



Surgical Management of Gastroesophageal Reflux Disease: A Systematic Review

Adam B. Goldin, Tim Jancelewicz, Monica E. Lopez
Outcomes and Evidence-Based Practice Committee



Historical context

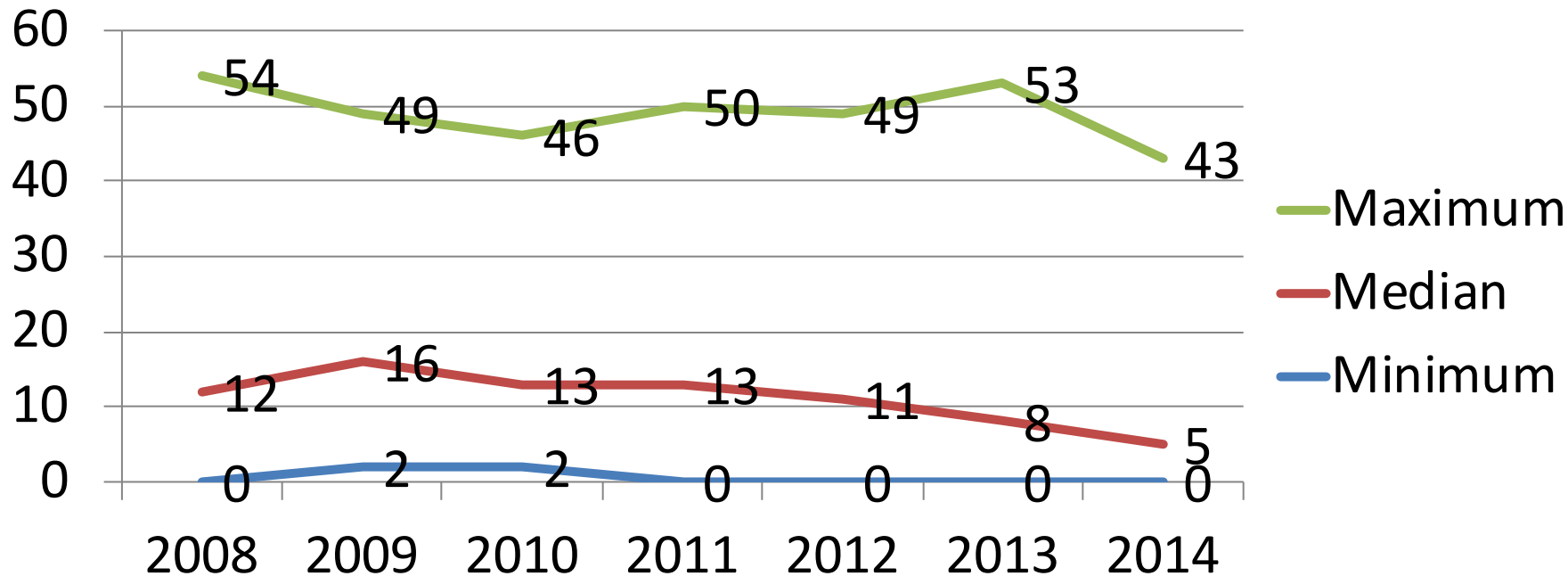
“Gastroesophageal reflux is manifest by: vomiting, failure to gain and grow normally, recurrent aspiration pneumonia and esophagitis.”

“All infants below the age of two months who require hospitalization because of malnutrition secondary to gastroesophageal reflux and who do not respond promptly to conservative therapy **should be operated on.**”

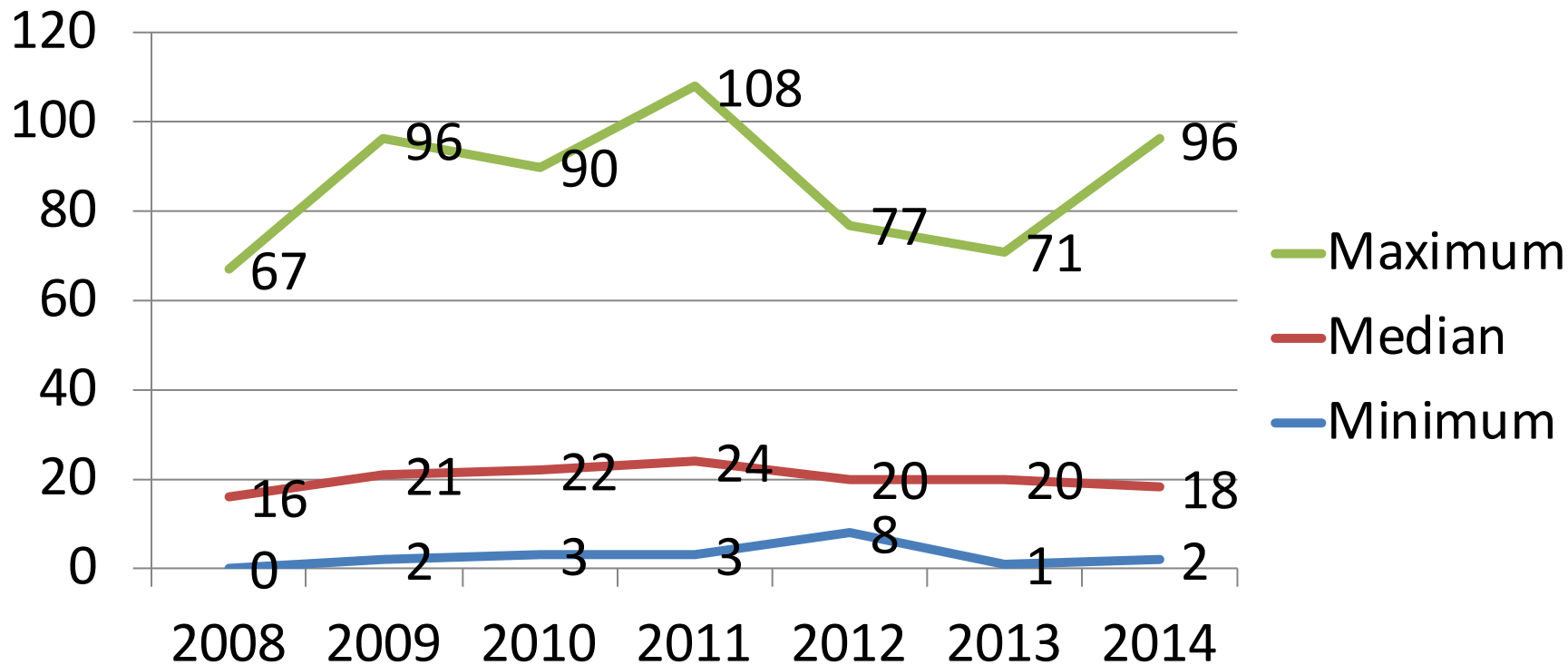
“Results of surgery to correct reflux in infants are **highly satisfactory** and, in this group of patients, unattended by serious complications or mortality.”

