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Canadian Consensus Conference on the Management of Gastroesophageal Reflux Disease in Adults – Update 2004

**March 1st – 2nd 2004
Banff, Alberta**

CAG GERD Consensus Meetings

- **First GERD Consensus – 1992**
- **Second GERD Consensus – 1996**
 - **Can J Gastroenterol 1997;11(Suppl B):7B-20B, 1997**
- **Developments & changes in:**
 - **Investigation**
 - **Therapy**
 - **Reimbursement**

GERD – Key Considerations 1

- **Changing prevalence of GERD**
- **Re-evaluation of burden of disease**
- **Re-evaluation of GERD symptomatology**
- **Re-evaluation of role of investigations**
 - **Symptom-based management (CanDys)**
 - **'Endoscopy negative reflux disease'**
 - **Endoscopic severity of esophagitis**
 - **Ambulatory pH monitoring**

GERD – Key Considerations 2

- **Changes in medical therapy**
 - **Increased used of PPIs**
 - **Multiple PPIs available**
 - **Use of high-dose PPIs**
 - **Step-up vs Step-down vs Step-in**
 - **Reduced availability of 'prokinetics'**
 - **Long-term strategies**
 - **Continuous, Intermittent *or* On-demand**
- **Changes in 'non-medical' therapy**
 - **Laparoscopic surgery**
 - **Endoscopic therapy**

GERD – Key Considerations 3

- Re-evaluation of disease severity
- Re-evaluation of long-term risks
 - Barrett's esophagus
 - Esophageal adenocarcinoma
- Re-evaluation of health economics
- *Re-evaluation of pediatric GERD*
- *Re-evaluation of extra-esophageal disease*

Process for Guideline Development

- 1. Determination of need for guidelines**
Needs assessment; review literature & previous guidelines
- 2. Membership of the Consensus group**
Participants with expertise;
Representation of relevant disciplines / societies
- 3. Determination of clinically relevant issues**
Based on literature review and clinical needs assessments
- 4. Nature and extent of background preparation**
Review key articles; develop narrative & systematic reviews
- 5. Delphi consensus process**
Circulate preliminary statements & evidence
- 6. The Consensus Conference**
Present statements; summarise and grade evidence, vote
- 7. Preparation process and format of the report**
Draft manuscript reviewed by participants and non-voting chair

GERD Consensus – Update 2004

- **Discussion with C.A.G.**
 - **Identification of potential participants:**
 - GI (adult & pediatric)
 - Surgery
 - Industry
 - Primary Care Physicians
 - Pharmacy
 - Provincial / Federal
 - **Invitation of Steering Committee**
- **Needs Assessments:**
 - **Primary Care – CANGUT June 2003**
 - **Gastroenterologists – October 2003**
- **Evaluate responses to determine areas of uncertainty & controversy**
- **Develop statements to address areas of uncertainty**

GERD Consensus – Update 2004

“Delphi Approach”

- **Review of statements by Steering Committee**
- **Revision of statements & provisional assignment of evidence base**
- **Circulation of statements to participants**
 - **Solicit comments**
 - **Assign priority for discussion at GERD Update Meeting**
- **Development of abridged list of statements for discussion**
- **Invitation to experts to present summary of key evidence in relevant areas**

GERD Consensus – Update 2004

- **Presenters – 12**
 - 'Top line' summary of evidence / data relevant to topic and 'key area'
- **Facilitator**
 - John Marshall
- **External observers**
 - Peter Kahrilas, Ronnie Fass, Paul Moayyedi
- **Medical writer**
 - Pauline Lavigne
- **Literature search resource**
 - Cathy Yuan

Agenda – Monday, March 1st

Session I	13:00	Introduction	Armstrong
	13:30	Prevalence of GERD	Mayrand
	13:45	QOL / Disease Burden	Hunt
	14:00	DISCUSSION	
	15:45	Break	
Session II	16:00	GERD Symptoms	Moayyedi
	16:15	GERD Investigation	Paterson
	16:30	DISCUSSION	
	18:30	Dinner	
Session III	19:30	Initial Medical Therapy	Chiba
	19:45	DISCUSSION	
	22:30	Close for day	

Agenda – Tuesday, March 2nd

Session IV	07:30	Continuous Therapy	Armstrong
	07:45	Alternative Long-Term Rx	Van Zanten
	08:00	Endoscopic Therapy	Enns
	08:15	Surgical Therapy	Duranceau
	08:30	DISCUSSION	
	10:15	Break	
Session V	10:30	Barrett's Esophagus	Fallone
	10:45	DISCUSSION	
	12:00	Working Lunch	
Session VI	12:15	Economics in GERD Rx	Sadowski
	12:30	DISCUSSION	
	13:00	Close	

GERD Consensus – Update 2004

- 23 voting participants – multidisciplinary group
- Presentations to highlight key evidence
- Discussion of key prioritised statements
 - Voting on level of support
- Review of lower priority statements
 - Completion of hard copy voting forms
- Levels of Support
 - Grade for Quality of Evidence (I-III)
 - Classification for Strength of Recommendation (A-E)
 - Vote of individual's agreement with statement / stated recommendation (a-e)

GERD Consensus – Update 2004

- **Compilation of statements**
 - Statements with voting available from mid-March 2004 – CAG, Provincial Ministries
- **Management algorithms**
 - Draft May 2004 – Steering Committee
- **Manuscript**
 - Draft to Steering Committee – Summer 2004
 - Revision to Participants – late Summer 2004
 - Posted to CAG website – Fall 2004
 - Submission to Can J Gastroenterol – Fall 2004
- **Publication**
 - **Can J Gastroenterol: January 2005 (Vol 19(1):pp15-35)**

Canadian GERD Consensus January 2005

Canadian Consensus Conference on the management of gastroesophageal reflux disease in adults – Update 2004

David Armstrong MD¹, John K Marshall MD¹, Naoki Chiba MD^{1,2}, Robert Enns MD³, Carlo A Fallone MD⁴,
Ronnie Fass MD⁵, Roger Hollingworth MD⁶, Richard H Hunt MD¹, Peter J Kahrilas MD⁷, Serge Mayrand MD⁴,
Paul Moayyedi MD^{1,8}, William G Paterson MD⁹, Dan Sadowski MD¹⁰, Sander JO Veldhuyzen van Zanten MD¹¹,
for the Canadian Association of Gastroenterology GERD Consensus Group*

D Armstrong, JK Marshall, N Chiba, et al; for the Canadian Association of Gastroenterology GERD Consensus Group. Canadian Consensus Conference on the management of gastroesophageal reflux disease in adults – Update 2004. *Can J Gastroenterol* 2005;19(1):15-35.

BACKGROUND: Gastroesophageal reflux disease (GERD) is the most prevalent acid-related disorder in Canada and is associated with significant impairment of health-related quality of life. Since the last Canadian Consensus Conference in 1996, GERD management has evolved substantially.

OBJECTIVE: To develop up-to-date evidence-based recommendations relevant to the needs of Canadian health care providers for the management of the esophageal manifestations of GERD.

unnecessary before starting GERD therapy. GERD is associated with Barrett's epithelium and esophageal adenocarcinoma but the risk of malignancy is very low. Endoscopic screening for Barrett's epithelium may be considered in adults with GERD symptoms for more than 10 years; Barrett's epithelium and low-grade dysplasia generally warrant surveillance; endoscopic or surgical management should be considered for confirmed high-grade dysplasia or malignancy.

CONCLUSION: Prospective studies are needed to investigate clinically relevant risk factors for the development of GERD and its complications; GERD progression, on and off therapy; optimal management strategies for typical GERD symptoms in primary care patients; and optimal management strategies for atypical GERD symptoms, Barrett's epithelium and esophageal adenocarcinoma.



**CAG GERD Consensus
Statements**

CAG Canadian Consensus Conference on the Management of GERD in Adults – Update 2004

- **GERD is the most prevalent acid-related disorder in Canada**
- **GERD is associated with significant impairment of health-related quality of life**
- **GERD management has evolved since the last Canadian GERD Consensus Conference (1996)**

CAG GERD Update 2004

Objective

- To develop up-to-date, evidence-based recommendations relevant to the needs of **Canadian health care providers** for the management of the **esophageal** manifestations of gastroesophageal reflux disease

Statement Groups

- **Impact of GERD**
 - Statement 1-2
- **Definitions**
 - Statement 3-6
- **Assessing Severity**
 - Statement 7-9
- **Diagnosis**
 - Statement 10-11
- **Investigations**
 - Statement 12-14
 - Statement 15-19
 - Statement 20

Alarm features
Endoscopy
pH monitoring

Statement Groups

- **Initial Therapy**

- Statement 21-22
- Statement 23-29
- Statement 30

OTCs, Lifestyle modifications

PPIs, H₂-RAs

Prokinetics

- **Long-term Therapy**

- Statement 31-33
- Statement 34-38
- Statement 39
- Statement 40
- Statement 41-42

Definitions

Continuous, On-demand

Prokinetics

H₂-RA & NAB

Surgical & endoscopic therapy

- ***Helicobacter pylori***

- Statement 43-46

***H. pylori* therapy; effect on GERD**

Statement Groups

- **Barrett's esophagus**

- Statement 47-48
- Statement 49-51
- Statement 52-53
- Statement 54-58
- Statement 59-61

Definitions

Esophageal adenocarcinoma

Screening

Surveillance

Management

- **Economics**

- Brief overview

- **Future Directions**

- Brief overview

GERD – Summary of Topics Addressed

- Impact of GERD Statements 1-2
- Definitions Statements 3-6
- Assessing Severity Statements 7-9
- Diagnosis Statements 10-11
- Investigations Statements 12-20
- Initial Therapy Statements 21-30
- Long-term Therapy Statements 31-42
- *Helicobacter pylori* Statements 43-46
- Barrett's esophagus Statements 47-61
- Economics Overview
- Future Directions Overview

Quality of Evidence

- I** Evidence obtained from at least one properly randomized controlled trial.
- II-1** Evidence obtained from well-designed controlled trials without randomization.
- II-2** Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.
- II-3** Evidence obtained from comparisons between times or places with or without the intervention, or dramatic results in uncontrolled experiments.
- III** Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Classification of Recommendations

- A** There is good evidence to support the procedure or treatment.
- B** There is fair evidence to support the procedure or treatment.
- C** There is poor evidence to support the procedure or treatment, but recommendations may be made on other grounds.
- D** There is fair evidence that the procedure or treatment should not be used.
- E** There is good evidence that the procedure or treatment should not be used.

