI use; Complications of surgery; GI quality of life
SETTING:	International
PERSPECTIVE:	Patient-surgeon

ASSESSMENT

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT

○ Trivial
○ Small
○ Moderate
○ Large
● Varies
○ Don't know

RESEARCH EVIDENCE

From the original systematic review, four randomized control trials on robotic versus laparoscopic fundoplication in adults were used to inform the panel's decision.

Outcomes	**Relative effect (95% CI)**	**Anticipated absolute effects* (95% CI)**			**Certainty of the evidence (GRADE)**	**Importance**
		With robotic approach	**With laparoscopic approach**	**Difference**		
Short term GI quality of life (< 5 year) № of participants: 90 (2 RCTs [1-2])	-	-	-	SMD **0.01 SD higher** (0.4 lower to 0.42 higher)	⊕⊕◯◯ LOW [a,d]	CRITICAL
Post-intervention PPI use № of participants: 40 (1 RCT [2])	**RR 0.14** (0.01 to 2.60)	**2.1%** (0.1 to 39)	15.0%	**12.9% fewer** (14.8 fewer to 24 more)	⊕⊕◯◯ LOW [a,b]	VARIES

ADDITIONAL CONSIDERATIONS

The main desirable effect for robotic approach was decreased postoperative PPI use. GI quality of life favored neither intervention nor comparator. The panel believed the degree of desirable effect ultimately varies based on the value taking a PPI post-intervention has for a patient. The panelists varied in whether post-intervention PPI should even be included as a decision-making outcome as PPI use does not correlate with reflux symptoms. The panel further observed the inconsistency in the direction of effect between symptom control and PPI use. As such, an important proportion of informed patients would likely consider PPI use as of low importance for decision-making.

Notwithstanding, the panel acknowledged a subgroup of patients for whom PPI-use would be an important or even critical decision-making outcome, particularly patients who opt for the procedure because of their concerns about long-term PPI use. For this subgroup of patients, PPI use would be an important outcome for decision-making, with small magnitude of the observed desirable effect.

a. Wide confidence interval and small sample size suggest the potential for both important benefit and harm.
b. PPI use was considered an imperfect proxy for "need for PPI" based on reflux
c. One observational study additionally has too few events to obtain an effect estimate.
d. The referestudies had opposite direction, but both have greatly overlapping confidence intervals with no statistical heterogeneity (Chi2 p=0.75, I2=0%).

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ● Trivial ○ Varies ○ Don't know	From the original systematic review, four randomized control trials on robotic versus laparoscopic fundoplication in adults were used to inform the panel's decision based.	All panel members agreed the undesirable effects of robotic approach were either trivial (2/3) or small (1/3). The main undesirable effects were complications and symptomatic reflux control.

Outcomes	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Certainty of the evidence (GRADE)	Importance
		Without robotic approach	With robotic approach	Difference		
Short-term symptomatic reflux control (№ of participants: 90 (2 RCTs [1-2])	**RR 0.95** (0.85 to 1.07)	Study population			⨁⨁◯◯ LOW [a]	CRITICAL
		95.6%	**90.8%** (81.2 to 100)	**4.8% fewer** (14.3 fewer to 6.7 more)		
Re-operation due to wrap failure № of participants: 40 (1 RCT [2])	**RR 3.00** (0.13 to 69.52)	Study population			⨁⨁◯◯ LOW [a]	IMPORTANT
		0.0%	**0.0%** (0 to 0)	**0.0% fewer** (range not estimable due to no events)		
Complication (Clavien-Dindo ≥3 № of participants: 140 (3 RCTs [1-3])	**RR 1.34** (0.27 to 6.70)	Study population			⨁⨁◯◯ LOW [a,c]	CRITICAL
		2.9%	**3.8%** (0.8 to 19.1)	**1.0% more** (2.1 fewer to 16.3 more)		

a. Wide confidence interval and small sample size suggest the potential for both important benefit and harm.
b. PPI use was considered an imperfect proxy for "need for PPI" based on reflux
c. One observational study additionally has too few events to obtain an effect estimate.
d. The studies had opposite direction, but both have greatly overlapping confidence intervals with no statistical heterogeneity (Chi2 p=0.75, I2=0%).

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Critical outcomes, including those which varied and had the potential to be critical for some patients, were used to inform the overall certainty of evidence.	For patients who critically value their long-term PPI consumption, the overall certainty would be very low.

Outcomes	Importance	Certainty of the evidence (GRADE)
Symptomatic reflux control < 5 year	CRITICAL	⨁⨁◯◯ LOW
Re-operation due to wrap failure	IMPORTANT	⨁⨁◯◯ LOW
PPI	VARIES	⨁◯◯◯ VERY LOW
Complication (Clavien dindo >= 3; peri-operative - 12 months)	CRITICAL	⨁⨁◯◯ LOW
GI quality of life (< 5 year)	CRITICAL	⨁⨁◯◯ LOW

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability		The panelists agreed there would unlikely be any variability in how patients value the desirable and undesirable outcomes above. Based on experience with this patient population, the panel was certain patients value symptom resolution and complications as critical decision-making outcomes. However, there was extensive debate as to the value of other outcomes, notably PPI, for patient decision-making. After extensive discussion, it was agreed that the value of post-procedure PPI use for decision-making likely is important for some patients while not important for others when deciding between robotic and laparoscopic fundoplication.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ● Varies ○ Don't know	With the exception of post-procedure PPI use, which had variable importance for decision making and thus small desirable effect for robotic approach, all remaining evidence suggested trivial desirable and trivial undesirable effects for robotic compared to laparoscopic fundoplication in adults. This included primary efficacy and safety outcomes (symptom control and complications). For the majority of patients, the balance does not favor either the intervention or the comparison. For those patients who are particularly concerned about long-term PPI use, the balance probably favors the intervention (robotic approach).	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know		The panel felt there may be some stakeholders, including some hospitals and a minority of practicing surgeons, who would not find the robotic approach for fundoplication acceptable, regardless of feasibility.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	Per patient costs for robotic versus laparoscopic fundoplication Study | Robotic | Laparoscopic | Details of cost Owen 2014 | 10644 | 7968 | US dollars. Perioperative cost Morino 2006 | 3157 | 1527 | EURO. Inpatient cost Muller-Stitch 2007 | 3244 | 2743 | EURO. Inpatient cost Nakadi 2006 | 27561 | 5907 | EURO. In hospital costs Nakadi 2006 | 26,088 | 936 | EURO. Yearly investment and maintenance	While robotic surgery has become more common than historically, the robotic approach still requires additional training and an investment in the actual robot. The feasibility thus varies based on access to facilities who have made that investment and have surgeons trained on the robot. This panel did not choose the societal perspective nor had the expertise needed to fully evaluate cost-effectiveness. However, the panel agreed that higher costs for robotic fundoplication could contribute to decreased feasibility. The research evidence presented does NOT mean patient out-of-pocket cost is greater, but that due to expense, the robotic approach may be less feasible.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		**Varies**	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		**Varies**	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	**Conditional recommendation for either the intervention or the comparison**	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	●	○	○