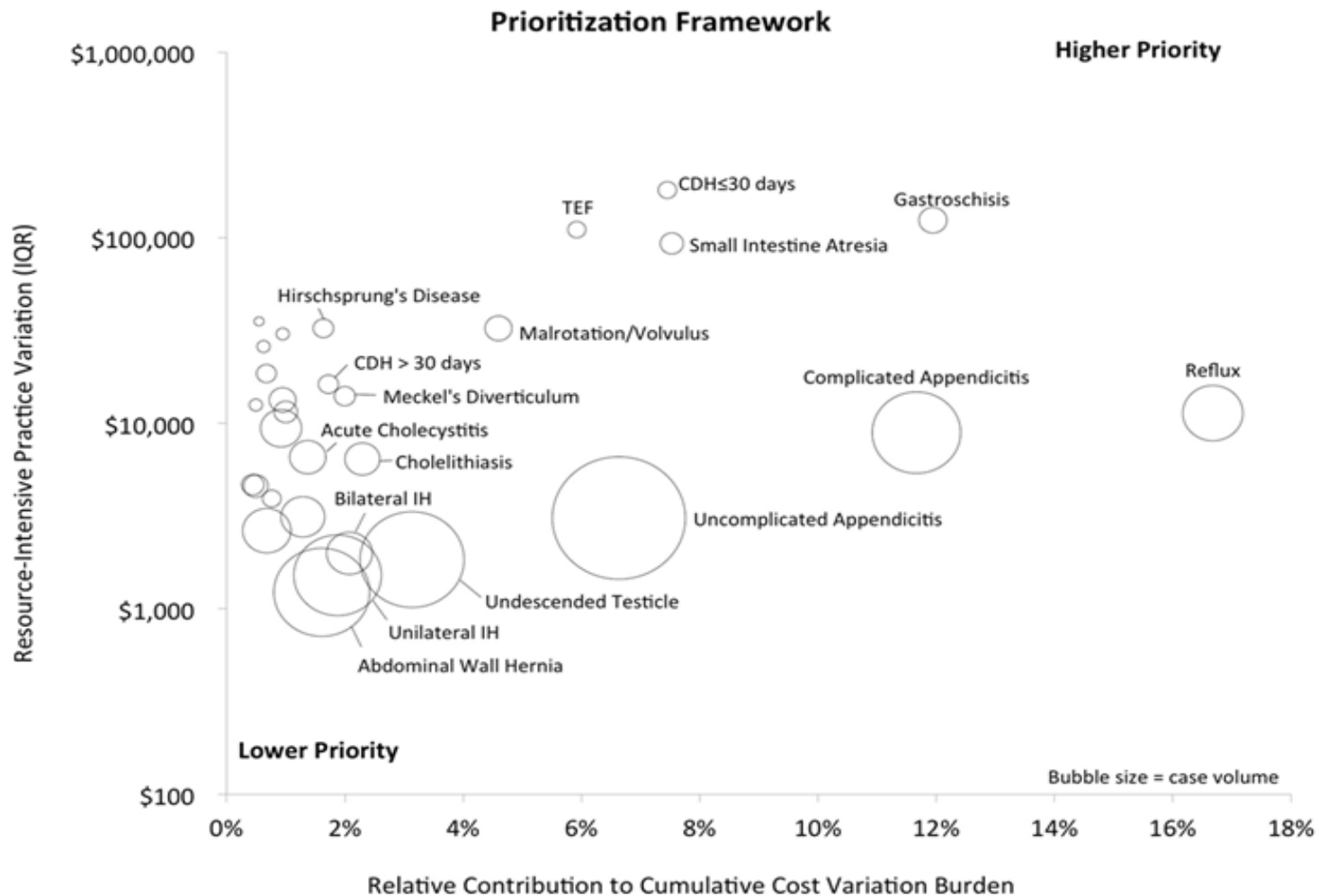
Randolph et al, *Surgical treatment of gastroesophageal reflux in infants*, 1974

ACGME reported Open ARP cases



ACGME reported Laparoscopic ARP cases





Questions in this Review

1. Is fundoplication effective treatment for observed symptoms attributed to reflux?
2. Is fundoplication effective treatment for objective measurements of GERD?
3. Does the effectiveness of fundoplication vary by age?
4. Is there a difference in the effectiveness of the different approaches to antireflux procedures in children?
5. Does the effectiveness of fundoplication vary by diagnosis?
6. Do antireflux procedures provide long-term benefits or complications in children?

Search Strategy

- Terms: Fundoplication, GERD, Ages 0-18, English, no date restriction
 - Medline – 1350 articles
 - Cochrane Database – 6 articles (1 duplicate removed)
 - Embase – 199 articles (5 duplicates removed)
 - Central – 55 articles (4 duplicates removed)
 - National Guideline Clearinghouse – 1 article
- Total 1,601 abstracts

1601 articles

711 dropped
after abstract
review

890 articles allocated
to one of 6 questions
for full review

Question 1
94 articles

Question 2
91 articles

Question 3
25 articles

Question 4
279 articles

Question 5
300 articles

Question 6
104 articles

14 articles
included

16 articles
included

12 articles
included

89 articles
included

106 articles
included

26 articles
included

Described surgical interventions

- | | | |
|--|--|--|
| 1. Nissen | 18. Cardiaplication | 34. Roux-en-Y gastrojejunal bypass (with Nissen/gastrostomy) |
| 2. Nissen-Rossetti | 19. Mediogastric plication | 35. Lortab-Jacob |
| 3. Transthoracic Nissen | 20. Jejunal Implement | 36. Allison |
| 4. Toupet | 21. Jejunal interposition | 37. Mutaf Procedure |
| 5. Thal | 22. STRETTA | 38. Gastric tube cardioplasty |
| 6. Belsey-Mark IV | 23. Transesophageal endoscopic plication (TEP) | 39. Technical modifications: |
| 7. Hill | 24. Trans-oral incisionless fundoplication (TIF) | 1. Crural plication/repair |
| 8. Dor | 25. Physiological antireflux procedure | 2. Hiatoptasty, with/without mesh |
| 9. Watson Anterior | 26. Anastomotic wrap | 3. Pyloroplasty |
| 10. EsophyX | 27. Erstra Procedure (hemifundoplication) | 4. Gastrostomy |
| 11. Boerema anterior gastropexy | 28. Bianchi | 40. Approach |
| 12. Collis-Belsey | 29. Esophagectomy | 1. Open |
| 13. Boix-Ochoa | 30. Esophagogastric disassociation | 2. Laparoscopic |
| 14. Uncut Collis-Nissen | 31. Angelchik prosthesis | 3. Needlescopic |
| 15. Magnetic esophageal sphincter device | 32. Vertical gastric plication | 4. Microlaparoscopy |
| 16. Husfeldt Hernia repair | 33. Lap-assisted jejunostomy | 5. Robotic |
| 17. L. Braun transthoracal hiatoptasty | | 6. CATS |
| | | 7. Telesurgical |
| | | 8. Transthoracic v. transabdominal |
| | | 9. SIPES (single-incision pediatric endosurgery) |

Question 1: Is a fundoplication effective treatment for observed symptoms attributed to reflux?