Voting on the Recommendations

- a Accept completely**
- b Accept with some reservation**
- c Accept with major reservation**
- d Reject with reservation**
- e Reject completely**

Accept statement if $>50\%$ of participants voted a, b, or c

Impact of GERD – Statement 1

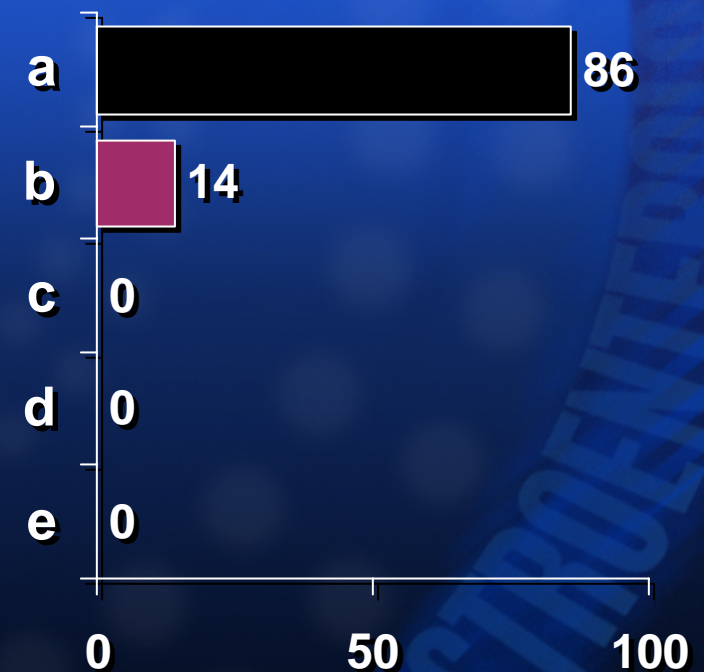
- *Gastroesophageal reflux disease (GERD) is the most prevalent acid-related disorder in Canada.*
- **Population survey in > 1,000 Canadians*:**
 - 17% - heartburn in last 3 mo.
 - 13% - moderate to severe symptoms, at least weekly
- **CADET-PE:**
 - 37.8% dominant heartburn,
 - 54.7% erosive esophagitis

Quality

- Level II-1

Classification

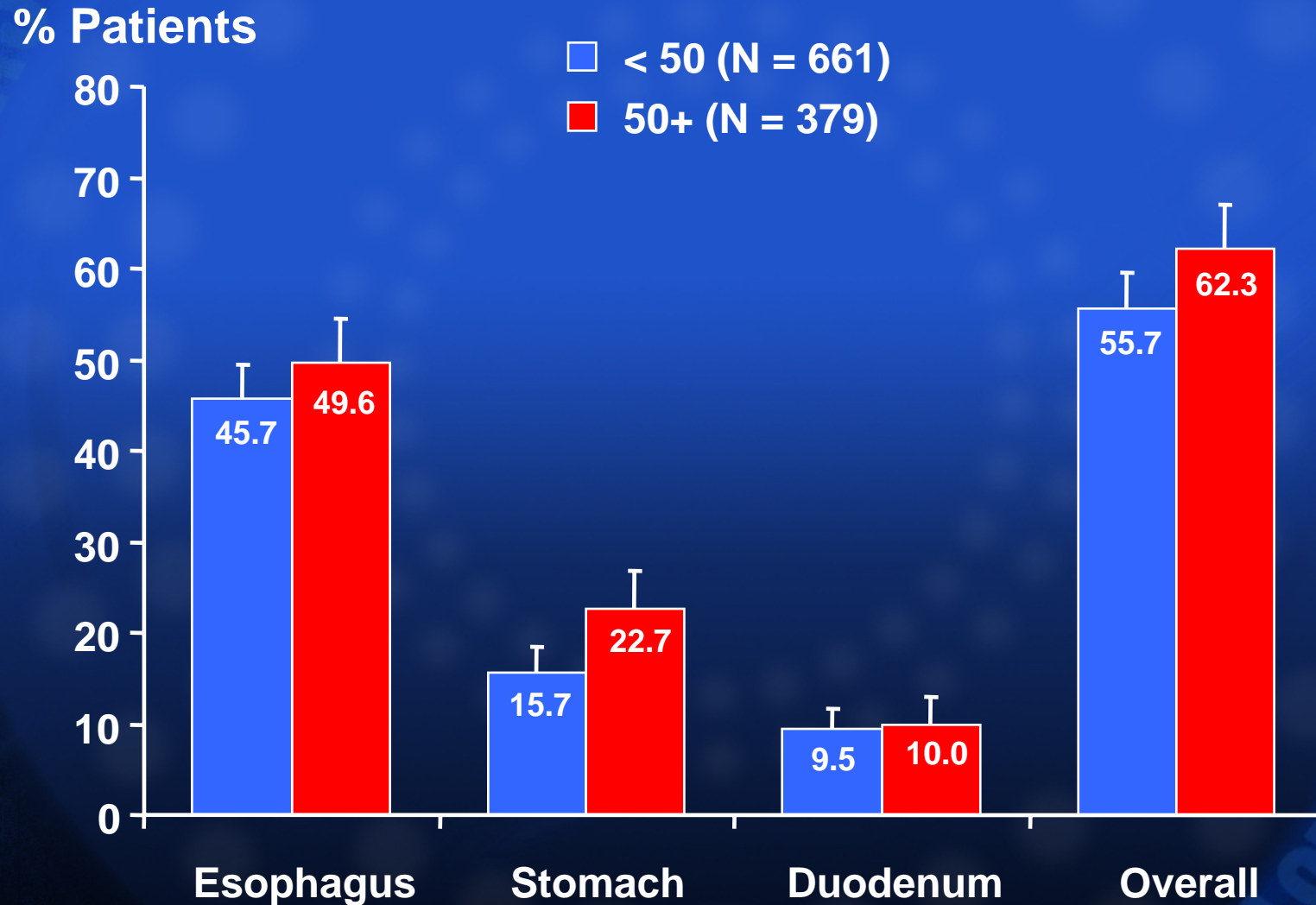
- Grade A



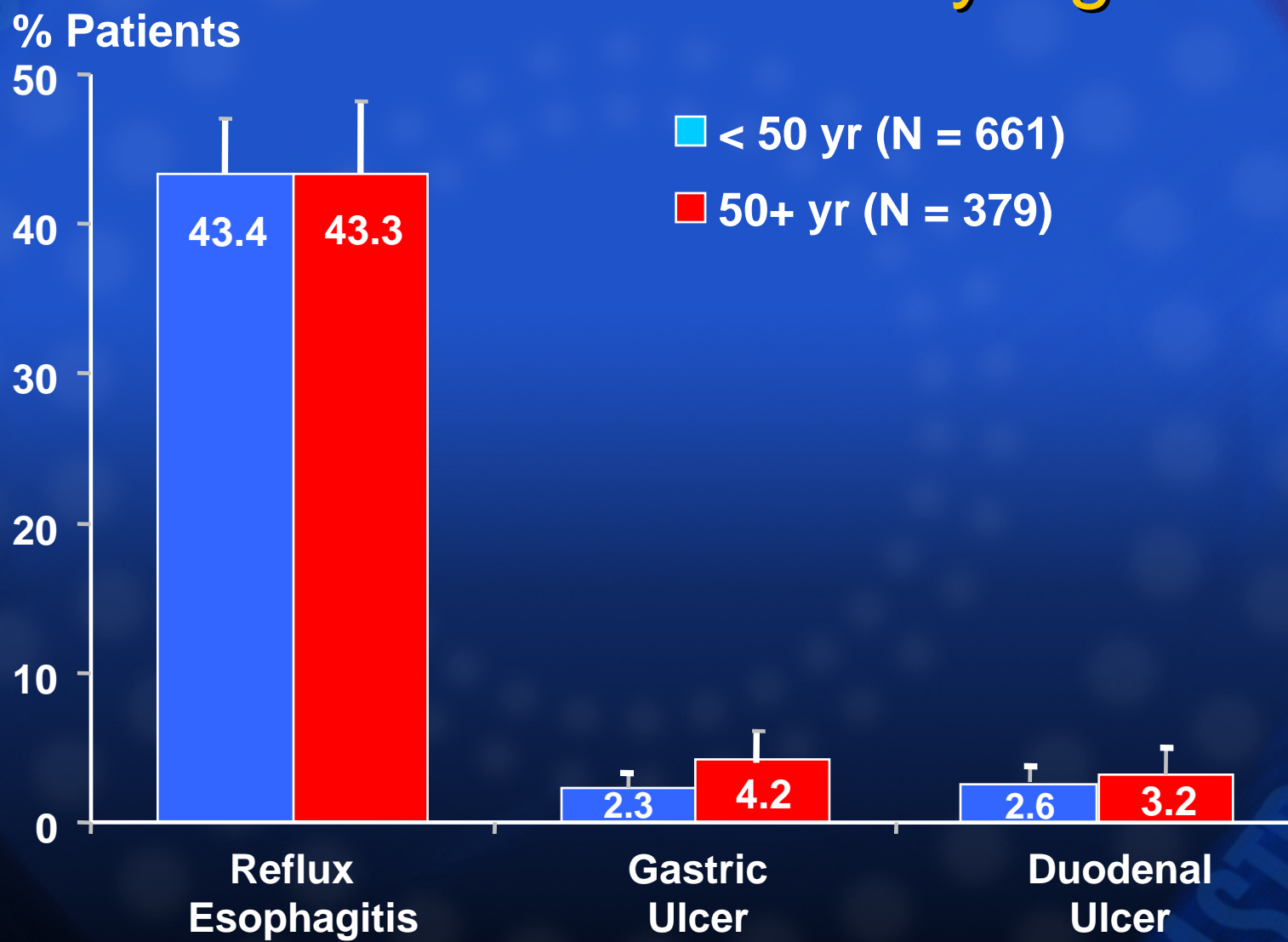
*Tougas G et al. Am J Gastroenterol 1999;94:2845-54