CONCLUSIONS

Recommendation

We suggest that adult patients with gastroesophageal reflux may be treated with either robotic or laparoscopic fundoplication (conditional recommendation based on low certainty in the evidence about effects). For patients who are particularly concerned about long-term PPI use, we suggest robotic surgery over laparoscopic fundoplication when expertise and resources are available (conditional recommendation based on very low certainty in the evidence about effects). No evidence-based recommendation can be made for patients who are undergoing revisional fundoplication.

Justification

Based on low certainty evidence available, the panel judged there are trivial differences in efficacy and safety between robotic and laparoscopic fundoplication.

Patients' values and preferences for outcomes, overall certainty about the estimates of effect, and the feasibility of performing robotic fundoplication were considered in making recommendations. This data may not reflect balance of effects for revisional cases, however. This population requires further research before a recommendation can be made.

Subgroup considerations

Implementation considerations

To improve feasibility for robotic fundoplication, considerations for increased surgeon training are needed.

Monitoring and evaluation

Research priorities

The panel made multiple recommendations for future studies on robotic versus laparoscopic fundoplication in adults with GERD.

- Long term effectiveness data
- Long term cost- effectiveness studies, including cost of both operation (laparoscopic versus robotic) and long-term care (medications and reoperation)
- PPI use
- Redo fundoplication benefits
- Additional studies comparing patient-reported pain in robotic vs laparoscopic surgery.

Studies

1. Draaisma, W. A., et al. "Randomized clinical trial of standard laparoscopic versus robot-assisted laparoscopic Nissen fundoplication for gastro-oesophageal reflux disease." *British Journal of Surgery: Incorporating European Journal of Surgery and Swiss Surgery* 93.11 (2006): 1351-1359.
2. Müller-Stich, B. P., et al. "No relevant difference in quality of life and functional outcome at 12 months' follow-up—a randomised controlled trial comparing robot-assisted versus conventional laparoscopic Nissen fundoplication." *Langenbeck's archives of surgery* 394.3 (2009): 441-446.
3. Morino, Mario, et al. "Randomized clinical trial of robot-assisted versus laparoscopic Nissen fundoplication." *British Journal of Surgery: Incorporating European Journal of Surgery and Swiss Surgery* 93.5 (2006): 553-558.
4. El Nakadi, Issam, et al. "Evaluation of da Vinci Nissen fundoplication clinical results and cost minimization." *World journal of surgery* 30.6 (2006): 1050-1054.

QUESTION 2B: Children

Should robotic approach vs. laparoscopic approach be used for fundoplication in children with GERD?	
POPULATION:	Fundoplication in children with GERD
INTERVENTION:	robotic approach
COMPARISON:	laparoscopic approach
MAIN OUTCOMES:	Symptom control; Reoperation for wrap failure; Complications of surgery; Dysphagia; Length of stay; Patient reported pain
SETTING:	International
PERSPECTIVE:	Patient-surgeon

ASSESSMENT

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT

- ● Trivial
- ○ Small
- ○ Moderate
- ○ Large
- ○ Varies
- ○ Don't know

RESEARCH EVIDENCE

From the original systematic review, four observational studies on robotic versus laparoscopic fundoplication in children were used to inform the panel's decision. Three (Albassam 2009, Anderberg 2007, Copeland 2008) used Nissen and Lehnert 2006 used Thal fundoplication. There was no heterogeneity between Lehnert 2006 and those with Nissen fundoplication for any outcome.

Outcomes	**Relative effect (95% CI)**	**Anticipated absolute effects*** **(95% CI)**			**Certainty of the evidence (GRADE)**	**Importance**
		Robotic approach	**Laparoscopic approach**	**Difference**		
Patient reported symptom control № of participants: 82 (3 observational studies [1-3])	**RR 1.00** (0.93 to 1.07)	Study population			⊕◯◯◯ VERY LOW a, b (1-2)	IMPORTANT
		100.0% (93 to 100)	100.0%	**0.0% fewer** (7 fewer to 7 more)		
Reoperation for wrap failure № of participants: 50 (1 observational study [1])	not estimable	Study population			⊕◯◯◯ VERY LOW c	CRITICAL
		0.0% (0 to 0)	0.0%	**0.0% fewer** (0 fewer to 0 fewer)		
		Study population				IMPORTANT

ADDITIONAL CONSIDERATIONS

The main desirable effect for robotic approach was decreased Clavien-Dindo 3 or greater complications and decreased patient-reported dysphagia. The panel believed the degree of the combined desirable effect was trivial.

Complications (clavien-Dindo ≥ 3) № of participants: 182 (4 observational studies [1-4])	**RR 0.88** (0.34 to 2.23)	**7.7%** (3 to 19.6)	8.8%	**1.1% fewer** (5.8 fewer to 10.8 more)	⊕◯◯◯ VERY LOW a,d (1,2,4), e		
Patient reported dysphagia № of participants: 50 (1 observational study [1])	**RR 0.33** (0.01 to 7.81)	Study population			⊕◯◯◯ VERY LOW a	IMPORTANT	
		1.3% (0 to 31.2)	4.0%	**2.7% fewer** (4 fewer to 27.2 more)			

a. Small sample size and wide confidence interval suggest potential for both harm and benefit.
b. Two of three studies were high risk of bias due to poor comparability given baseline differences between interventions without corrections (older robotic patients in one study, older and heavy laparoscopic patients in the other)
c. No effect could be estimated due to no events.
d. Three of four studies were high risk of bias due to poor comparability given baseline differences between interventions without correction (statistically older robotic cohort in two studies and different baseline weight in two studies - robotic greater in 1, less in 1.)
e. While the relative effect estimates were similar (no heterogeneity when RR also calculated), three studies had no events in either arm, whereas the fourth (Copeland 2008) had all the events.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ● Trivial ○ Varies ○ Don't know	From the original systematic review, four observational studies on robotic versus laparoscopic fundoplication in children were used to inform the panel's decision. Three (Albassam 2009, Anderberg 2007, Copeland 2008) used Nissen and Lehnert 2006 used Thal fundoplication. There was no heterogeneity between Lehnert 2006 and those with Nissen fundoplication for any outcome.	There were no undesirable effects based on the available evidence.