- 14 articles < 20 years since publication
 1. Cough – 1 paper
 2. Aspiration/ALTE/Apnea – 7 papers
 3. Emesis v. Emetic reflex – 1 paper
 4. Esophageal/Gi symptoms – 4 papers
 5. Practice Guideline – 1 paper

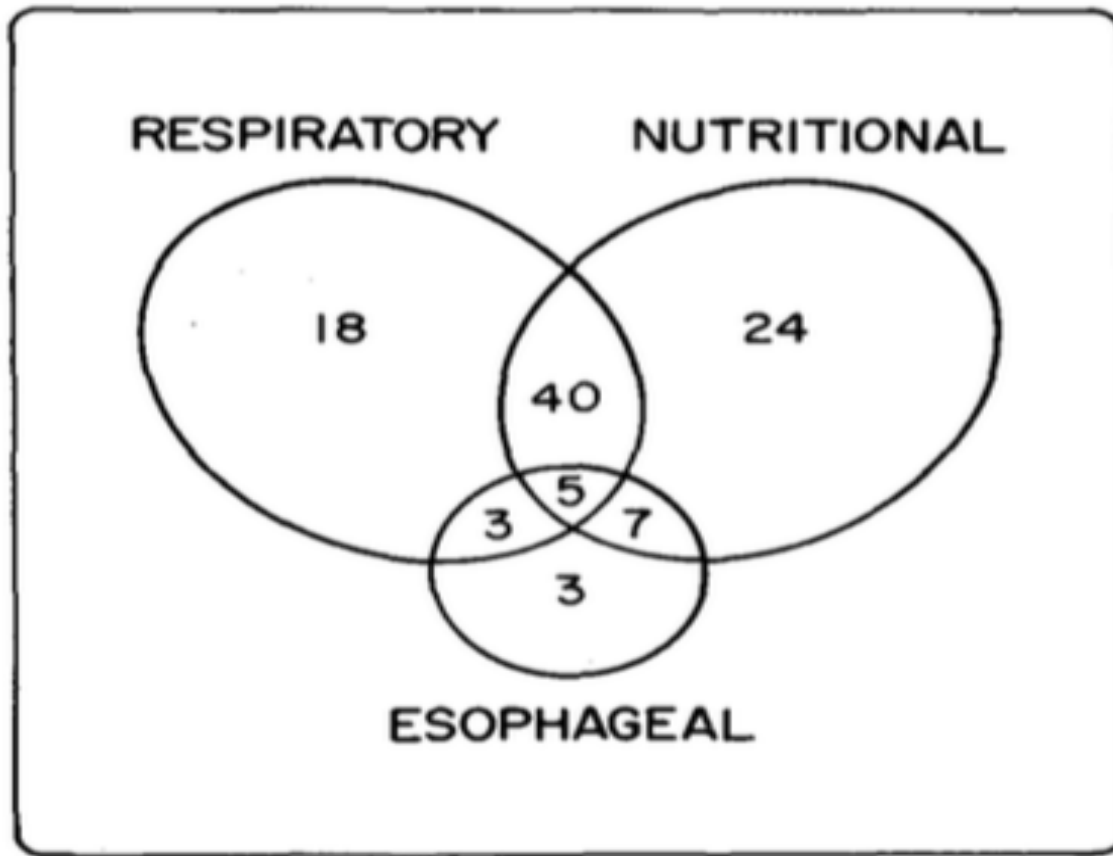


Fig. 1. This graph illustrates that more than half the patients in this series had overlapping systems affected by severe GER.

Cough

- 1 paper: Cochrane review
- *No trials addressing effectiveness of surgical interventions on prolonged non-specific cough in children have been performed*
- **Recommendation:**
 - **Insufficient evidence for the use of ARP to treat cough**

Aspiration/Apnea/ALTE

- 7 papers (1 level 2, 6 level 4)
 1. No difference in hospitalizations before v. after ARP
 2. 3.7% of 81 with recurrent ALTE
 3. 40% mortality; 100% off medication, transferred from NICU, and on feeds
 4. 34% with post-op sx
 5. 1.6 aspiration admissions to 0.6 admissions, 53% complications, 8% GERD recurrence, 13% mortality
 6. 69% without symptoms
 7. 38/61 (62%) decreased pneumonia (not resolution), ALTE in 26% pre-op, 4% post-op.

Aspiration/Apnea/ALTE

- **Recommendation:**
 - **ARP does not affect rate of hospitalization for aspiration pneumonia, apnea**
 - Grade C recommendation
 - **ARP may decrease the risk of ALTE, though only in patients with symptoms clearly related to gastric reflux**
 - Grade C recommendation

Emesis v. Emetic reflex

- 1 paper (Level 3 evidence)
 - Compared
 - “effortless vomiting” (0/8 patients)
 - “activation of emetic reflex” (8/12 patients)
- **Recommendation**
 - **An ARP is not appropriate treatment for children with symptoms caused by activation of the emetic reflex, and fundoplication may make these children’s symptoms worse and predispose to wrap failure.**
 - Grade C recommendation

Esophageal/GI Symptoms

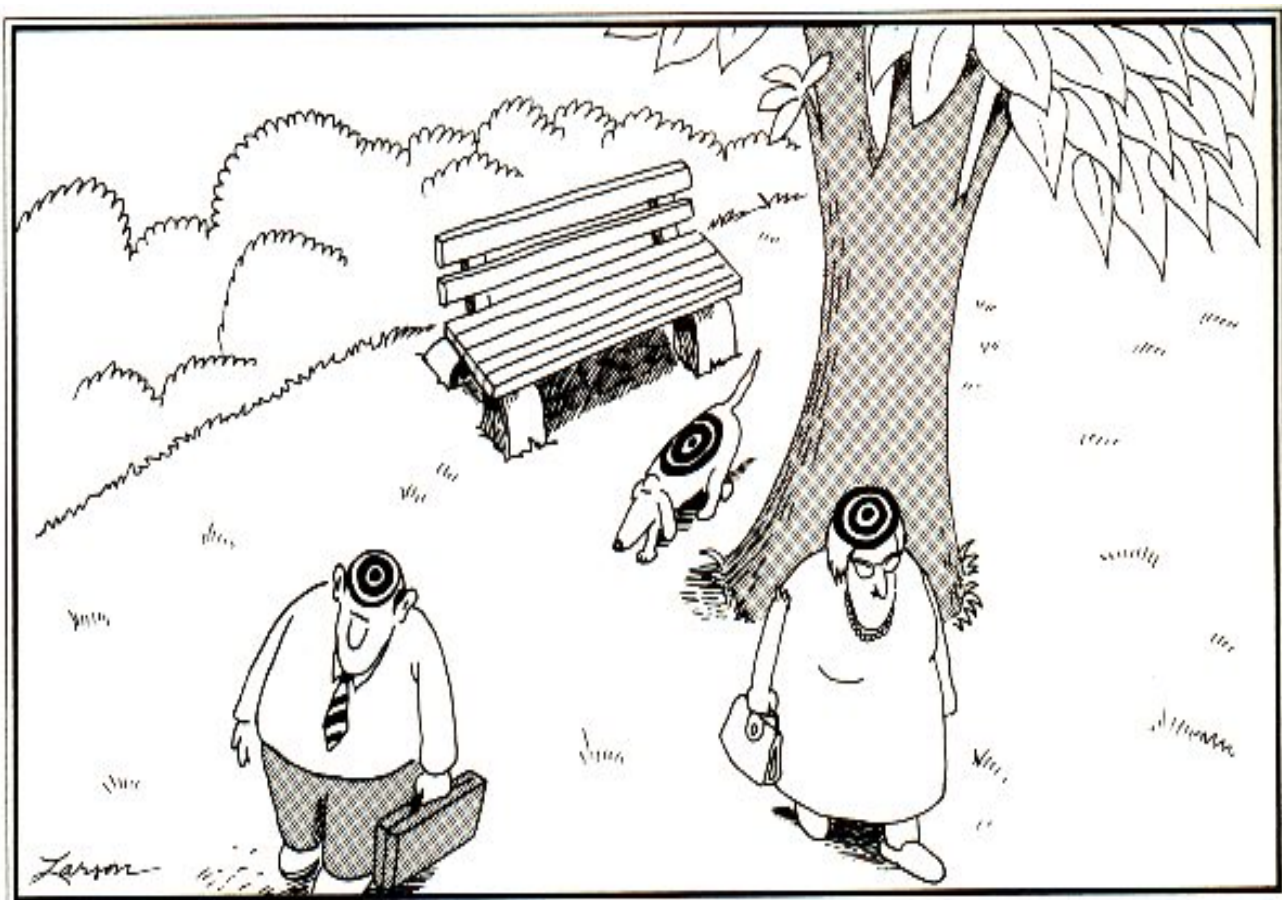
- 4 papers (all level 4 evidence):
 1. 91/105 (87%) resolution of GI Sx by pediatrician interview
 2. By parent survey: 88% felt better, 2% worse, 10% no change
 3. 22/26 (85%) had no recurrent reflux
 4. 22/34 (65%) symptomatic improvement; no difference in reflux-related hospitalizations