CADET PE Study

Clinically Significant Findings by Age



CADET PE Study Acid-Related Lesions by Age



Impact of GERD – Statement 2

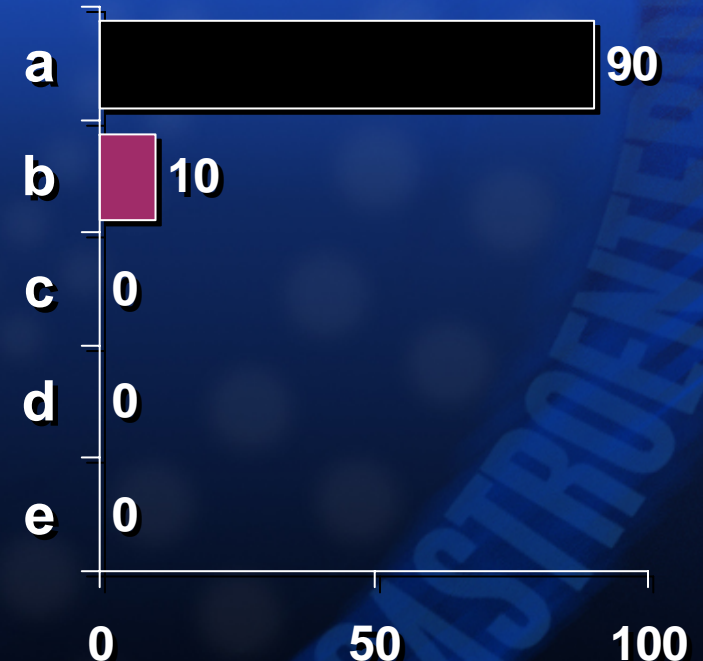
- ***GERD is associated with significant impairment of health-related quality of life (HRQL).***
- **HRQL is worse in patients with GERD than in patients with diabetes, hypertension, mild heart failure or arthritis**
(Revicki D et al. Am J Med 1998;104:252-8)
- **A survey of 102 GERD patients: 41% reported lost work productivity because of their disease** *(Henke C et al. Am J Gastroenterol 2000;95:788-92.)*

Quality

- Level I

Classification

- Grade A



Definitions – Statement 3

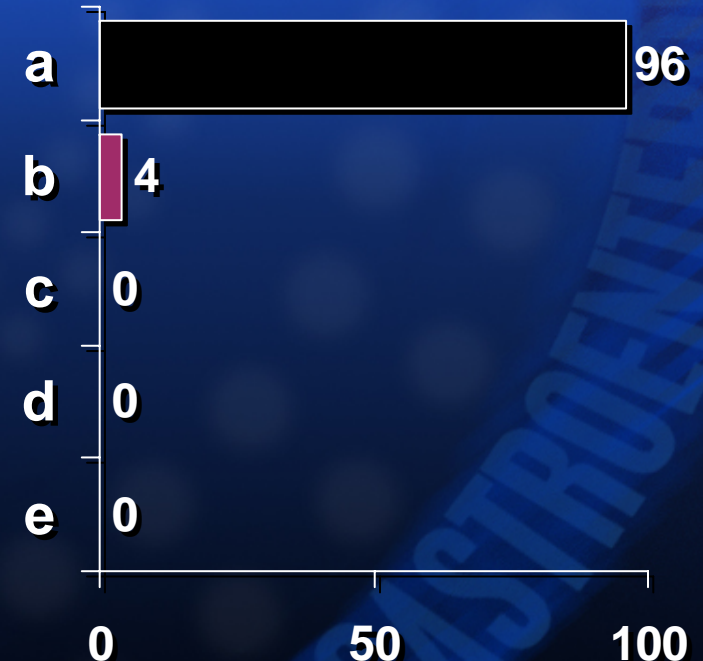
- ***GERD applies to individuals with reflux of gastric contents into the esophagus causing:***
(a) symptoms sufficient to reduce quality of life and/or
(b) esophageal injury.
- **The disease definition is based on symptoms and endoscopic findings, not on other tests (pH monitoring, radiology)**
- **Extra-esophageal reflux disease is not covered by this definition**

Quality

- N/A

Classification

- N/A



Definitions – Statement 4

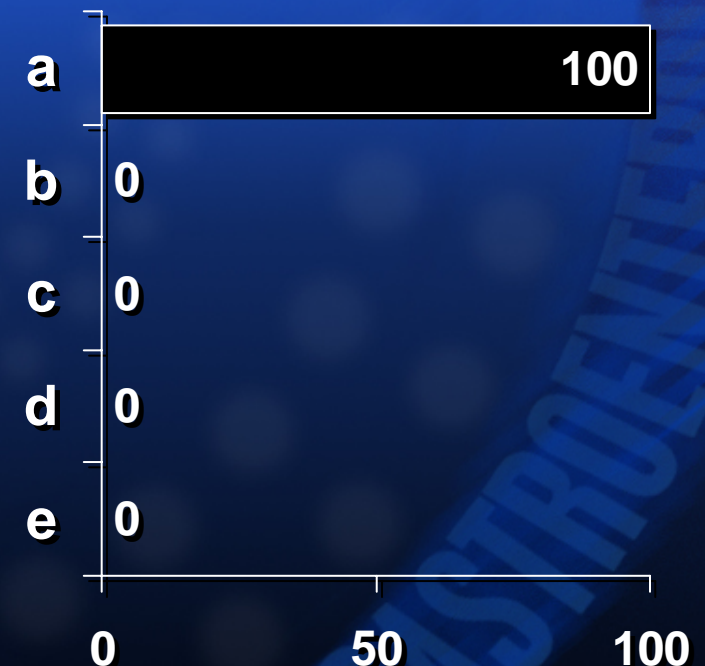
- **Heartburn** (a retrosternal burning sensation which may rise to the back of the throat) and **acid regurgitation** are the archetypal symptoms of GERD, which can be treated empirically without further investigation, provided there are no alarm features.
- Heartburn & regurgitation are the most common but **NOT** the only symptoms of GERD
- In the absence of alarm features, including age < 50 years, upper GI malignancy is very rare in Canada.

Quality

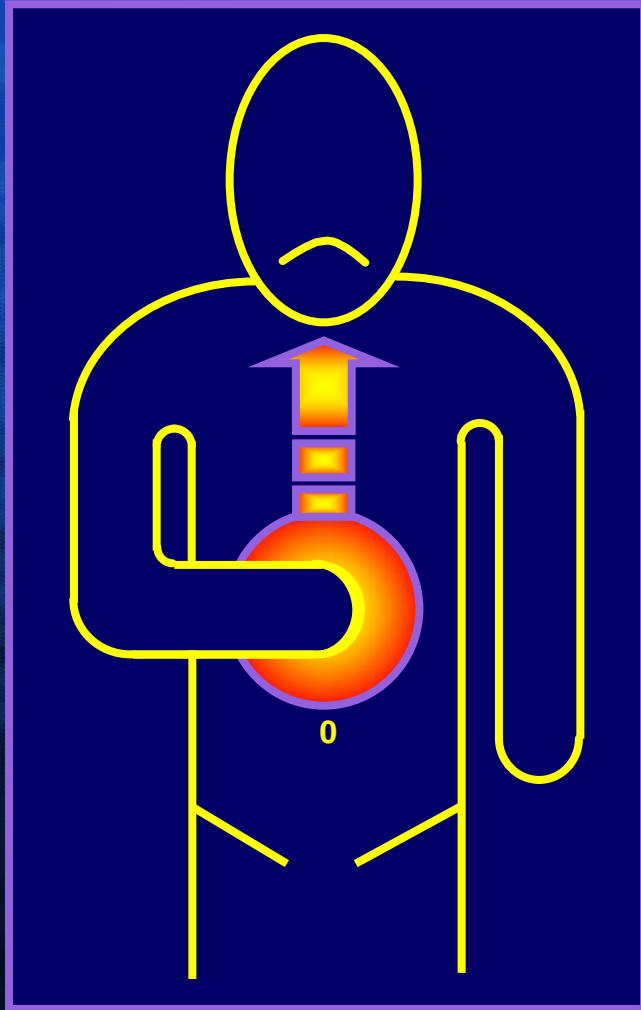
- Level I

Classification

- Grade A



GERD Symptoms



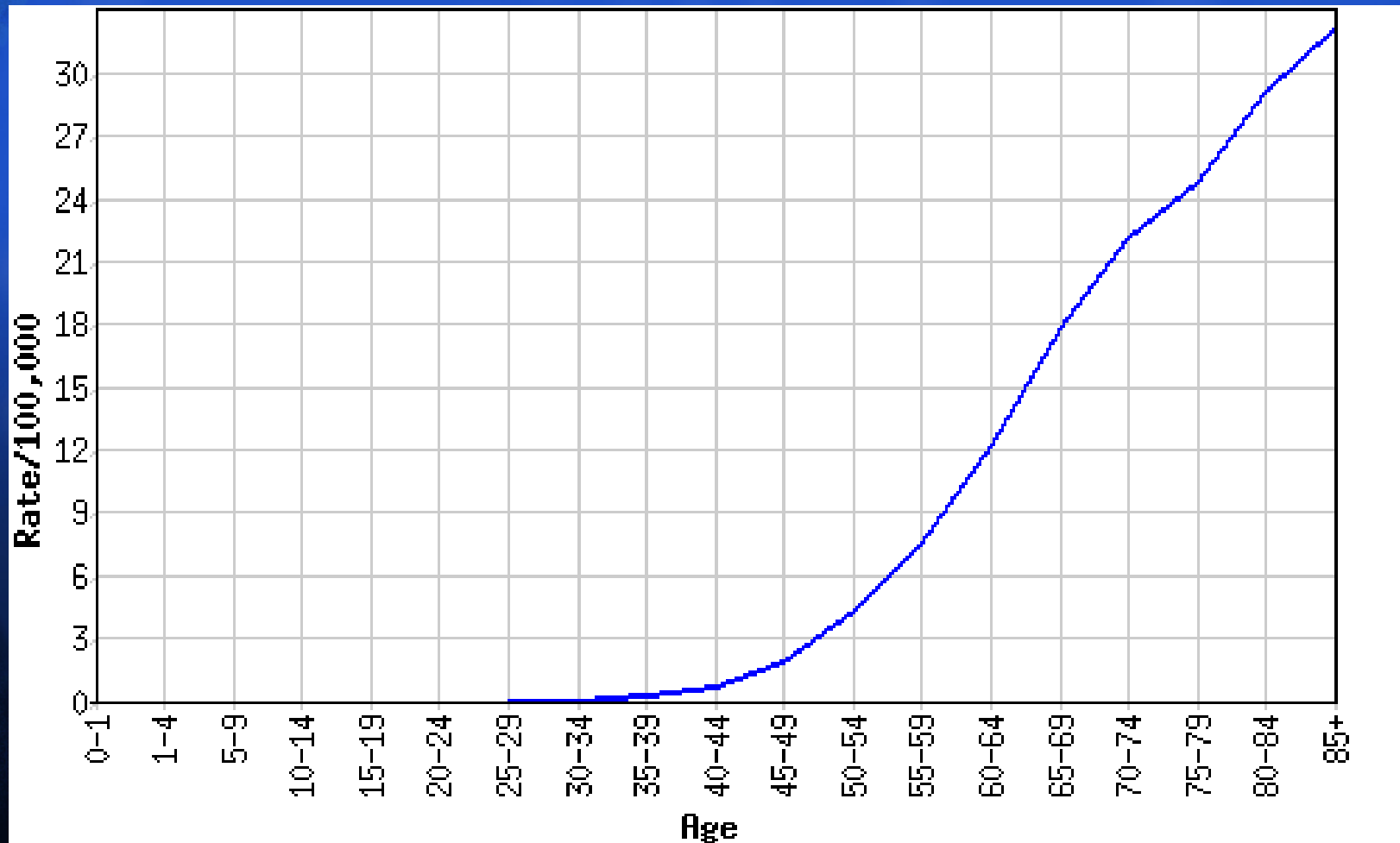
“A burning feeling rising from the stomach or lower chest towards the neck”