Outcomes	**Relative effect (95% CI)**	**Anticipated absolute effects* (95% CI)**			**Certainty of the evidence (GRADE)**	**Importance**
		Robotic approach	**Laparoscopic approach**	**Difference**		
Patient reported symptom control № of participants: 82 (3 observational studies [1-3])	**RR 1.00** (0.93 to 1.07)	Study population			⊕◯◯◯ VERY LOW a, b (1-2)	IMPORTANT
		100.0% (93 to 100)	100.0%	**0.0% fewer** (7 fewer to 7 more)		
Reoperation for wrap failure № of participants: 50 (1 observational study [1])	not estimable	Study population			⊕◯◯◯ VERY LOW c	CRITICAL
		0.0% (0 to 0)	0.0%	**0.0% fewer** (0 fewer to 0 fewer)		

	a. Small sample size and wide confidence interval suggest potential for both harm and benefit. b. Two of three studies were high risk of bias due to poor comparability given baseline differences between interventions without corrections (older robotic patients in one study, older and heavy laparoscopic patients in the other) c. No effect could be estimated due to no events. d. Three of four studies were high risk of bias due to poor comparability given baseline differences between interventions without correction (statistically older robotic cohort in two studies and different baseline weight in two studies - robotic greater in 1, less in 1.) e. While the relative effect estimates were similar (no heterogeneity when RR also calculated), three studies adno events in either arm, whereas the fourth (Copeland 2008) had all the events.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● **Very low** ○ Low ○ Moderate ○ High ○ No included studies	All outcomes had very low certainty.	

Outcomes	Importance	Certainty of the evidence (GRADE)
Patient reported symptom control (< 5years)	IMPORTANT	⊕◯◯◯ VERY LOW
Reoperation for wrap failure	CRITICAL	⊕◯◯◯ VERY LOW
Complications (Clavien-Dindo ≥3)	IMPORTANT	⊕◯◯◯ VERY LOW
Dysphagia	IMPORTANT	⊕◯◯◯ VERY LOW

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● **No important uncertainty or variability**		The panelists agreed there would unlikely be any variability in how patients value the main outcomes involving efficacy and safety as presented for this key question.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ● Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know	There is both trivial desirable and trivial undesirable effect of using robotic fundoplication compared to laparoscopic fundoplication.	

Acceptability

Is the option from balance of effects acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know		The panel felt there may be some stakeholders, including some hospitals and a minority of practicing surgeons, who would not find the robotic approach for fundoplication acceptable, regardless of feasibility.

Feasibility

Is the option from balance of effects feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	Per patient costs for robotic versus laparoscopic fundoplication Study | Robotic | Laparoscopic | Details of cost Anderberg 2009 | 9584 | 8982 | Euros. Combined anesthesia, surgical instruments, in hospital care	While robotic surgery has become more common than historically, the robotic approach still requires additional training and an investment in the actual robot. This panel did not choose the societal perspective and did not evaluate cost-effectiveness. However, the panel agreed that higher costs for robotic fundoplication could contribute to decreased feasibility. The research evidence presented does NOT mean patient out-of-pocket cost is greater, but that due to expense, the robotic approach may be less feasible. An additional obstacle to feasibility in children, is the size of the patient. Small children posing additional difficulty due to the size of robotic instruments relative to their body size.

		The feasibility thus varies based on access to facilities who have made that investment and have surgeons trained on the robot as well as size of the patient.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	**No important uncertainty or variability**			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		**Varies**	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	**Conditional recommendation for either the intervention or the comparison**	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	●	○	○

CONCLUSIONS

Recommendation

The panel suggests that children with gastroesophageal reflux may be treated with either robotic or laparoscopic fundoplication based on surgeon and patient's shared decision-making and feasibility (conditional recommendation based on very low certainty in the evidence about effects). No evidence-based recommendation can be made for patients who are undergoing revisional fundoplication.

Justification

Based on the limited and low certainty evidence available, the panel judged there are trivial differences in efficacy and safety between robotic and laparoscopic fundoplication. Each patient's values for other decision-making outcomes and the local feasibility of performing robotic fundoplication need to be discussed to make a final decision. This data may not reflect balance of effects for revisional cases, however. This population requires further research before a recommendation can be made.

Subgroup considerations

Implementation considerations

To improve feasibility for robotic fundoplication, considerations for increased surgeon training are needed.
Robotic instruments are not currently sized for convenient use in small children. 5mm instruments will improve feasibility.

Monitoring and evaluation

Research priorities

The panel made multiple recommendations for future studies on robotic versus laparoscopic fundoplication in children with GERD.

- Standardization of surgeon experience level in research on robotic surgery compared to alternative approaches
- Additional studies comparing patient-reported pain in robotic vs laparoscopic surgery.

Studies

1. Albassam, A. A., et al. "Nissen fundoplication, robotic-assisted versus laparoscopic procedure: a comparative study in children." *European journal of pediatric surgery* 19.05 (2009): 316-319.
2. Anderberg Magnus, Christina Clementson Kockum, and Einar Arnbjörnsson. "Robotic fundoplication in children." *Pediatric surgery international* 23.2 (2007): 123-127.
3. Lehnert, Mark, et al. "A prospective study comparing operative time in conventional laparoscopic and robotically assisted Thal semifundoplication in children." *Journal of pediatric surgery* 41.8 (2006): 1392-1396.
4. Copeland, Daniel R., et al. "Evaluation of initial experience and comparison of the da Vinci surgical system with established laparoscopic and open pediatric Nissen fundoplication surgery." *JSLS: Journal of the Society of Laparoendoscopic Surgeons* 12.3 (2008): 238.

Appendix 3 (KQ3): Complete or partial fundoplication in adult and pediatric patients with GERD?

QUESTION 3A: Adults

Should partial fundoplication vs. complete fundoplication be used for adults with GERD?	
POPULATION:	adults with GERD
INTERVENTION:	Partial fundoplication
COMPARISON:	complete fundoplication
MAIN OUTCOMES:	Complications; Demeester score ; Long-term dysphagia; Endoscopic dilation; Failure (reoperation due to symptom recurrence); Long-term gas bloat; Percent time abnormal pH (< 4.0) ; Postoperative PPI use ; quality of life; symptom control
SETTING:	International
PERSPECTIVE:	Patient-surgeon

ASSESSMENT

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT

○ Trivial
● Small
○ Moderate
○ Large
○ Varies
○ Don't know

RESEARCH EVIDENCE

From the original systematic review, 22 randomized controlled studies on partial versus complete fundoplication in adults were used to inform the panel's decision.