Esophageal/GI Symptoms

- **Recommendation:**
 - **ARP may result in subjective resolution of GI manifestation of gastric reflux symptoms in patients who have failed medical management**
 - Grade C
 - **ARP does not affect rate of hospitalization for GI manifestation of gastric reflux symptoms in patients who have failed medical management**
 - Grade C

Practice Guidelines

- Vandenplas 2009: J Pediatr Gastr Nutr
 - Joint practice guidelines of NASPGHAN/ESPGHAN
 - **Antireflux surgery should be considered only in children with GERD and failure of optimized medical therapy, or long-term dependence on medical therapy where compliance or patient preference preclude ongoing use, or life-threatening complications**



How Surgeons see the World

Question 2: Is fundoplication effective treatment for objective measurements of GERD?

- 16 articles
 - UGI: 1 paper
 - 24-h pH : 3 papers
 - pH-MII : 1 paper
 - pH-MII-Imp: 5 papers
 - GES: 6 papers
 - EGD: 0 papers

Objective Measures
Upper GI Series (UGI)
24-hour pH monitoring (24-h pH)
Multichannel intraluminal impedance (MII)
Manometry
pH-MII; pH-Manometry; MII-Manometry
Gastric Emptying Scan (GES)
Esophago-gastro-duodenoscopy with/without biopsy (EGD/Bx)

UGI

- 1 paper addressed use of UGI:
 - Did not address question of impact on post-op outcome
 - UGI abnormality affected the operative plan in 4.5% of cases
 - 656/843 (78%) had an UGI
 - 30/656 (5%) with abnormality other than GERD, HH (malrotation, stricture, DGE, duodenal obstruction)
- No studies identified
- **Recommendation**
 - **There is insufficient evidence for the use of UGI as a measure of the effectiveness of fundoplication to treat GERD.**

24-hour pH

- 3 papers (all level 4 evidence)
 - 3.6% abnormal postcibal 2-hour esophageal pH studies <12 weeks post-op (pre-op not reported)
 - Significant decrease in median pH values
 - Pre-op to post-op:
 - Median RI 5.7% to 0.15%
 - Median longest reflux episode 12.1 to 1.15 minutes
 - Median episodes >5 min 4 to 0.5

24-hour pH

- **Recommendation**
 - **Fundoplication may be effective in reducing parameters of esophageal acid exposure as measured by 24-hour pH**
 - Grade D based on inconsistent or inconclusive level 4 evidence

pH-MII

- 1 paper (level 4 evidence)
 - No significant difference in pH or MII parameters before v. after ARP
 - One additional paper noted no significant difference in post-op *symptom* improvement with respect to the proportion of patients that had normal or abnormal pre-operative pH-probe or pH-MII results, but no post-op study

pH-MII

- **Recommendation:**
 - **Fundoplication is not effective in reducing parameters of either esophageal acid or non-acid exposure as measured by combined 24-hour pH-MII**
 - Grade C based on level 4 evidence

pH/MII/Manometry

- 5 papers (all level 4 evidence)
 - Fundoplication decreases:
 - Esophageal acid exposure
 - Non-acid exposure
 - RI
 - *Without altering esophageal motility.*
 - No relationship between manometry and outcome
 - Fundoplication decreases 24-hour pH parameters, without improving esophageal motility
 - Post-op RI decreased to 0%, basal LES pressures increased/unchanged, and no patients had TLESR

pH/MII/Manometry

- **Recommendation:**
 - **Fundoplication is effective in reducing all parameters of esophageal acid exposure without altering esophageal motility**
 - Grade C based on level 4 evidence

GES

- 6 papers (one level 3, five level 4)
 - Mean gastric retention was lower post-op in both groups – with/without GEP (no values provided)
 - Mean gastric retention decreased from 72% to 40% mean 3.6 years after ARP, antroplasty, GT.
 - Gastric residual activity improved overall after ARP without drainage procedure (22% to 17%).

GES

- 6 papers (one level 3, five level 4)
 - One year after surgery, patients with DGE and ARP/pyloroplasty had improved GE.
 - GE significantly improved after ARP ($t_{1/2}$: 107 to 76 min; DGE 55% to 9% of patients; 90/120 min retention improved)
 - After ARP, no change in median % GE for solids, significant improvement in GE for liquids.

GES

- **Recommendation:**
 - **Fundoplication improves gastric emptying. This benefit in infants may be greater for liquids than solids.**
 - **DGE identified pre-operatively is not an indication for GEP**
 - Grade C based on level 3/4 evidence

EGD

- No papers
- **Recommendation: None**

Question 3:

Does the effectiveness of fundoplication vary by age?

Number of Articles	Study Type	Level of Evidence	Quality of Evidence Rating
10	Case series, Retrospective cohort	4	Poor
1	Database	2	Fair
1	Review	5	Poor

The surgical treatment of gastro-esophageal reflux in neonates and infants.

Pacilli M, Chowdhury MM, Pierro A. Seminars in Pediatric Surgery 2005; 14 (1): 34-41

- Review of literature
- 16 studies (1983-2003) laparoscopic or open fundoplication
- All single center, inclusion criteria varied
 - By weight <2500 g, <3.5 kg, <5 kg, <8 kg
 - By age <3 mo, <4 mo, <1 yr, <2yrs
- Overall success rate 67-100%
- Re-do rate 7-26%
- Worse recurrence rates in patients with associated congenital anomalies, such as esophageal atresia
- Selection bias, heterogeneity of indications for surgery, unstandardized assessment and poor definition of outcomes, no adjustment for confounders, reporting bias, attrition bias

Antireflux procedures for gastroesophageal reflux disease in children: influence of patient age on surgical management.