- not necessarily congruent with “Heartburn” - interpreted differently by many patients / physicians

Sensitivity	- 73%
Specificity	- 43%

Esophageal Cancer Incidence by Age 1990-2000, Canada (Male & Female)

Age-Standardized Incidence Rate per 100,000 (Canada 1991)



Definitions – Statement 5

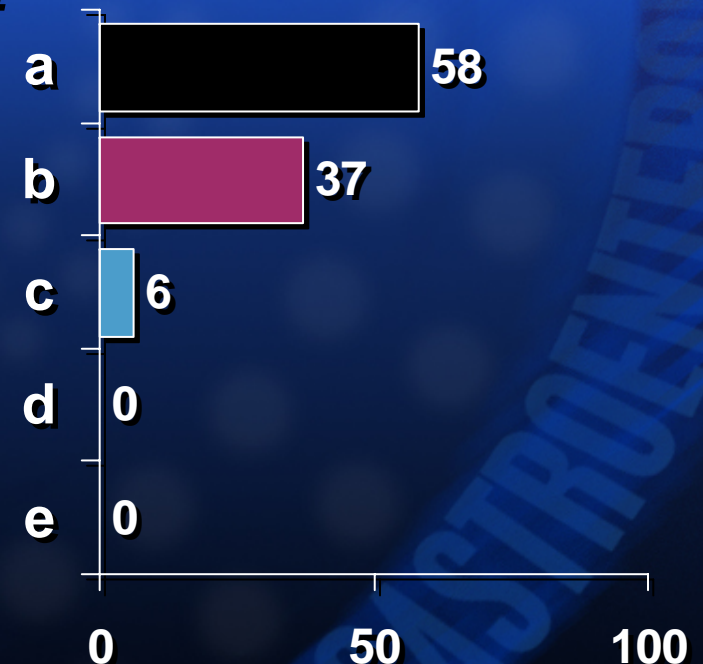
- ***Heartburn-dominant uninvestigated dyspepsia, applies to individuals who have symptoms, referable to the esophagus, or a reduced quality of life attributable to gastro-esophageal reflux, in the absence of any prior investigations.***
- **CADET & CanDys definitions of dyspepsia and GERD relevant to primary care practice:**
 - **Due to limited availability of timely investigations**

Quality

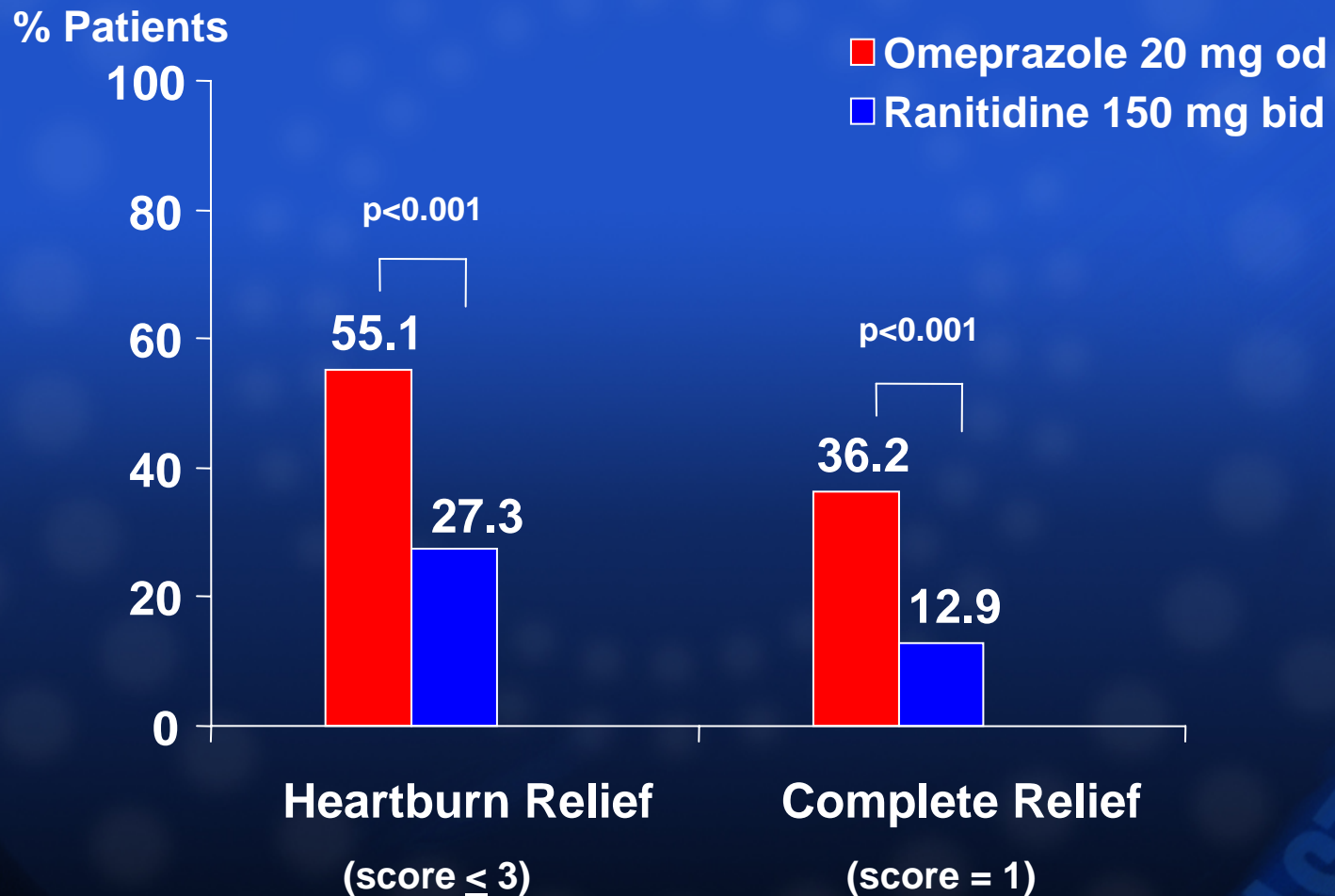
- **Level III**

Classification

- **Grade A**



Heartburn Relief at 4 Weeks (CADET-HR) Uninvestigated Heartburn Dominant Dyspepsia



Armstrong D et al. Aliment Pharmacol Ther 2005;21:1189-202

Definitions – Statement 6

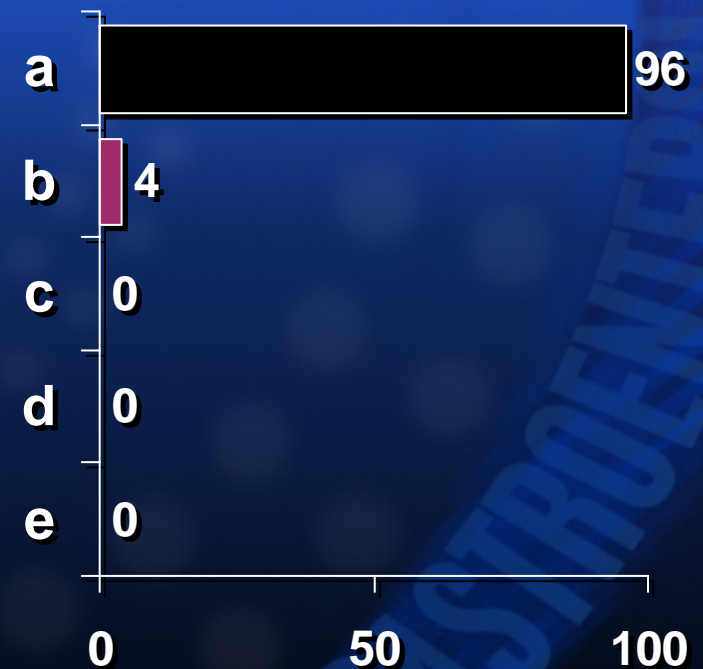
- *Endoscopy negative reflux disease (ENRD) applies to individuals with GERD, who have a normal endoscopy (while off treatment).*
- **30-70% of patients with GERD symptoms have no esophageal abnormality at endoscopy**
- **ENRD is, arguably, the most common subgroup of GERD and symptoms will often respond to effective acid-suppressive therapy**

Quality

- N/A

Classification

- N/A



Prevalence of E.N.R.D.