Outcomes	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)			Certainty of the evidence (GRADE)	Importance
		With Partial fundoplication	With complete fundoplication	Difference		
Long-term dysphagia № of participants: 400 (4 RCTs [1,16-18])	**RR 0.73** (0.52 to 1.02)	Study population			⊕⊕◯◯ LOW [a]	CRITICAL
		20.0% (14.3 to 28)	27.5%	**7.4% fewer** (13.2 fewer to 0.5 more)		
Failure (reoperation due to symptom recurrence) № of participants:	**RR 0.97** (0.66 to 1.45)	Study population			⊕⊕⊕◯ MODERATE [b]	CRITICAL
		5.8% (3.9 to 8.6)	5.9%	**0.2% fewer** (2 fewer to 2.7 more)		

ADDITIONAL CONSIDERATIONS

As noted in values below, some patients may place greater or less value on long-term dysphagia, influencing its estimated effect for them. Most panel members believed the size of the overall desirable effect, independent of value placed on different outcomes, however, was small. A minority felt that the effect magnitude could be moderate.

1936 (15 RCTs [1-3,5-11,13,15,16,18,19])						
Short-term quality of life (< 5 year follow-up) № of participants: 754 (5 RCTs [3,5,11,15,21])	-	-	-	SMD **0.12 SD higher** (0.02 lower to 0.26 higher)	⊕⊕⊕◯ MODERATE [a]	IMPORTANT

a. Small sample size and wide confidence interval suggest the potential for both benefit and no effect.
b. Wide confidence interval suggests potential for both harm and benefit.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT

- ○ Large
- ○ Moderate
- ● Small
- ○ Trivial
- ○ Varies
- ○ Don't know

RESEARCH EVIDENCE

Outcomes	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)			Certainty of the evidence (GRADE)	Importance
		With Partial fundoplication	With complete fundoplication	Difference		
Failure (reoperation due to symptom recurrence) № of participants: 1936 (15 RCTs [1-3,5-11,13,15,16,18,19])	**RR 0.97** (0.66 to 1.45)	Study population			⊕⊕⊕◯ MODERATE [b]	CRITICAL
		5.8% (3.9 to 8.6)	5.9%	**0.2% fewer** (2 fewer to 2.7 more)		
Postoperative PPI use (> 5 year follow-up) № of participants: 496 (5 RCTs [13,17,20])	**RR 1.46** (0.95 to 2.24)	Study population			⊕⊕◯◯ LOW [c (14,18), d]	IMPORTANT
		17.7% (11.5 to 27.2)	12.1%	**5.6% more** (0.6 fewer to 15.1 more)		
Long-term symptom control (> 5 year follow-up) № of participants: 865 (6 RCTs [1-2,14,16-18])	**RR 0.94** (0.85 to 1.04)	Study population			⊕◯◯◯ VERY LOW [b,e (16, 18),f (14), g]	IMPORTANT
		80.0% (72.4 to 88.5)	85.1%	**5.1% fewer** (12.8 fewer to 3.4 more)		

From the original systematic review, 22 randomized controlled studies on partial versus complete fundoplication in adults were used to inform the panel's decision.

ADDITIONAL CONSIDERATIONS

	a. Small sample size and wide confidence interval suggest the potential for both benefit and no effect. b. Wide confidence interval suggests potential for both harm and benefit. c. Two studies with high and unclear RoB (Roks 2017, Qin 2013) were not pooled because statistically significant heterogeneity resolved when they were removed. d. Wide confidence interval and small sample size suggest the potential for both no effect and harm e. Two studies were high risk of bias due to incomplete outcome data f. An additional study had unclear risk of bias due to unclear bias from all aspects of randomization and blinding, as well as noncomparable groups (Qin 2013) g. There is moderate heterogeneity (p = 0.06 I2=53%). When removing the high risk of bias studies the heterogeneity improves (p=0.16, I2 = 46%), but the effect estimate remains the same.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Critical outcomes were used to judge the overall certainty of evidence.	

Outcomes	Importance	Certainty of the evidence (GRADE)
Long-term dysphagia (long-term)	CRITICAL	⊕⊕◯◯ LOW
Failure (reoperation due to symptom recurrence)	CRITICAL	⊕⊕⊕◯ MODERATE
Postoperative PPI use	IMPORTANT	⊕⊕◯◯ LOW
Short-term quality of life (< 5 year follow-up)	IMPORTANT	⊕⊕⊕◯ MODERATE
Long-term symptom control	IMPORTANT	⊕◯◯◯ VERY LOW

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability		The use of postoperative dilation may especially vary in decision-making importance. Additionally, the indication for fundoplication and concurrent symptoms patients have can influence the value of different symptoms for decision-making. Patients getting fundoplication for lung transplant for example may find risks for other symptoms as overall not important.

		The panel additionally agreed there would possibly be patients who value dysphagia, post intervention PPI use, and symptom control differently.
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ● Varies ○ Don't know		Some patient populations would favor minimizing reflux and some would favor minimizing dysphagia. For the former as well as those patients who greatly value decreased PPI intake, the balance would probably favor the comparison (complete fundoplication) and for the latter, the balance would probably favor the intervention (partial fundoplication).
Acceptability Is the option from the balance of effects acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know		While the option of either intervention or comparator based on patient values, is likely to be acceptable to stakeholders, the acceptability may be subject to the influence of individual training and local practice.
Feasibility Is the option from the balance of effects feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know		

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	**Conditional recommendation for either the intervention or the comparison**	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	●	○	○

CONCLUSIONS

Recommendation

For adult patients with GERD, the panel suggest either partial or complete fundoplication approaches may be used guided by patient values. For patients who value improvement in reflux symptoms higher over the risk of dysphagia, complete fundoplication may be the preferred option. Patients who value dysphagia highly, partial fundoplication may be offered preferentially. (Conditional recommendations based on low certainty in the evidence about effects)

Justification

There are mixed data to support both the intervention and the comparator. While the magnitude of overall effect is similar for desirable and undesirable effects, the values patient place on individual outcomes possibly varies such that these values can change the balance of effects.