McAteer J, Larison C, LaRiviere C, et al. JAMA Surg. 2014 Jan;149(1):56-62

- PHIS database study 2002-2010; 141,190 patients
- Evaluated proportional hazard of progression to ARP during hospitalization for GERD
- 8% (11,621) underwent ARP
- 57% **<6 months of age**
- Preoperative work up not uniform (65% UGI)
- Increased hazard of progression to ARP in those **< 2 months**
- **HR increased for comorbidities**
- 10% risk of ARF at each subsequent GERD-related hospitalization
- Providers more likely to offer ARP to infants compared to older children, independent of indications
- Higher risk of ARP in <2 months of age infants suggests these patients are not given an adequate medical treatment trial

Recommendation

Does the effectiveness of fundoplication vary by age?

- Very limited data
- Long term outcomes unknown
- Evidence is insufficient to support a recommendation on the effectiveness of fundoplication in infants
- Other factors may be considered in determining appropriate choice of intervention in these patients

Level of evidence 2, 4 and 5; Grade D recommendation

Question 4:

Is there a difference in the effectiveness of various approaches to antireflux procedures?

- **106** articles critically appraised and categorized

Open vs. Laparoscopic	SILS
Nissen	Transoral/Endoluminal
Rossetti	Fundoplication with gastrostomy
Thal	Fundoplication with gastric emptying procedure
Toupet	Esophagogastric dissociation
Robotic	Technical modifications of various fundoplication procedures

- Most single center retrospective reviews and case series (Level 4, poor-fair quality evidence)
- Focused only on comparative studies
- Effectiveness of **open vs. laparoscopic**, and **partial vs. complete** fundoplication

Thirty-day outcome in children randomized to open and laparoscopic Nissen fundoplication

Knatten CK, FyhnTJ, Edwin B, et al. J Pediatr Surg 2012; 47: 1990–1996

- 2 center randomized clinical trial in Norway
- Inclusion: Symptoms of GERD despite medical therapy
 - pH testing and/or UGI
- Primary Outcome: Recurrence of GERD
 - Poor accrual, study closed prior to achieving sample size
- 88 patients (44 open, 44 laparoscopic)
- No difference in early postoperative complications (<30 days)
 - 24/44 (54%) Clavien-Dindo classification
- No difference in LOS (7.0 vs 7.5, $p=0.74$) or readmission rate (25%)
- Limitations: heterogeneous population, unable to enroll sufficient patients to achieve power, block randomization with no stratification for center or other patient factors, post hoc power calculation, no blinding

Clinical outcome of a randomized controlled blinded trial of open versus laparoscopic Nissen fundoplication in infants and children

McHoney M, Wade AM, Eaton S, et al. Ann Surg. 2011 Aug;254(2):209-16

- Inclusion: >1 mo GERD (pH, UGI, endoscopy or combination)
- Primary outcome: Resting Energy Expenditure (reported in separate publication)
- Secondary outcomes: GERD recurrence, need for re-do fundoplication, persistent retching
- 39 patients (19 lap, 20 open); median follow up 22 months
- No difference in dysphagia, recurrence or need for redo fundoplication
- No difference in time to full feeds, LOS, or postoperative analgesic requirement
- Retching was higher after open surgery (56% vs. 6%; $P = 0.003$)
- Equal efficacy of open and lap approach for early postoperative outcomes
- Limitations: per-protocol analysis, outcome measurement instruments subjective or not validated, not powered to detect differences in secondary outcomes

A meta-analysis of outcomes after open and laparoscopic Nissen fundoplication for gastro-oesophageal reflux disease in children

Siddiqui MR, Abdulaal Y, Nisar A, et al. Pediatr Surg Int. 2011 Apr;27(4):359-66

- Systematic review and meta-analysis
- 6 studies met inclusion criteria: 4 retrospective, 2 prospective
- 721 patients (466 lap, 255 open)
- Outcomes: Operative time, hospital LOS, time to feed, morbidity, 12-month recurrence
- No significant difference in operative time (SMD -0.55, 95% CI -1.69, 0.6)
- LOS, time to feed, and morbidity favor laparoscopic approach
 - SMD 0.93, 95 % CI (0.41, 1.44); SMD 4.13, 95% CI (1.0, 7.3); SMD 2.90, 95% CI (1.49, 5.66)
- No significant difference in recurrence at 12 months SMD 2.61, 95% CI (0.44, 15.2)
- Authors conclude laparoscopic approach is a safe and effective alternative to open surgery
- Limitations: Significant heterogeneity for most outcomes, included studies graded 8-14 (poor- fair) methodological quality score, most subject to significant and multiple sources of bias

Recommendation

Is there a difference in the effectiveness of various approaches to antireflux procedures?

Laparoscopic versus open fundoplication

Laparoscopic fundoplication may be comparable to open fundoplication with regard to short term clinical outcomes. Data on long term effectiveness are lacking.

Level 1 and 2 evidence; Grade D recommendation

Long-term outcome of laparoscopic Nissen fundoplication compared with laparoscopic Thal fundoplication in children: a prospective, randomized study.

Kubiak R, Andrews J, Grant HW. Ann Surg. 2011 Jan;253(1):44-9

- Inclusion: <21 yo GERD unresponsive to medical therapy, failed treatment, serious complications or hiatal hernia
- Primary Outcome: Recurrence warranting re-do fundoplication or GJ; early mortality
- Secondary Outcomes: Recurrence with reintroduction of antireflux medication, postoperative complications
- 167 Patients (85 Nissen, 82 Thal); 60% concomitant gastrostomy
- Median follow-up 30 months (95% patients)
- **Nissen** group had **lower recurrence** compared to Thal (5.9% vs. 15.9%; $p = 0.038$)
- Most recurrences occurred in **NI** children (17/18)
- In **normal children**, **no difference in recurrence rate** between two techniques (0/18 Nissen, 1/22 Thal; $p=NS$)
- No significant difference in “relative failure rate” between groups
- Dysphagia same for both, but **Nissen required more dilatations** (11.8% vs. 2.4%; $p=0.02$)
- 31 deaths; only 1 in perioperative period, others due to pre-existing comorbidities

Complete versus partial fundoplication in children with gastroesophageal reflux disease: results of a systematic review and meta-analysis.

Mauritz FA, Blomberg BA, Stellato RK, et al. J Gastrointest Surg. 2013 Oct;17(10):1883-92

- 8 trials met inclusion criteria: 7 retrospective, 1 prospective
- 1183 patients (588 complete- Open or Lap Nissen +/- SGV division; 595 Open or Lap partial anterior or posterior- Thal or Watson, Toupet)
- Outcomes: Short (<6 mo) and long-term (>12 mo) postoperative reflux control
- Subjective reflux control was not significantly different between groups at early RR 0.64 (0.29, 1.3; p=0.28) and long term follow-up RR 0.85 (0.57, 1.27; p=0.42)
- No significant difference in postoperative dysphagia between partial and complete, but excessive heterogeneity for this analysis
- Complete fundoplication required significantly more endoscopic dilatations for severe dysphagia (RR 7.26; p=0.007) than partial fundoplication
- No significant difference in re-intervention rate, gas bloat syndrome or in-hospital complications
- Poor methodological quality of studies; publication bias in some of the funnel plots

Recommendation

Is there a difference in the effectiveness of various approaches to antireflux procedures?

Complete versus Partial Fundoplication

Partial and complete fundoplication are comparable in effectiveness for control of GERD in neurologically normal children.