- **53%** of community GERD patients
(Robinson et al 1998)
- **68%** of general practice GERD patients
(Venables et al 1997)
- **71%** of GERD patients
(Galmiche et al 1997)
- **49%** of primary care GERD patients
(Carlsson et al 1997)

GERD Severity – Statement 7

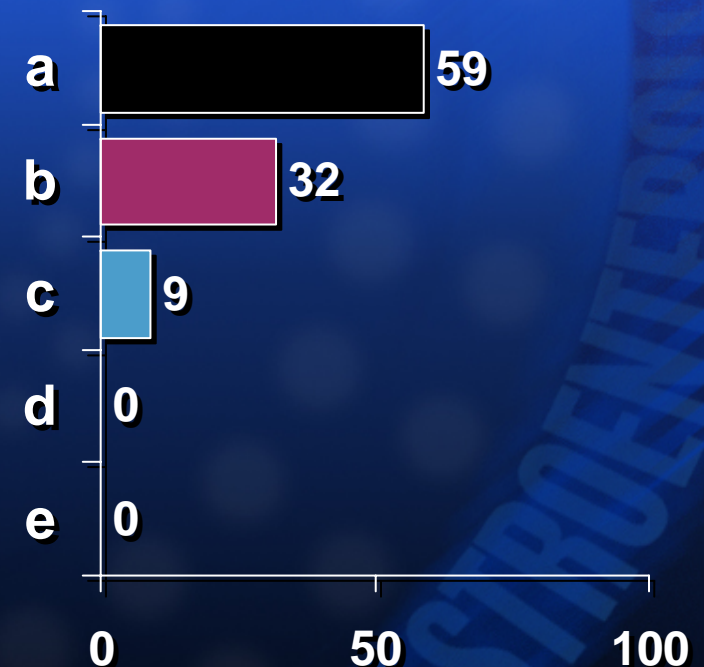
- ***GERD symptom severity, incorporating the frequency, intensity and duration of symptoms, is defined by the extent to which the sufferer indicates that it has an adverse effect on his or her daily activities and HRQL.***
- **Reduction in HRQL and work productivity is greater for individuals with more severe symptoms**

Quality

- II-3

Classification

- B



GERD Severity – Statement 8

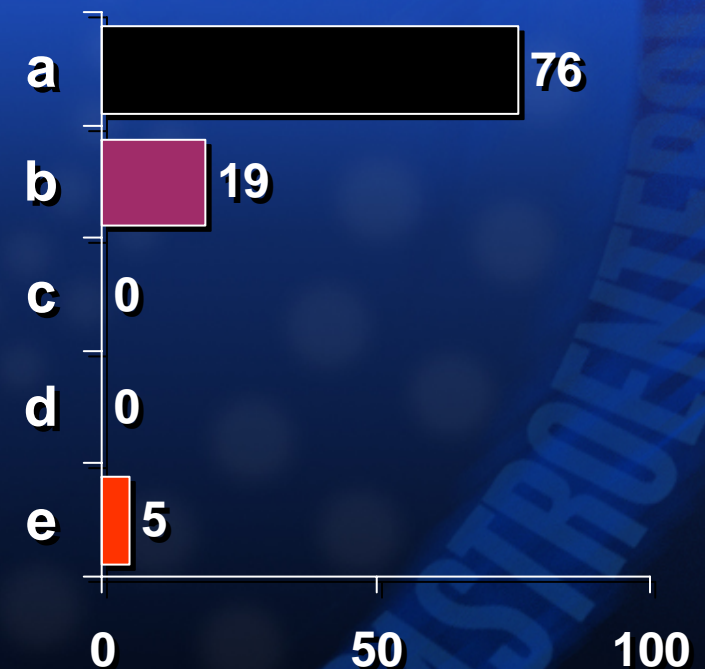
- ***GERD severity is determined by the severity and frequency of the associated symptoms or by the presence and extent of reflux-related lesions such as esophageal erosions, ulcers, hemorrhage, strictures or columnar metaplasia (Barrett's epithelium).***
- **Disease severity is determined both by symptoms and by the extent and nature of any mucosal lesions.**

Quality

- I

Classification

- A



GERD Severity – Statement 9

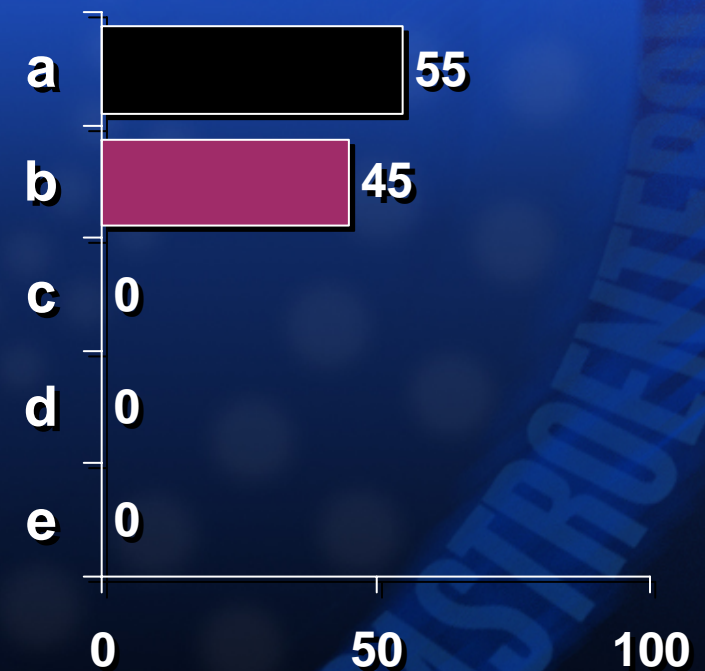
- *In the context of symptomatic management of GERD, ‘mild disease’ is applicable to patients who have symptoms that are infrequent (**fewer than three times/week**), of low intensity and short duration, and that have minimal long-term effect on the patient’s activities of daily living or HRQL. The terms ‘moderate disease’ or ‘severe disease’ are applicable to patients who have more frequent, intense or prolonged symptoms that have a significant effect on the patient’s daily activities or HRQL.*
- Symptom severity is largely subjective, but objective criteria are necessary for developing management strategies

Quality

- N/A

Classification

- N/A



Diagnosis – Statement 10

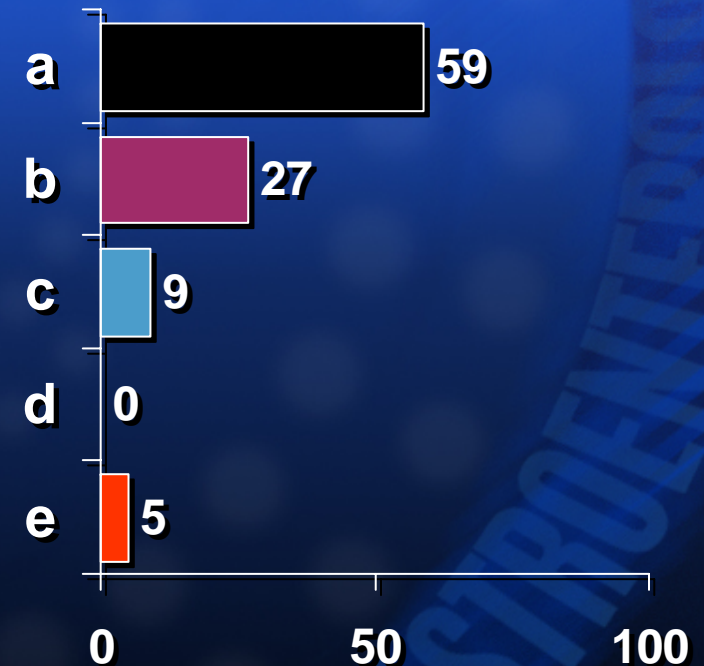
- *In clinical practice, a diagnosis of GERD can be made without investigation, based on the presence of the typical symptom of heartburn, with or without regurgitation.*
- **No clear ‘gold standard’**
- **Dominant heartburn or acid regurgitation have high specificity (89% & 95%) but low sensitivity (38% & 6%) for GERD, as defined by abnormal acid exposure on 24-hour pH monitoring**

Quality

- Level II-1

Classification

- Grade A



Diagnosis – Statement 11

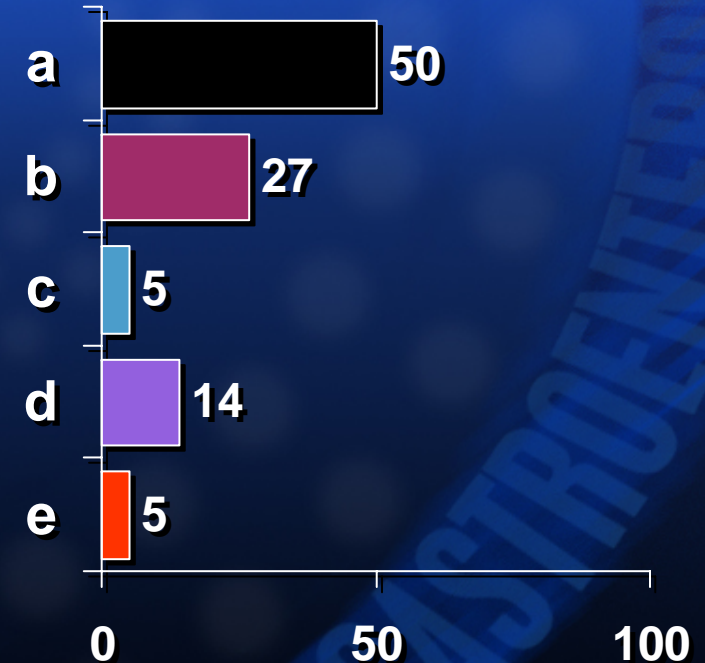
- ***A diagnosis of GERD can be made regardless of the frequency or severity of the individual's GERD-related symptoms.***
- **In general, neither symptom severity nor frequency constitutes a diagnostic criterion for GERD**
 - **e.g. Reflux-related NCCP is consistent with a diagnosis of GERD even if symptoms are infrequent, but**
 - **Mild, infrequent heartburn, not affecting quality of life is not, on its own, sufficient to diagnose GERD**

Quality

- **Level II-2**

Classification

- **Grade A**



Diagnosis – Statement 12

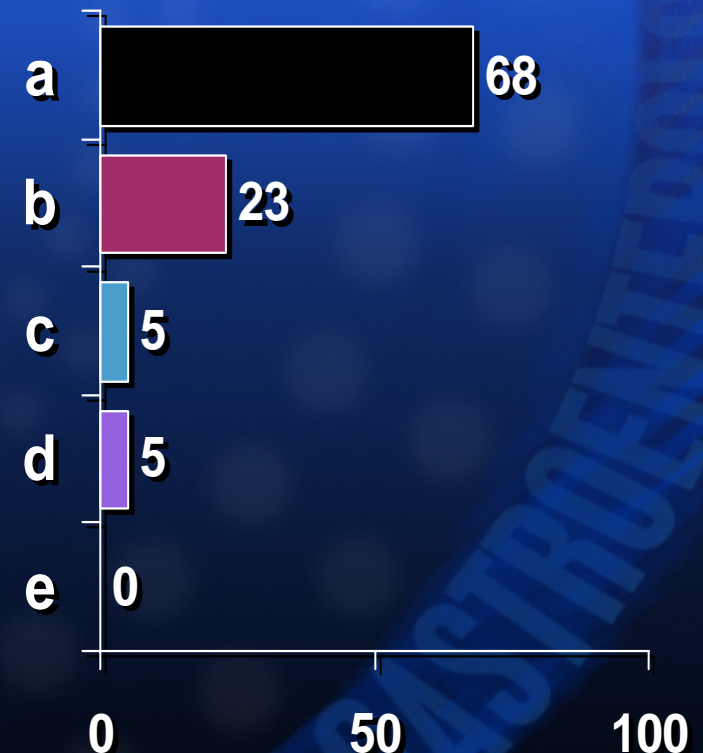
- **Alarm features in the presence of GERD symptoms include vomiting, evidence of gastrointestinal tract blood loss, anemia, involuntary weight loss, dysphagia, or chest pain.**
- **Recent guidelines (dyspepsia & GERD) identify alarm features that require prompt investigation**
 - **Canadian Dyspepsia Working Group** (Veldhuyzen van Zanten et al CMAJ 2000)
 - **A.G.A.** (DeVault et al AJG 1999; Spechler, Gastro 1999)
 - **NICE (UK)** www.nice.org.uk