Subgroup considerations

Subgroup considerations, including degree of wrap and presence of preoperative dysmotility, were not addressed due to limited evidence available.

Implementation considerations

Training and familiarity with both partial and complete fundoplication is needed for this recommendation.

Monitoring and evaluation

Research priorities

The panel made recommendations for future stratified studies including these populations:

- People who failed PPI (medically refractory) versus those whose symptoms are controlled on PPI
- Reoperation population
- Lung transplant vs not transplant
- Previous endoscopic reflux operations
- Use of bougie clearly reported as a subgroup analysis or as its own comparator.
- Additional evidence on types of partial wrap as a subgroup analysis or as its own comparator.
- Studies with long-term effectiveness outcomes (reflux control and dysphagia and other side effects) in a larger sample of patients with minimal attrition.

Studies

1. Mickevičius, Antanas,et al. "Influence of wrap length on the effectiveness of Nissen and Toupet fundoplications: 5-year results of prospective, randomized study." *Surgical endoscopy* 27.3 (2013): 986-991.
2. Cao, Z., et al. "Randomized clinical trial of laparoscopic anterior 180 partial versus 360 Nissen fundoplication: 5-year results." *Diseases of the Esophagus* 25.2 (2012): 114-120.
3. Djerf, Pauline, et al. "One-and ten-year outcome of laparoscopic anterior 120° versus total fundoplication: a double-blind, randomized multicenter study." *Surgical endoscopy* 30.1 (2016): 168-177.
4. Booth, M. I., et al. "Randomized clinical trial of laparoscopic total (Nissen) versus posterior partial (Toupet) fundoplication for gastro-oesophageal reflux disease based on preoperative oesophageal manometry." *British journal of surgery* 95.1 (2008): 57-63.
5. Aye, Ralph W., et al. "A randomized multiinstitution comparison of the laparoscopic Nissen and Hill repairs." *The Annals of thoracic surgery* 94.3 (2012): 951-958.
6. Strate, U., et al. "Laparoscopic fundoplication: Nissen versus Toupet two-year outcome of a prospective randomized study of 200 patients regarding preoperative esophageal motility." *Surgical endoscopy* 22.1 (2008): 21-30.
7. Spence, Gary M., et al. "Single center prospective randomized trial of laparoscopic Nissen versus anterior 90° fundoplication." *Journal of gastrointestinal surgery* 10.5 (2006): 698-705.
8. Mucio, Moreno, et al. "Novel surgical concept in antireflux surgery: Long-term outcomes comparing 3 different laparoscopic approaches." *Surgery* 151.1 (2012): 84-93.
9. Khan, Mansoor Ali, et al. "Randomized controlled trial of laparoscopic Nissen versus Lind fundoplication for gastro-oesophageal reflux disease." *Scandinavian journal of gastroenterology* 44.3 (2009): 269-275.
10. Watson, David I., et al. "Multicenter, prospective, double-blind, randomized trial of laparoscopic Nissen vs anterior 90º partial fundoplication." *Archives of Surgery* 139.11 (2004): 1160-1167.
11. Hakanson, Bengt S., et al. "Comparison of Laparoscopic 270 degrees Posterior Partial Fundoplication vs Total Fundoplication for the Treatment of Gastroesophageal Reflux Disease A Randomized Clinical Trial." *JAMA SURGERY* 154.6 (2019): 479-486.

12. Wang, Bin, et al. "A Chinese randomized prospective trial of floppy Nissen and Toupet fundoplication for gastroesophageal disease." *International Journal of Surgery* 23 (2015): 35-40.
13. Shaw, John M., et al. "Long-term outcome of laparoscopic Nissen and laparoscopic Toupet fundoplication for gastroesophageal reflux disease: a prospective, randomized trial." *Surgical endoscopy* 24.4 (2010): 924-932.
14. Qin, Mingfang, Guoqian Ding, and Huiqi Yang' *Surgical Techniques* 23.7 (2013): 601-604.
15. Koch, Oliver O., et al. "Laparoscopic Nissen versus Toupet fundoplication: objective and subjective results of a prospective randomized trial." *Surgical endoscopy* 26.2 (2012): 413-422.
16. Broeders, Joris A., et al. "Objective outcomes 14 years after laparoscopic anterior 180-degree partial versus nissen fundoplication: results from a randomized trial." *Annals of surgery* 258.2 (2013): 233-239.
17. Nijjar, Rajwinder S., et al. "Five-year follow-up of a multicenter, double-blind randomized clinical trial of laparoscopic Nissen vs anterior 90 partial fundoplication." *Archives of Surgery* 145.6 (2010): 552-557.
18. Roks, D. J., J. A. Broeders, and R. J. Baigrie. "Long-term symptom control of gastro-oesophageal reflux disease 12 years after laparoscopic Nissen or 180° anterior partial fundoplication in a randomized clinical trial." *British Journal of Surgery* 104.7 (2017): 852-856.
19. Koch, Oliver O., et al. "Effectiveness of laparoscopic total and partial fundoplication on extraesophageal manifestations of gastroesophageal reflux disease: a randomized study." *Surgical Laparoscopy Endoscopy & Percutaneous Techniques* 22.5 (2012): 387-391.
20. Cai, W., et al. "Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180° partial fundoplication." *British Journal of Surgery: Incorporating European Journal of Surgery and Swiss Surgery* 95.12 (2008): 1501-1505.
21. Baigrie, R. J., et al. "Randomized double-blind trial of laparoscopic Nissen fundoplication versus anterior partial fundoplication." *British Journal of Surgery: Incorporating European Journal of Surgery and Swiss Surgery* 92.7 (2005): 819-823.
22. Guérin, Eric, et al. "Nissen versus Toupet fundoplication: results of a randomized and multicenter trial." *Surgical endoscopy* 21.11 (2007): 1985-1990.

Question 3B: Children

Should partial fundoplication vs. complete fundoplication be used for children with GERD?	
POPULATION:	Children with GERD (without large hiatal hernia)
INTERVENTION:	Partial fundoplication
COMPARISON:	Complete fundoplication
MAIN OUTCOMES:	Complication rate; Long term dysphagia; Endoscopic dilation; Wrap failure (requiring reoperation); Postoperative PPI use; Short term symptom control
SETTING:	International
PERSPECTIVE:	Patient-surgeon

ASSESSMENT

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	From the original systematic review, 2 observational studies and a randomized controlled study on partial versus complete fundoplication in children were used to inform the panel's decision.	While the number of dilations was not explicitly stated in the study by Kubiak et al., the panel recognized that repeat dilations are often required and this factors into the magnitude of effect for this outcome in particular. The panel noted that in some small subpopulations, such as neurologically impaired children who will never be able to swallow food independently, the desirable benefit of decreased dysphagia will not be as important for decision-making. However, the panel felt these patients would still have an overall moderate desirable effect from the intervention.