Complete fundoplication may lead to increased postoperative dysphagia requiring endoscopic dilatation.

Level 1 and 2 evidence; Grade B recommendation

Summary of Evidence for Other Approaches

Number of Articles	Surgical Approach	Study Type	Level of Evidence	Focus
7	Robotic	Case series, Retrospective cohort	4	Single institution, Feasibility, Learning curve, Costs
9	SILS, Endoluminal, Transoral	Case series	4	
20	Technical modifications	Case series, retrospective cohort, 2 poor quality RCTs	1, 4	Multiple techniques*

* Mesh hiatal reinforcement, pledgeted sutures, cardiaplication, anastomotic wrap, left-sided fundoplication, extent of esophageal mobilization, intraoperative manometry

- Very limited evidence to make conclusions on the effectiveness of these approaches

Question 5. Does the effectiveness of fundoplication vary by diagnosis?

- Achalasia (49 studies) - **dropped**
 - Neurologic impairment (26)
 - Esophageal atresia (8)
 - Reactive airway disease (8)
-
- | | |
|---|---|
| <ul style="list-style-type: none">• Lung transplant (6)• Cystic fibrosis (6)• Cardiac anomalies (5)• CDH (4)• Esophageal dysmotility (4), stricture (3), esophagitis• VP shunt (3) | <ul style="list-style-type: none">• Barrett's esophagus• Previous gastrostomy• Malrotation (2)• Obesity• Swallowing dysfunction• Pulmonary hypertension• SCID• Apnea |
|---|---|

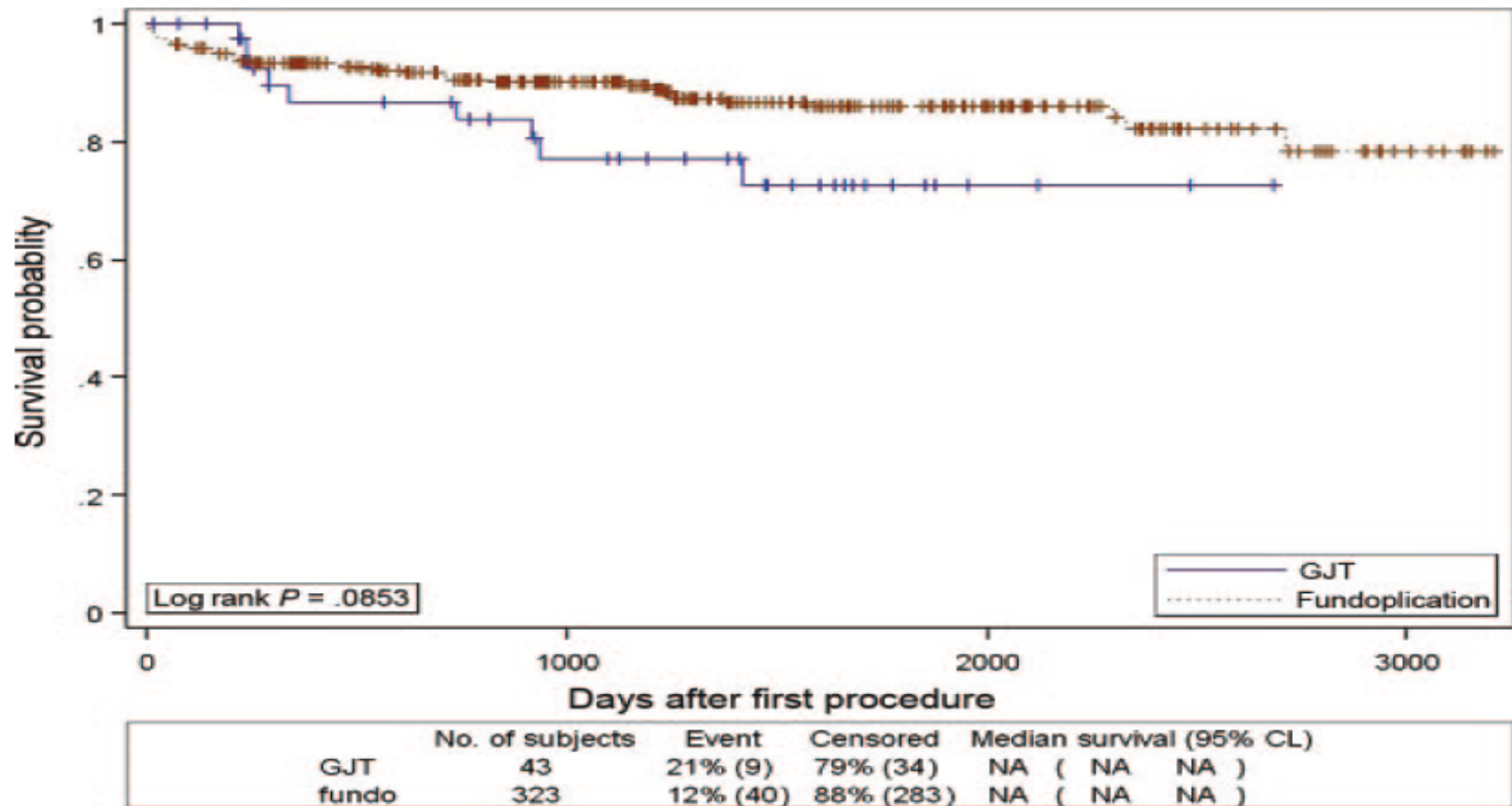
Does fundoplication effectiveness vary in children with underlying neurologic impairment (NI)?

- 23 retrospective case series
- 1 prospective cohort
- 1 large retrospective cohort (database) study
- **1 Cochrane review** (Vernon-Roberts 2013): could not identify any RCT comparing outcomes with PPI vs fundo