Quality

- Level III

Classification

- Grade A



Diagnosis – Statement 13

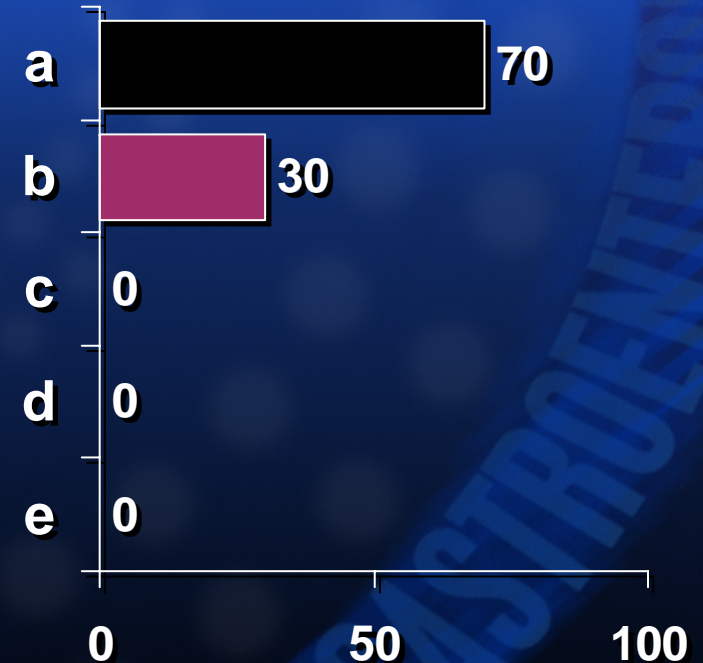
- *In patients with GERD, dysphagia should be investigated if it does not completely resolve with adequate PPI therapy (2-4 weeks).*
- **Dysphagia can often be elicited in erosive esophagitis:**
 - Usually mild & infrequent
 - Often resolves with PPI therapy
- **Solid food dysphagia: alarm feature**
 - Suggests peptic stenosis, stricture, a ring or web or malignancy
 - Needs prompt investigation, especially if progressive or unresponsive

Quality

- Level III

Classification

- Grade C



Diagnosis – Statement 14

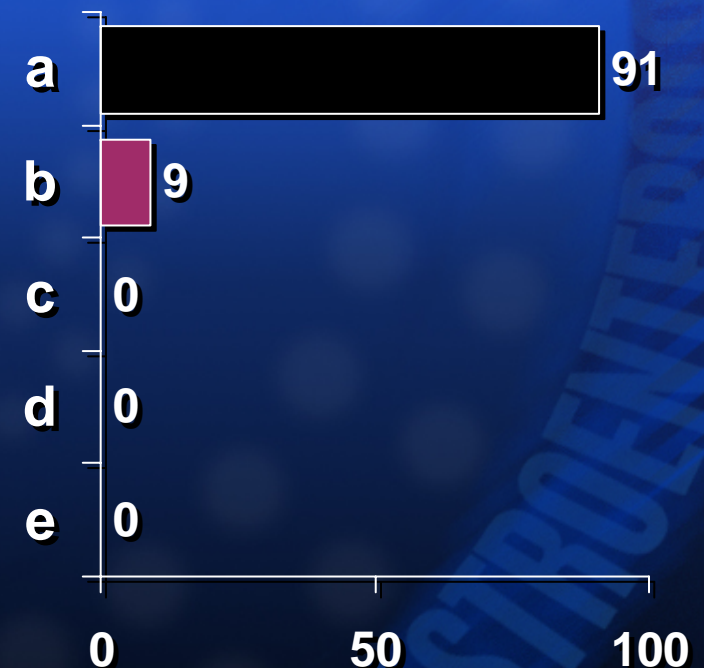
- *There is no age threshold (e.g., 50 years) that is, by itself, an indication for further investigation for GERD.*
- **Esophageal cancer is more prevalent over 50 years of age, but not enough to justify prompt investigation in all patients with GERD symptoms for the first time over the age of 50 years.**
- **This does not preclude investigation for Barrett's esophagus in patients over the age of 50**

Quality

- Level II-2

Classification

- Grade B



Endoscopy – Statement 15

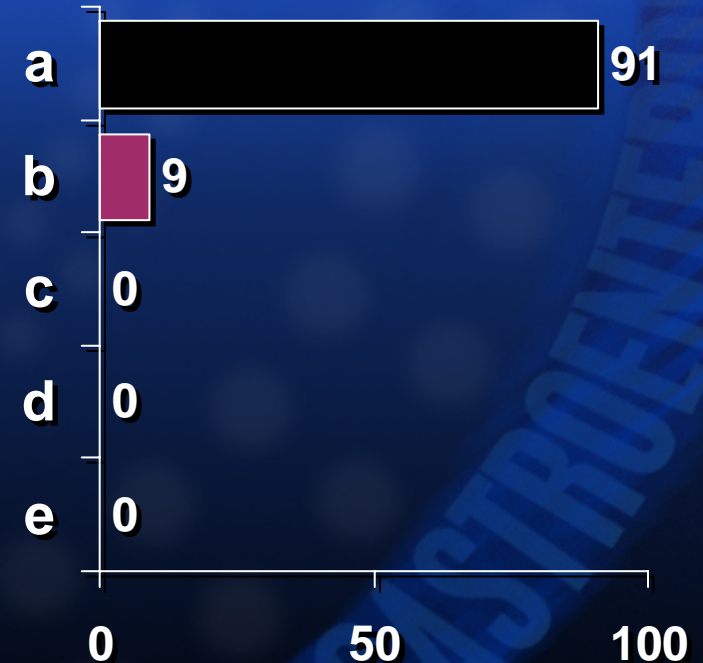
- ***Endoscopy is not required to make a diagnosis of GERD.***
- **Up to 70% of patients with symptoms of GERD have ENRD.**
- **Thus, endoscopy is highly specific (>90%) with lower sensitivity (40-60%) and it is not essential for a diagnosis of GERD.**
- **Endoscopy should not be a prerequisite for any form of pharmacological acid suppression therapy.**

Quality

- Level I

Classification

- Grade A



Endoscopy – Statement 16

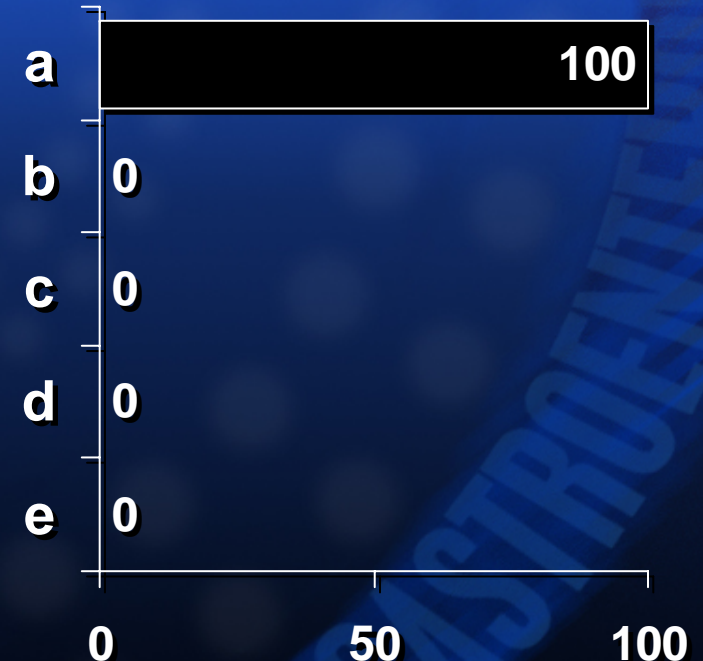
- *The role of endoscopy in patients with GERD symptoms is to investigate atypical or alarm features and to detect Barrett's esophagus.*
- The role of endoscopy for atypical symptoms is ill defined;
 - A normal endoscopy does **not** rule out GERD.
- Treatment (eg PPIs) generally does **not** need to be stopped before endoscopy

Quality

- Level III

Classification

- Grade B



Endoscopy – Statement 17

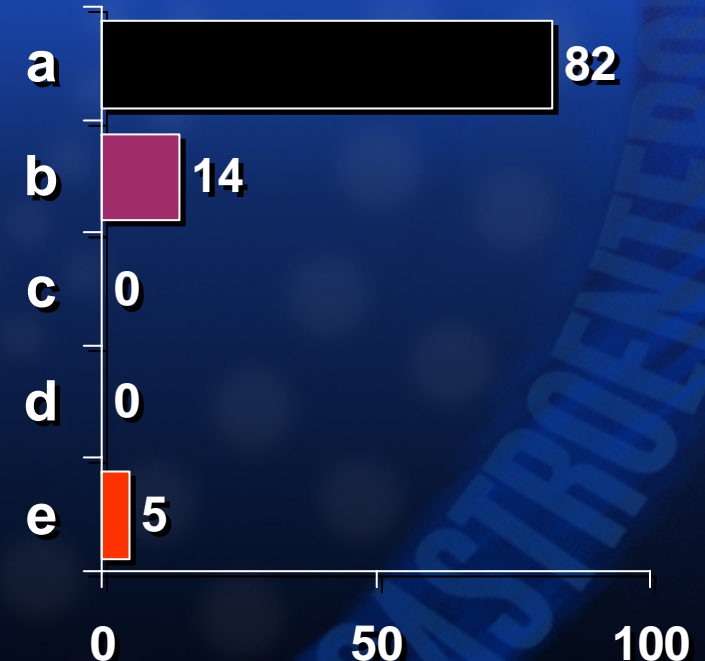
- *The severity of erosive esophagitis is determined endoscopically by the presence and extent of reflux-related “**mucosal breaks**” (erosions or ulcers) as defined by the Los Angeles classification.*
- **Los Angeles (‘LA’) system favoured because of:**
 - Extensive validation
 - Widespread use in clinical studies and clinical practice