Outcomes	Relative effect (95% CI)	Anticipated absolute effects[*] (95% CI)			Certainty of the evidence (GRADE)	Importance
		With Partial fundoplication	With Complete fundoplication	Difference		
Long term dysphagia (> 5 years) № of participants: 238 (1 observational study [2])	**RR 0.49** (0.11 to 2.14)	Study population			⨁◯◯◯ VERY LOW [a,b]	CRITICAL
		2.1% (0.5 to 9.1)	4.3%	**2.2% fewer** (3.8 fewer to 4.9 more)		
EGD +/- dilation* № of participants: 167 (1 RCT [3])	**RR 0.21** (0.05 to 0.92)	Study population			⨁⨁◯◯ LOW [c]	CRITICAL
		2.5% (0.6 to 10.8)	11.8%	**9.3% fewer** (11.2 fewer to 0.9 fewer)		
		Study population				IMPORTANT

Postoperative PPI use № of participants: 167 (1 RCT [3])	**RR 0.75** (0.32 to 1.78)	**9.7%** (4.1 to 23)	12.9%	**3.2% fewer** (8.8 fewer to 10.1 more)	⨁⨁◯◯ LOW [b]		

a. Esposito 2006 had high risk of bias due to insufficient information on baseline characteristics or establishment of GERD as well as no controls for possible confounders.
b. Small sample size and wide confidence interval suggest potential for both harm and benefit
c. Small sample sizes (less than OIS - optimal information size) and low fragility index
d. Small sample size and wide confidence interval suggest potential for both no effect and harm

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ● Moderate ○ Small ○ Trivial ○ Varies ○ Don't know	From the original systematic review, 2 observational studies and a randomized controlled study on partial versus complete fundoplication in children were used to inform the panel's decision.	

Outcomes	Relative effect (95% CI)	Anticipated absolute effects [c] (95% CI)			Certainty of the evidence (GRADE)	Importance
		With Partial fundoplication	With Complete fundoplication	Difference		
Wrap failure (requiring reoperation) № of participants: 167 (1 RCT [3])	**RR 2.70** (1.01 to 7.22)	Study population			⨁⨁◯◯ LOW [d]	CRITICAL
		15.9% (5.9 to 42.5)	5.9%	**10.0% more** (0.1 more to 36.6 more)		

a. Esposito 2006 had high risk of bias due to insufficient information on baseline characteristics or establishment of GERD as well as no controls for possible confounders.
b. Small sample size and wide confidence interval suggest potential for both harm and benefit
c. Small sample sizes (less than OIS - optimal information size) and low fragility index
d. Small sample size and wide confidence interval suggest potential for both no effect and harm

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies		

Outcomes	Importance	Certainty of the evidence (GRADE)
Long term dysphagia (> 5 years)	CRITICAL	⨁◯◯◯ VERY LOW
Endoscopic dilation (follow-up 30 mo)	CRITICAL	⨁⨁◯◯ LOW
Wrap failure (requiring reoperation, follow-up 30 mo)	CRITICAL	⨁⨁◯◯ LOW
Postoperative PPI use (follow-up 30 mo)	IMPORTANT	⨁⨁◯◯ LOW

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability		

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ● Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know		For both the intervention as well as the comparison there are undesirable effects that are important and have good evidence.

Acceptability Is the option from balance of effects acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know		With shared surgeon-patient decision-making approach, no acceptability concerns were noted for either options
Feasibility Is the from balance of effects feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know		Given the balance of effects favors EITHER intervention or comparator, the panel felt this option would be feasible as it allows surgeons to choose the procedure.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	**Moderate**	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	**Conditional recommendation for either the intervention or the comparison**	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	●	○	○

CONCLUSIONS

Recommendation

Guided by shared surgeon-patient decision-making, we suggest either partial or complete fundoplication approaches be used for pediatric patients with GERD but without large hiatal hernia. (Conditional recommendations based on low certainty in the evidence about effects).

Justification

There is balanced evidence and choice is likely influenced by surgeon practice patterns.

Subgroup considerations

The panel noted that in some small subpopulations, such as neurologically impaired children who will never be able to swallow food independently, the desirable benefit of decreased dysphagia will not be as important for decision-making. However, the recommendation for either is still supported by the presented evidence.

Implementation considerations

Monitoring and evaluation

Research priorities

The panel made multiple recommendations for future studies on robotic versus laparoscopic fundoplication in children with GERD.

- Neurologically impaired versus not neurologically impaired
- Effect of bougie on partial versus complete fundoplication outcomes
- Choice of partial wrap type
- Additional studies stratifying by different pediatric age groups to determine if partial versus complete varies with age of patient for long-term outcome. For example, does a partial wrap in an infant last as well as a complete wrap long term

Studies

1. Wagener, S., N. Sudhakaran, and E. Cusick. "Watson fundoplication in children: a comparative study with Nissen fundoplication." *Journal of pediatric surgery* 42.6 (2007): 1098-1102.
2. Esposito, C., et al. "Long-term outcome of laparoscopic Nissen, Toupet, and Thal antireflux procedures for neurologically normal children with gastroesophageal reflux disease." *Surgical Endoscopy and Other Interventional Techniques* 20.6 (2006): 855-858.
3. Kubiak, Rainer, James Andrews, and Hugh W. Grant. "Long-term outcome of laparoscopic nissen fundoplication compared with laparoscopic thal fundoplication in children: a prospective, randomized study." *Annals of surgery* 253.1 (2011): 44-49.

Appendix 4 (KQ4): Should division of short gastric vessels or no division be performed in adult patients with GERD?

QUESTION 4

Should division of short gastrics vs. no division be used for Nissen fundoplication in adult patients with GERD?	
POPULATION:	Adult patients with GERD undergoing fundoplication
INTERVENTION:	Division of short gastric vessels
COMPARISON:	No division of short gastric vessels
MAIN OUTCOMES:	Complications (Clavien-Dindo ≥ 3); Long-term Dysphasia; Long-term Gas bloat; long-term PPI use; Symptom control
SETTING:	International
PERSPECTIVE:	Patient-surgeon

ASSESSMENT

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	From the original systematic review, 8 reports on randomized controlled trials on division versus no division of the short gastric vessels were used to inform the panel's decision. All trials used Nissen fundoplication. While three reports pertained to the sample study (Watson 1007, O'Boyle 2002, and Kinsey-Trotman 2018), these were never pooled to avoid duplicate counting of the same patients, and the earlier studies were used for outcomes not reported in Kinsey-Trotman.	