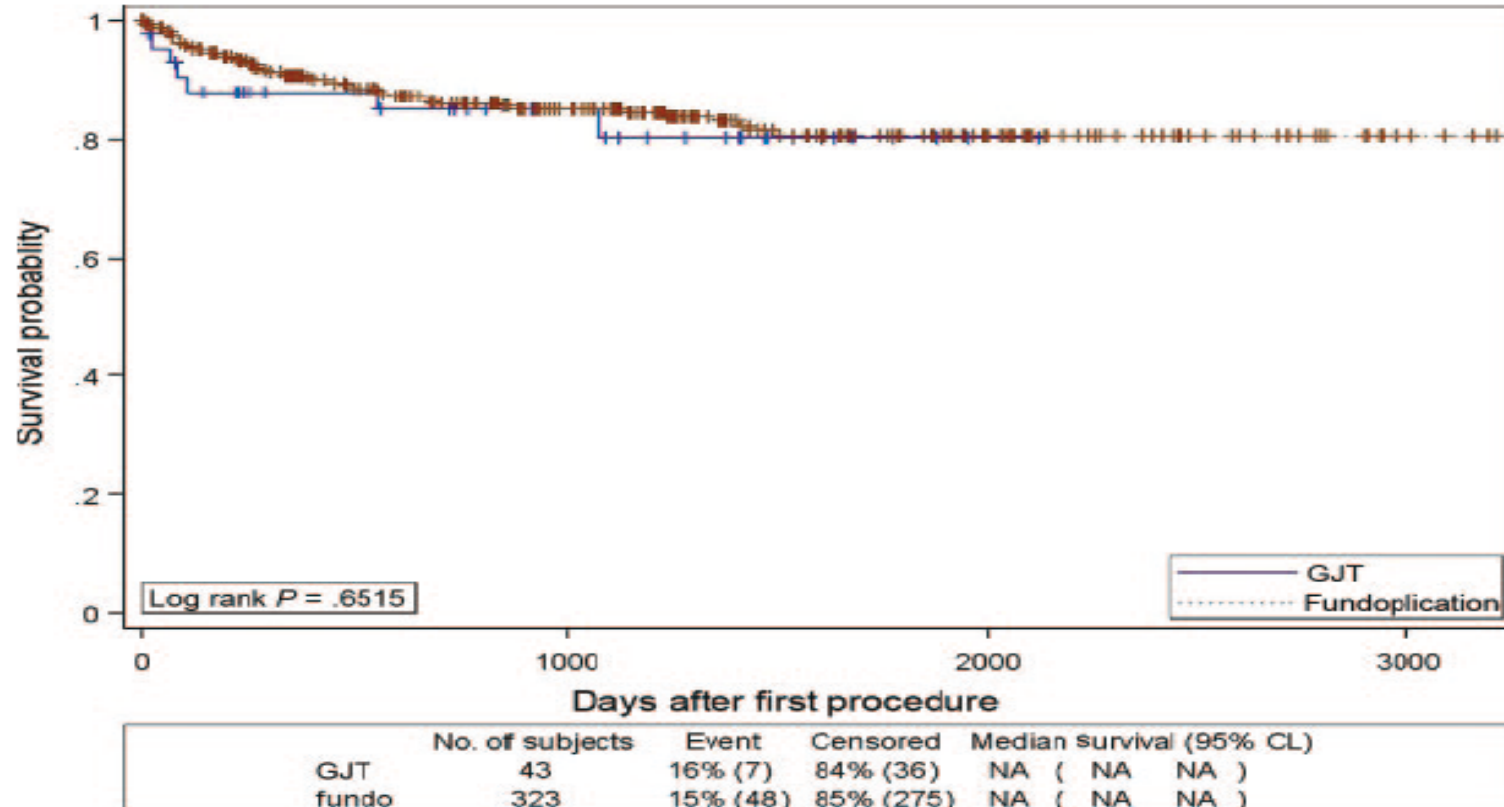
Does fundoplication effectiveness vary in children with underlying neurologic impairment (NI)?

- Srivastava 2009, retrospective cohort: N=366, GJ vs fundo, follow-up 3.4 years
 - Aspiration PNA, mortality common after either a first fundo or a first GJ feeding tube for GERD in children with NI
 - Neither treatment option is clearly superior in PNA prevention or survival

Survival, fundo vs. GJ in NI patients



Pneumonia-free survival, fundo vs. GJ in NI patients



Does fundoplication effectiveness vary in children with underlying neurologic impairment (NI)?

- Wales 2002, retrospective (N=111), open Nissen + G vs. GJ
 - No difference in PNA
 - No difference in mortality (12.5% GJ, 17.5% N+G, $P=.6$)
 - GJ failure 8.3%; 14.3% wrap failure
 - 14.5% of GJ improved and had GJ removed
 - 21% intussusception in GJ

Case series summary – Neurologic Impairment

- Highly variable in terms of population, intervention, selection criteria, outcomes criteria, length of follow-up
- For 14 studies reporting at least two of mortality, recurrence, or pneumonia in NI patients after open or lap Nissen or Thal:
 - median follow-up time of 17 months
 - N range 12-141
 - **17.1% mortality** (range 0-27%)
 - **10.6% recurrence or failure** (range 0-39%)
 - **2-17% pneumonia** (range 2-23%)

Recommendations – Neurologic Impairment

- **Fundoplication not superior or inferior to gastrojejunal feeds**
- **Cannot recommend for or against utility of fundoplication in patients with NI**
- **Great need for prospective RCT** (medical vs surgical management of GERD, fundoplication vs gastrojejunal feeds)

Level 4 evidence, grade D recommendations.

What are outcomes of fundoplication in patients with esophageal atresia (EA)?

Table 2. Failure of Nissen Fundoplication in Patients Who Had Prior EA/TEF Repair

Study	Year	EA/TEF (n)	FUNDO, n (%)	Failures, n (%)
Wheatley et al ¹	1993	80	21 (26)	7 (33)
Lindahl et al ²	1989	48	13 (27)	5 (38)
Curci and Dibbins ³	1988	31	14 (45)	5 (36)
Fonkalsrud ¹³	1979	14	9 (64)	0 (0)
Current study	1996	143	59 (41)	9 (15)
Totals*		173	57 (33)	17 (30)

NOTE. Nearly one third of patients had a poor outcome after complete wrap for GER associated with EA/TEF.

*Authors' data not included.

Recommendations – Esophageal Atresia

7 case series

- High incidence of reflux in EA patients (>90%)
- High wrap failure rate: 15-32% with 70 months median follow-up
- **Cannot recommend the type of wrap based on existing evidence but Dor has low morbidity**
- **Minimal data regarding outcomes after laparoscopic fundoplication**

Level 4 evidence, grade C recommendations.

Does fundoplication ameliorate asthma (RAD) symptoms or need for medication?

- **5 case series**
- **1 nonrandomized case-control**, 6 month follow-up
 - PPI (30) v. anti-histamine (14) v. fundo (9)
 - PPI = fundo for patients with asthma and GER (fewer exacerbations compared with anti-histamine group)
- **1 meta-analysis (2000):**
 - 5 ped, 14 adult level IV studies
 - 90% of children, 70% of adults improved symptoms
 - 1/3 improved PFT's
- **1 Cochrane review (2009):**
 - 11 adult RCT, 1 ped RCT; **11 medical, 1 surgical**
 - Med/surg rx does **not** improve RAD

Asthma after fundoplication – case series

- Rothenberg 2012 (N=235): 91% improved, 80% off steroids, 95% decreased inhaler use, 24% increased FEV after fundoplication
- Mattioli 2004 (N=48): No difference between groups in % patients with post-op Visick I (no respiratory symptoms)
- Tannuri 2008 (N=151): 45% of RAD patients had fewer bronchospasm events
- Ahrens 1999 (N=128): 65% decrease in asthma medication
- Tashjian 2002 (N=24): 75% symptom-free, off meds

Recommendations – Asthma

- Some evidence in support of fundoplication for RAD but best evidence is in adult studies
- Data (e.g. Rothenberg experience) are suggestive but an RCT is needed (with medical, surgical, and placebo arms)

Level 3-4 evidence, grade C recommendations.

Question 6. Do antireflux procedures provide long-term benefits or complications?