Quality

- Level I

Classification

- Grade A

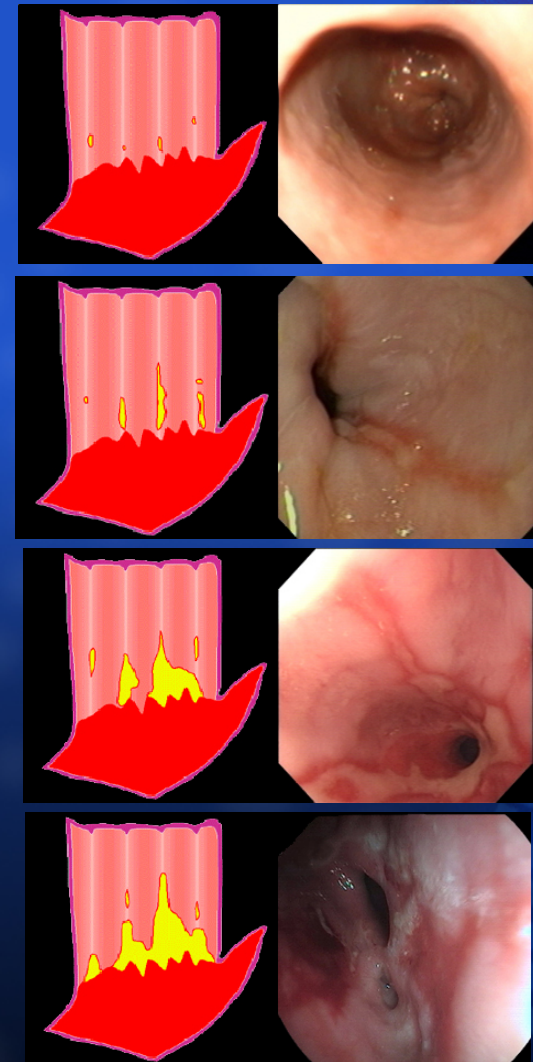


Los Angeles (L.A.) Classification

- A. One or more mucosal breaks < 5 mm in maximum length
- B. One or more mucosal breaks, > 5 mm, but not extending across 2 folds
- C. Non-circumferential mucosal breaks, continuous between 2 folds
- D. Mucosal break involving > 75% of esophageal circumference

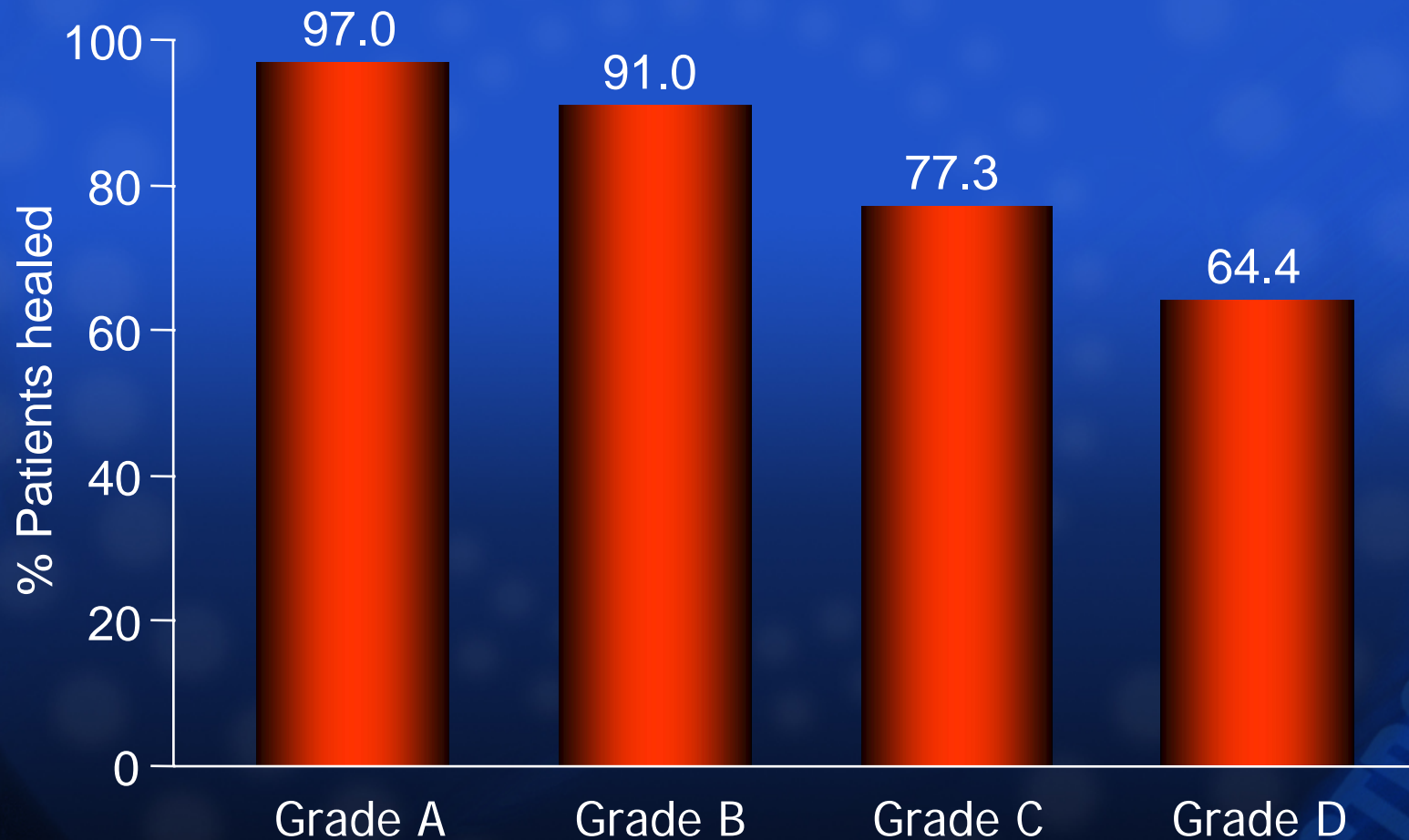
Los Angeles (L.A.) Classification

- A. ≥ 1 mucosal break < 5 mm in length
- B. ≥ 1 mucosal breaks, > 5 mm, but not extending across 2 folds
- C. Mucosal breaks, continuous between 2 folds but $< 75\%$ of circumference
- D. Mucosal break involving $> 75\%$ of esophageal circumference

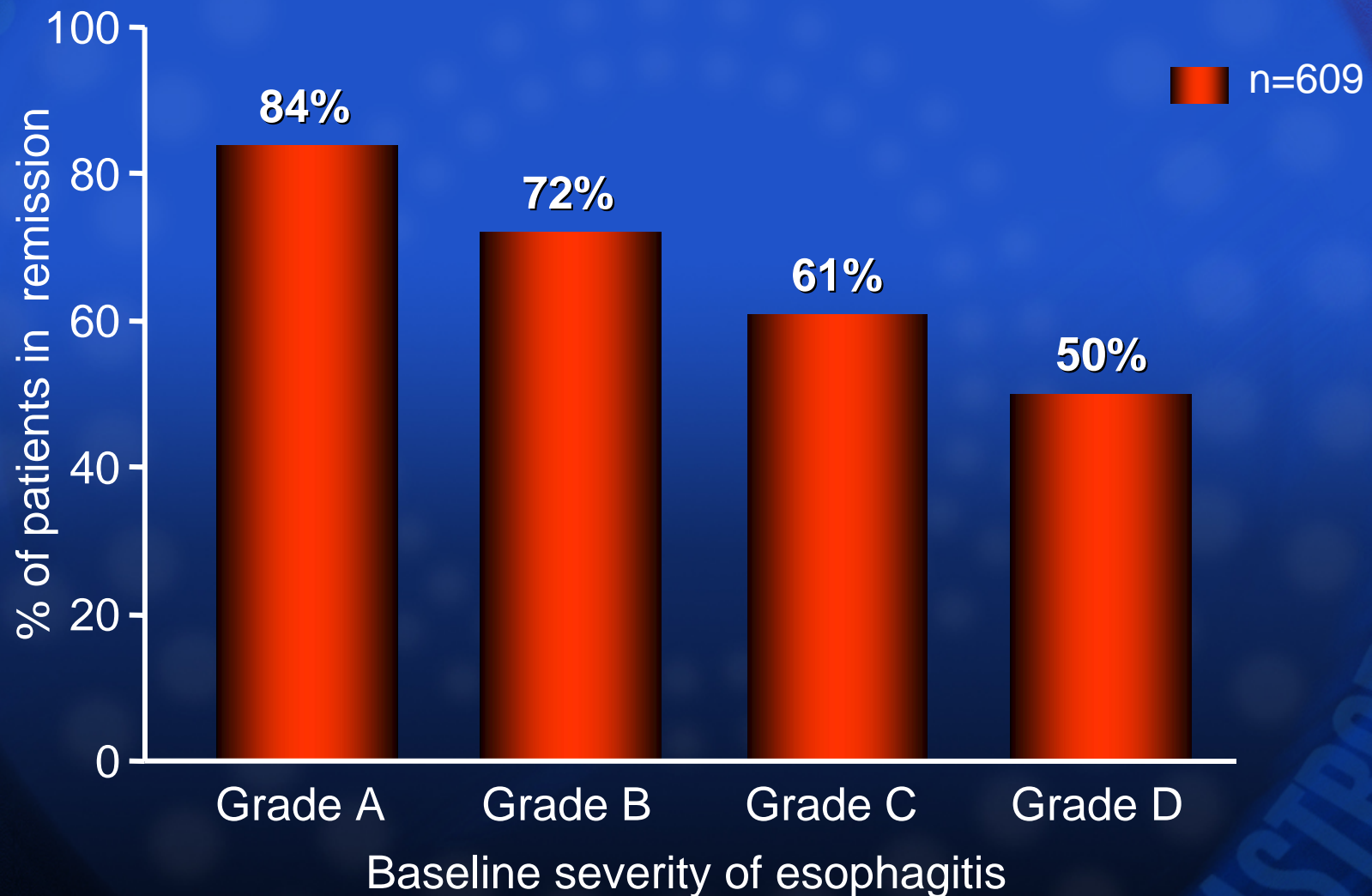


Armstrong D, et al. Gastroenterology 1996; 111:85-92
Lundell L, et al. Gut 1999; 45:172-180

Healing Rates by LA Grade at Week 8 (Once-daily, standard-dose PPI)



Remission Rates by LA Grade at Month 6 (Once-daily, half-dose PPI)