Outcomes	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)			Certainty of the evidence (GRADE)	Importance
		Division of short gastrics	NO division of short gastrics	Difference		
Long-term Dysphagia № of participants: 192 (3 RCTs [5-7])	**RR 0.97** (0.66 to 1.42)	Study population **31.7%** (21.6 to 46.4)	32.7%	**1.0% fewer** (11.1 fewer to 13.7 more)	⨁◯◯◯ VERY LOW b,c (3,4)	CRITICAL
PPI use № of participants: 151 (2 RCTs [6,7])	**RR 0.73** (0.36 to 1.47)	Study population **15.7%** (7.7 to 31.6)	21.5%	**5.8% fewer** (13.8 fewer to 10.1 more)	⨁◯◯◯ VERY LOW b,d (3)	IMPORTANT

Symptom control № of participants: 82 (1 RCT [7])	**RR 1.17** (0.96 to 1.42)	Study population			⊕⊕◯◯ LOW [b]	CRITICAL
		90.7% (74.4 to 100)	77.5%	**13.2% more** (3.1 fewer to 32.5 more)		

a. Two studies are high risk of bias due to selective outcomes reporting and incomplete outcome data bias on the Cochrane risk of bias tool 1.0.
b. Small sample sizes and confidence interval suggest the potential for important benefit as well as harm.
c. Two of the studies have high risk of bias due to incomplete outcome risk of bias and one also with high risk of bias from lack of blinding.
d. A single study was high risk of bias on the Cochrane Risk of Bias tool 1.0 due to incomplete outcome data.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ● Moderate ○ Small ○ Trivial ○ Varies ○ Don't know	From the original systematic review, 8 reports on randomized controlled trials on division versus no division of the short gastric vessels were used to inform the panel's decision. All trials used Nissen fundoplication. While three reports pertained to the sample study (Watson 1007, O'Boyle 2002, and Kinsey-Trotman 2018), these were never pooled to avoid duplicate counting of the same patients, and the earlier studies were used for outcomes not reported in Kinsey-Trotman.	The panel expressed concern for high complication rate that could be due to early learning curve and which does not seem congruous with recent complication rates for this procedure. The effect of a concurrent emptying procedure (pyloroplasty) or gastrostomy placement on gas bloat was contemplated. In these situations, gas bloat may be decreased but the certainty and degree of this effect is unknown.

Outcomes	**Relative effect (95% CI)**	**Anticipated absolute effects* (95% CI)**			**Certainty of the evidence (GRADE)**	**Importance**
		Division of short gastrics	**No division of short gastrics**	**Difference**		
Complications (Clavien-Dindo ≥ 3, 6 mo- 1 yr follow-up) № of participants: 347 (4 RCTs [1-4])	**RR 2.05** (0.59 to 7.15)	Study population			⊕◯◯◯ VERY LOW [a (1,2), b]	CRITICAL
		3.5% (1 to 12.3)	1.7%	**1.8% more** (0.7 fewer to 10.5 more)		
Long-term Gas bloat (10-20 yr follow-up) № of participants: 151 (2 RCTs [6,7])	**RR 1.41** (0.77 to 2.61)	Study population			⊕⊕◯◯ LOW [b,d (3)]	IMPORTANT
		75.0% (40.9 to 100)	53.2%	**21.8% more** (12.2 fewer to 85.6 more)		

a. Two studies are high risk of bias due to selective outcomes reporting and incomplete outcome data bias on the Cochrane risk of bias tool 1.0.
b. Small sample sizes and confidence interval suggest the potential for important benefit as well as harm.
c. Two of the studies have high risk of bias due to incomplete outcome risk of bias and one also with high risk of bias from lack of blinding.
d. A single study was high risk of bias on the Cochrane Risk of Bias tool 1.0 due to incomplete outcome data.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies		

Outcomes	Importance	Certainty of the evidence (GRADE)
Complications (Clavien-Dindo >= 3)	CRITICAL	⨁◯◯◯ VERY LOW
Long-term Dysphasia - (> 5years)	CRITICAL	⨁◯◯◯ VERY LOW
Long-term Gas bloat - (> 5 years)	IMPORTANT	⨁⨁◯◯ LOW
PPI use (> 5 years)	IMPORTANT	⨁◯◯◯ VERY LOW
Symptom control (> 5 years)	CRITICAL	⨁⨁◯◯ LOW

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability		

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ● Varies ○ Don't know		Balance of effect varies depending on patient preference between symptom control and gas bloat/ risk of complications. For patients who would be highly concerned about long-term gas bloat, the balance of desirable and undesirable effects probably favors no division. For patients who assign higher value to symptom control, the balance probably favors division.

Acceptability
Is the option chosen in balance of effects (both options) acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know		If a patient values bloating more than symptom control, then division of short gastrics would not be acceptable. If a patient values symptom control more, then division would be acceptable.

Feasibility
Is the chosen in balance of effects (both options) feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know		For those trained to do either division or no division, both options would be feasible. Technically, the feasibility varies based on individual patient anatomy. Division may be necessary in situations where a tension free anastomosis is not possible otherwise.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	**Moderate**	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies

VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		**Varies**	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		**Varies**	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	**Conditional recommendation for either the intervention or the comparison**	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	●	○	○

CONCLUSIONS

Recommendation

For adults undergoing fundoplication for GERD, the panel suggests either division or no division of short gastric vessels may be used guided by patient values and feasibility of the procedures. For patients who value reflux symptom relief more than the long-term risk of gas bloat or small risk of more procedural complications, division of short gastric vessels may be the preferred option. Patients who value long-term gas bloat, procedural complications, or both more than the improvement in their reflux symptoms, partial fundoplication may be offered preferentially. (Conditional recommendations based on very low certainty in the evidence about effects)

Justification

Based on the limited and low certainty evidence available, the panel judged there are moderate desirable and undesirable effects of division as opposed to no division during Nissen fundoplication. Each patient's values for other decision-making outcomes need to be discussed, and the feasibility of patient anatomy for performing division or no division considered, to make a final decision. This data may not reflect balance of effects for revisional cases, however. This population requires further research before a recommendation can be made.