- **26 studies** selected for full review: 22 case series, three retrospective database studies, one retrospective matched case-control
- Positive outcomes or “benefits” most often measured by improvement in subjective symptoms, rarely by objective tests
- Adverse outcomes or “complications” measured by:
 - Recurrent, new, or persistent symptoms
 - use of antireflux/antacid medication
 - aspiration pneumonia
 - mortality
 - abnormal objective tests (e.g. pH probe, endoscopy)
 - other morbidity

Summary of 18 papers with adequate data, lap & open Nissen fundo

- **Wrap reoperation** in mean 9% (4-18%), median follow-up 35 (range 9-156) months
- **All adverse outcomes (excluding mortality)** mean 18% (4-58%), median follow-up 60 (range 9-156) months
- **Favorable outcome** mean 83% (42-95%) of patients, median follow-up 60 months (range 9-156)

Surgical Treatment of Gastroesophageal Reflux in Children: A Combined Hospital Study of 7467 Patients

*Eric W. Fonkalsrud, Keith W. Ashcraft, Arnold G. Coran, Dick G. Ellis, Jay L. Grosfeld, William P. Tunell, Thomas R. Weber.
Pediatrics 101: 419-22, 1998*

- Questionnaire to seven US centers, 56% NN, 44% NI, Nissen (64%), Thal (34%), Toupet (1.5%), laparoscopic 2.6%
- 40% age <12 months, mean 7.3 years f/u
- 30-day mortality 0.07% NN, 0.8% NI
- Major complications in 4.2% NN, 12.8% NI
- Reoperation in 3.6%, 11.8% of NI children
- “Significant clinical improvement in preoperative symptoms” in 94% of NN, 85% of NI
- Selection and recall bias

Measures of adverse outcomes

- Lee 2008 (N=342): **Use of antireflux medication** decreased in NN after Nissen, but there was no significant change in NI
- Wockenforth 2011 (N=230): **Mortality 20% at 3 years**, GT (RR death 11.04, $P < 0.001$), cerebral palsy (RR 6.58, $P = 0.021$) associated with reduced survival
- Naerncham 2007 (N=325, case-control): **GERD recurrence 10.3%** at 50 months; predictors young age, hiatal hernia, postop retching; not significant: NI, EA, nutritional status

Outcomes - Recommendations

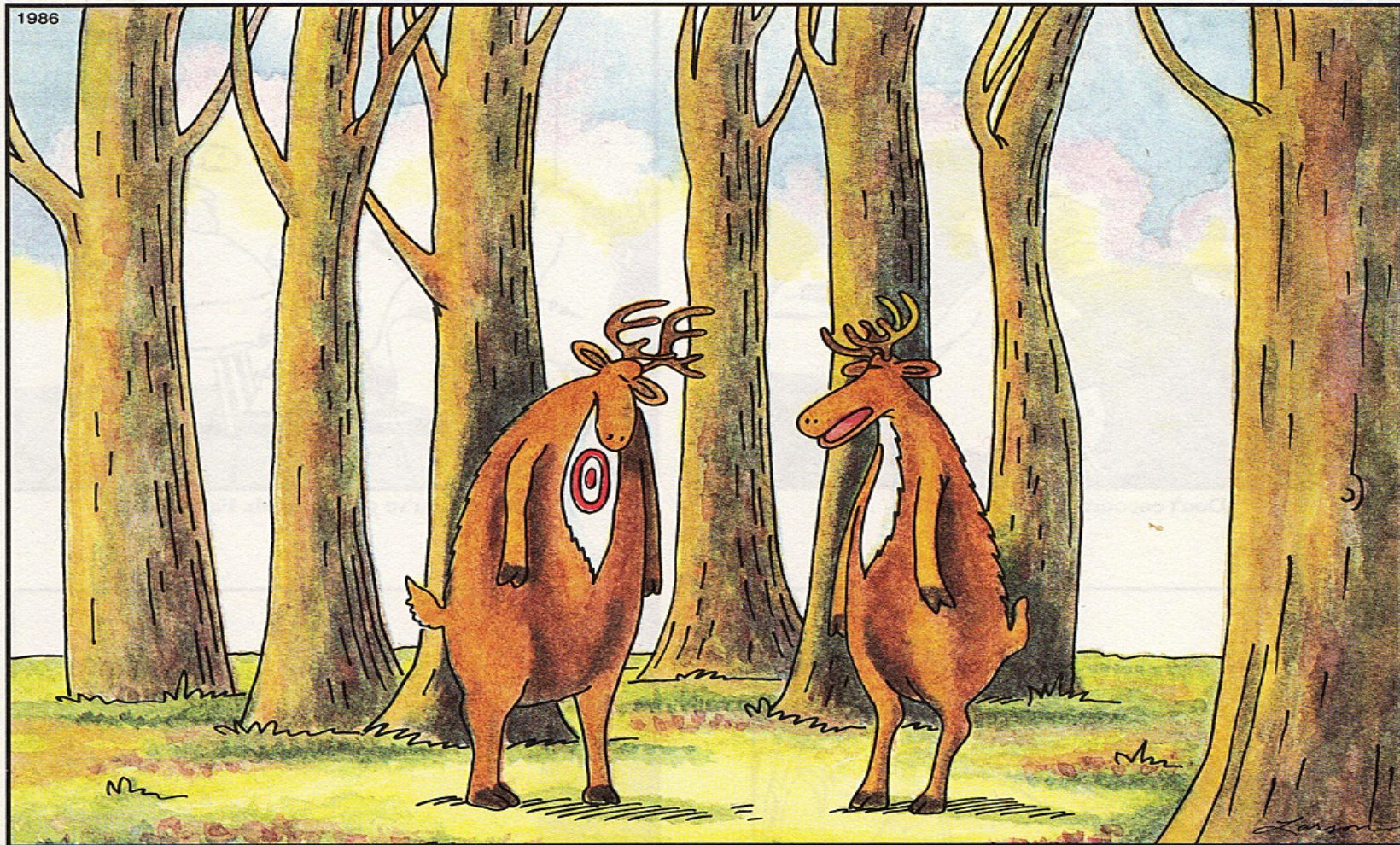
- **Comprehensive long-term outcomes data are lacking in the pediatric population**
- Elevated morbidity/mortality seen in NI patients may not be due to fundoplication
- Need to standardize both the definition of and workup for reflux and recurrent reflux
- Need to consistently define recurrence and failure with objective testing

Level 4 evidence, grade C recommendations.

Historical context

“During the past twenty years fundoplication has found widespread propagation. Due to its effectiveness it is today the most often applied operative procedure of reflux-preventing surgery. As such the method must be reserved for **clearly demonstrated reflux disease** and its organic complications. *False indication and incorrect technique have burdened results of such operations with unnecessary complications...*In the future, the results of this surgical method will have to be improved more by **correct indication** instead of changing the surgical technique.”

Nissen, Rossetti *20 years in the Management
of Reflux Disease Using Fundoplication*,
1977



“Bummer of a birthmark, Hal.”

Outcomes of pediatric laparoscopic fundoplication: A critical review of the literature

Martin K, Deshaies C, Emil S. Can J Gastroenterol Hepatol. 2014 Feb; 28(2): 97–102

- Systematic Review EMBASE, PubMed, CENTRAL 1996-2010
- Medium to long-term outcomes (> 6 month follow-up)
- Newcastle-Ottawa and Cochrane assessment tools for quality and risk of bias
- Extremely poor quality and level of evidence
- Significant heterogeneity precluded ability to pool outcomes
- Higher quality data needed before effectiveness can be demonstrated for this procedure in children

Total number of articles n=36	
Outcome/Criterion	%
Recurrence	0-48%
Reoperation	0.7-18%
Mortality	0-24%
No description of symptoms	36%
No disclosure of diagnostic modalities	11%
Definition of recurrence	17%
Controlled for confounders	14%