Subgroup considerations

Implementation considerations

Monitoring and evaluation

Research priorities

The panel recommended that modern, comparative studies would be beneficial.

Studies

1. Chrysos, Emmanuel, et al. "Prospective randomized trial comparing Nissen to Nissen-Rossetti technique for laparoscopic fundoplication." *The American journal of surgery* 182.3 (2001): 215-221.
2. Farah, José Francisco de Mattos, et al. "Randomized trial of total fundoplication and fundal mobilization with or without division of short gastric vessels: a short-term clinical evaluation." *Acta cirurgica brasileira* 22.6 (2007): 422-429.
3. Blomqvist, Anne, et al. "Impact of complete gastric fundus mobilization on outcome after laparoscopic total fundoplication." *Journal of Gastrointestinal Surgery* 4.5 (2000): 493-500.
4. Watson, David I., et al. "Prospective double-blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels." *Annals of surgery* 226.5 (1997): 642.
5. Kösek, Volkan, et al. "Division of the short gastric vessels during laparoscopic Nissen fundoplication: clinical and functional outcome during long-term follow-up in a prospectively randomized trial." *Surgical endoscopy* 23.10 (2009): 2208.
6. Kinsey-Trotman, Stephen P., et al. "Randomized trial of division versus nondivision of short gastric vessels during Nissen fundoplication: 20-year outcomes." *Annals of surgery* 268.2 (2018): 228-232
7. Mardani, J., et al. "Ten-year results of a randomized clinical trial of laparoscopic total fundoplication with or without division of the short gastric vessels." *British Journal of Surgery: Incorporating European Journal of Surgery and Swiss Surgery* 96.1 (2009): 61-65.
8. O'Boyle, Colm J., et al. "Division of short gastric vessels at laparoscopic Nissen fundoplication: a prospective double-blind randomized trial with 5-year follow-up." *Annals of surgery* 235.2 (2002): 165.

Appendix 5 (KQ5): Should minimal dissection or maximal dissection be used in pediatric patients with GERD?

QUESTION 5

Should “minimal” dissection vs. “maximal” dissection be used for Fundoplication in patients with GERD?	
POPULATION:	Patients (adults or children) getting fundoplication (excluding patients with large hiatal hernia)
INTERVENTION:	“minimal” dissection
COMPARISON:	“maximal” dissection
MAIN OUTCOMES:	Endoscopic dilation; Reoperation for wrap failure; Readmission for respiratory cause; Weight gain (lbs);
SETTING:	International
PERSPECTIVE:	Patient-surgeon

ASSESSMENT

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	From the original systematic review, a single randomized controlled trial on minimal dissection versus maximal dissection during fundoplication was used to inform the panel's decision. St. Peter et al. used Nissen fundoplication in a pediatric population. Minimal dissection was defined as minimal mobilization with no violation of the phrenoesophageal membrane, and maximal dissection was defined as circumferential division of the phrenoesophageal attachments.	No evidence was found for adult patients and the panel did not think that pediatric findings would be generalizable to adult patients

Outcomes	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)			Certainty of the evidence (GRADE)	Importance
		With "minimal" dissection	With "maximal" dissection	Difference		
Endoscopic dilation № of participants: 134 (1 RCT)	**RR 0.08** (0.00 to 1.46)	Study population			⊕⊕◯◯ LOW [a]	IMPORTANT
		0.7% (0 to 12.5)	8.6%	**7.9% fewer** (8.6 fewer to 3.9 more)		
Reoperation for wrap failure № of participants: 134 (1 RCT)	**RR 0.21** (0.06 to 0.67)	Study population			⊕⊕⊕◯ MODERATE [b]	CRITICAL
		4.8% (1.4 to 15.3)	22.9%	**18.1% fewer** (21.5 fewer to 7.5 fewer)		
Readmission for respiratory cause № of participants: 177 (1 RCT)	**RR 0.71** (0.35 to 1.46)	Study population			⊕⊕◯◯ LOW [a]	IMPORTANT
		12.2% (6 to 25.2)	17.2%	**5.0% fewer** (11.2 fewer to 7.9 more)		
Weight gain (lbs) № of participants: 177 (1 RCT)	**RR 1.08** (0.98 to 1.20)	Study population			⊕⊕◯◯ LOW [a]	IMPORTANT
		93.1% (84.5 to 100)	86.2%	**6.9% more** (1.7 fewer to 17.2 more)		

a. Small sample size and wide confidence interval suggest potential for both important harm and benefit.
b. Small sample sizes

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ● Trivial		Based on their experience and personal observations, the panel felt there would be no notable undesirable effects.

○ Varies ○ Don't know		No evidence was found for adult patients and the panel did not think that pediatric findings would be generalizable to adult patients

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies		

Outcomes	Importance	Certainty of the evidence (GRADE)
Endoscopic dilation	IMPORTANT	⨁⨁◯◯ LOW
Reoperation for wrap failure	CRITICAL	⨁⨁⨁◯ MODERATE
Readmission for respiratory cause	IMPORTANT	⨁⨁◯◯ LOW
Weight gain (lbs)	IMPORTANT	⨁⨁◯◯ LOW

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability		

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ● Favors the intervention ○ Varies ○ Don't know		The panel was in agreement that the evidence clearly favors the intervention, though minority felt the degree of certainty in the evidence may warrant a less definitive answer.

Acceptability Is the option from balance of effects acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know		
Feasibility Is the option from balance of effects feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know		

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

In the pediatric GERD population without large hiatal hernias undergoing surgery, we suggest the use of minimal dissection during fundoplication. (Conditional recommendations based on moderate certainty in the evidence about effects).
Given no comparative evidence in adults, no recommendation is given on adults.

Justification

A single RCT demonstrated moderate desirable effects and trivial undesirable effects for minimal dissection. Although there was moderate certainty in the evidence, the strength of the panel recommendation was tempered by the limited number of studies and long-term evidence available.

Subgroup considerations

Implementation considerations

Monitoring and evaluation

Research priorities

The panel made recommendations
- Need more studies in adults.
- Additional studies with longer follow-up and minimal attrition are needed to determine long-term failure rates
- Additional research on the degree of mobilization appropriate in the setting of concomitant hiatal hernia

Studies

St. Peter, Shawn D. St, et al. "Minimal vs extensive esophageal mobilization during laparoscopic fundoplication: a prospective randomized trial." *Journal of pediatric surgery* 46.1 (2011): 163-1