Endoscopy – Statement 18

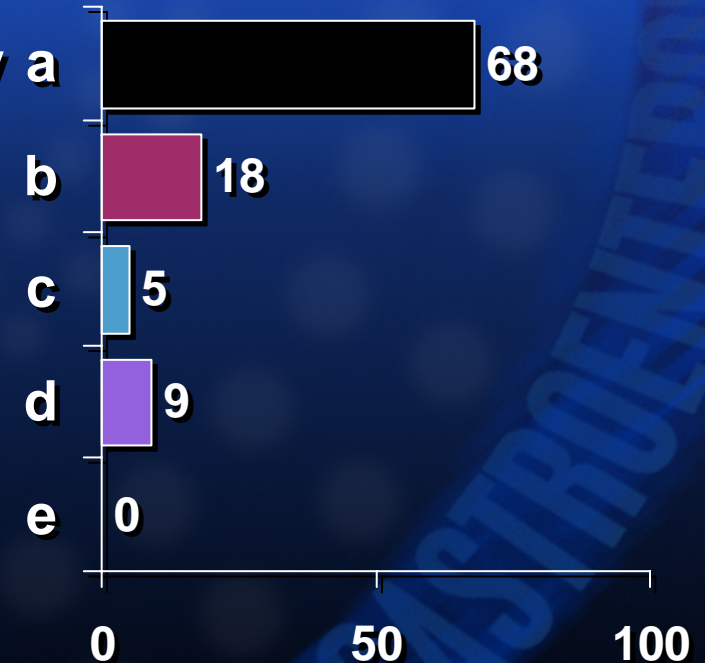
- *If a patient with GERD symptoms is to undergo endoscopy in clinical practice, it is not generally necessary to discontinue antisecretory therapy before the procedure.*
- **Mucosal breaks are best detected by a**
endoscopy but:
 - Mucosal breaks may not recur for weeks / months after stopping therapy
 - In clinical practice, the aim of treatment is to minimize symptoms
 - Detection of dysplasia is more reliable in the absence of underlying injury

Quality

- Level II-3

Classification

- Grade B



Endoscopy – Statement 19

- ***Esophageal histology is not required to diagnose GERD in a patient with typical symptoms.***
- **GERD is associated with basal cell layer hyperplasia, papillary elongation and intercellular space dilation *but* test sensitivity and specificity for GERD are not known**
(Stolte SJG 2000; Armstrong Gastro 2003; Ismail-Beigi Gastro 1970; Tobey N Gastro 1996; Armstrong D Gastro 2003; Solcia E Virchows Arch 2000)
- **Biopsies are appropriate for the diagnosis of Barrett's epithelium, dysplasia, malignancy (irregular or ulcerated lesions) and, for example, eosinophilic esophagitis**

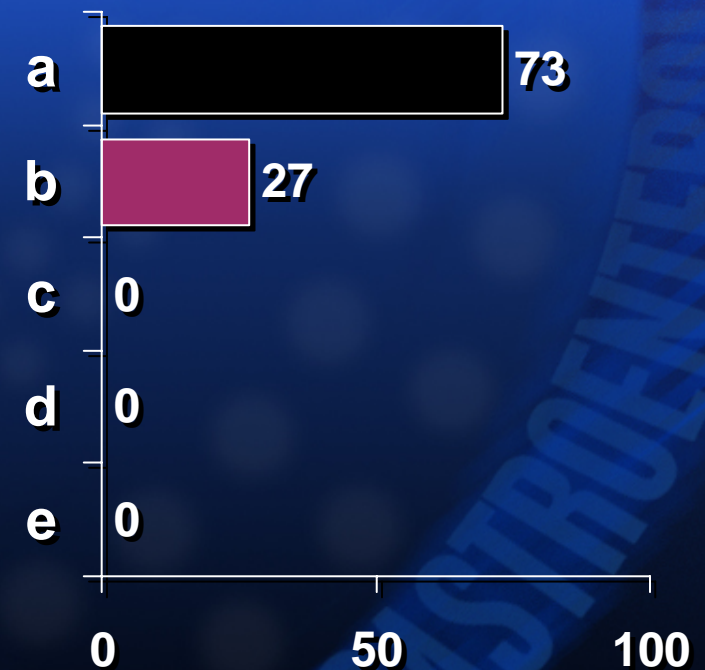
(Richter J. Am J Med Sci 2003)

Quality

- Level II-2

Classification

- Grade B



pH monitoring – Statement 20

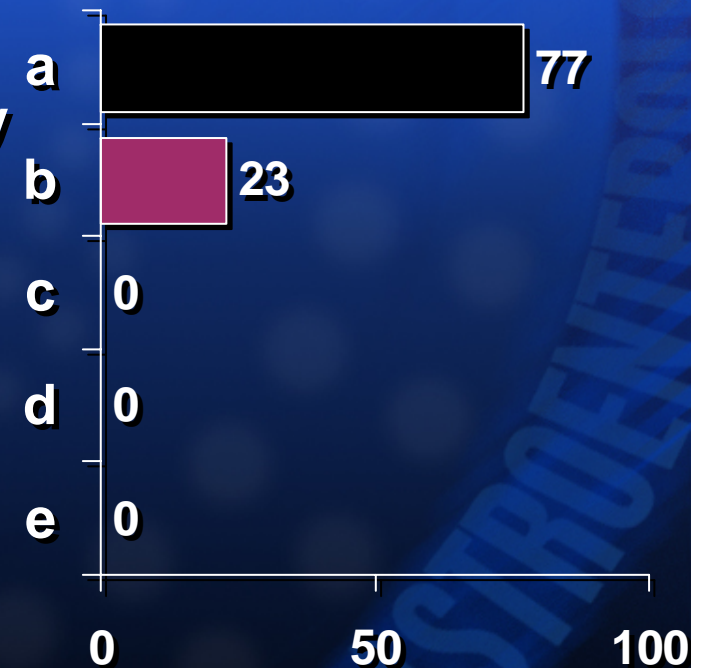
- ***In adult clinical practice, ambulatory esophageal pH monitoring is indicated primarily for investigation of atypical or persistent symptoms despite appropriate therapy.***
- **Esophageal pH monitoring used to be considered the gold standard:**
 - **Good sensitivity (77-100%) and specificity (85-100%) in esophagitis**
- **But, less reliable for ENRD diagnosis**
 - **Variable sensitivity (0-71%) and specificity (85-100%) vs symptoms**
(Kahrilas Gastro 1996; Martinez APT 2003)
- **Bravo capsule may provide a more accurate, better tolerated alternative**
(Pandolfino AJG 2003)

Quality

- **Level II-1**

Classification

- **Grade B**



Initial therapy – Statement 21

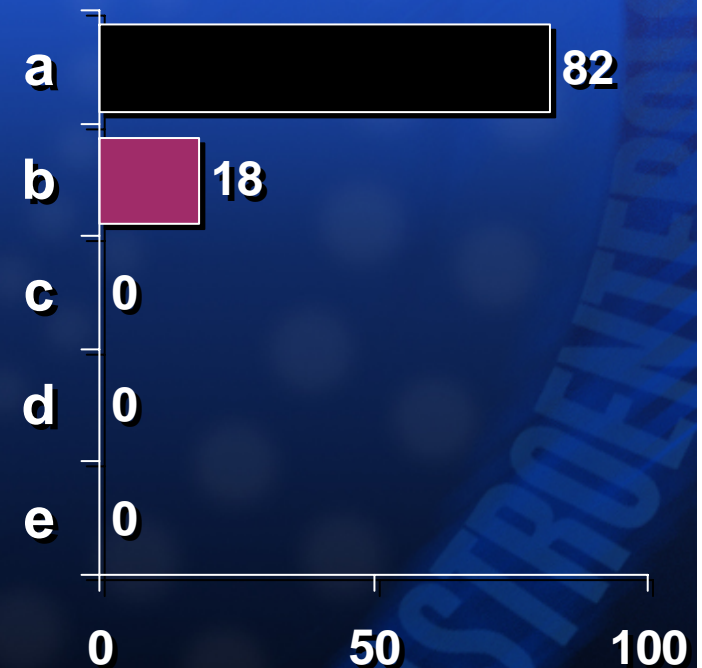
- **“Over the counter” medications, including alginates, antacids and low-dose H₂-RAs, are safe and effective for symptom management in individuals with mild GERD symptoms.**
- **OTC R_x is safe and effective for many with mild and infrequent GERD symptoms** (*Dent Gut 1999; Poynard APT 1998*)
- **OTC R_x has limited efficacy for more severe GERD (erosive esophagitis, complications, severe symptoms or severely-reduced HRQL)** (*Veldhuyzen van Zanten CMAJ 2000; Dent Gut 1999; Kitchin Arch Intern Med 1991*)

Quality

- Level I

Classification

- Grade A



Initial therapy – Statement 22

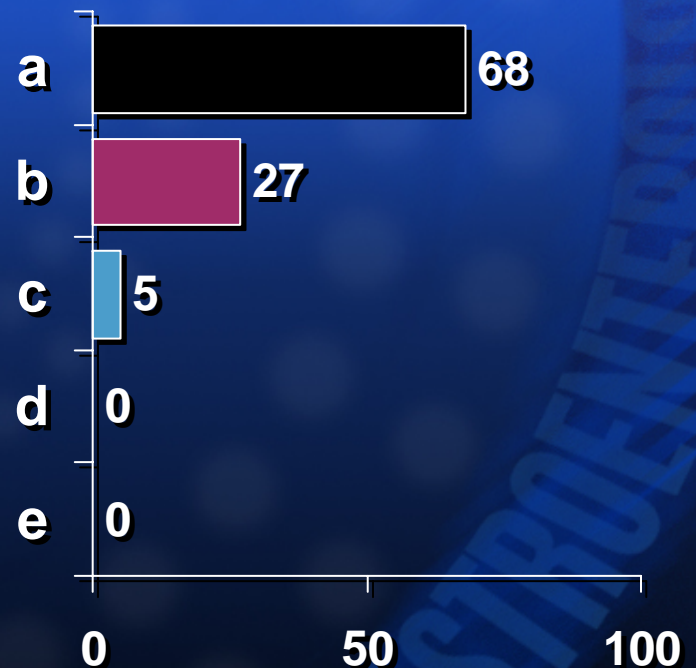
- ***Lifestyle modifications, with or without “over-the-counter” antacids or H₂-RAs, are not effective for the management of frequent or severe GERD symptoms.***
- **All patients should be educated about factors that may worsen their GERD symptoms,**
- **BUT – lifestyle modifications, alone, are inadequate for most patients.**
- **N.B. – Few data on the efficacy of lifestyle modifications for mild GERD.**

Quality

- Level II-2

Classification

- Grade A



Veldhuyzen van Zanten CMAJ 2000; Dent Gut 1999 (Suppl 2)

Initial therapy – Statement 23

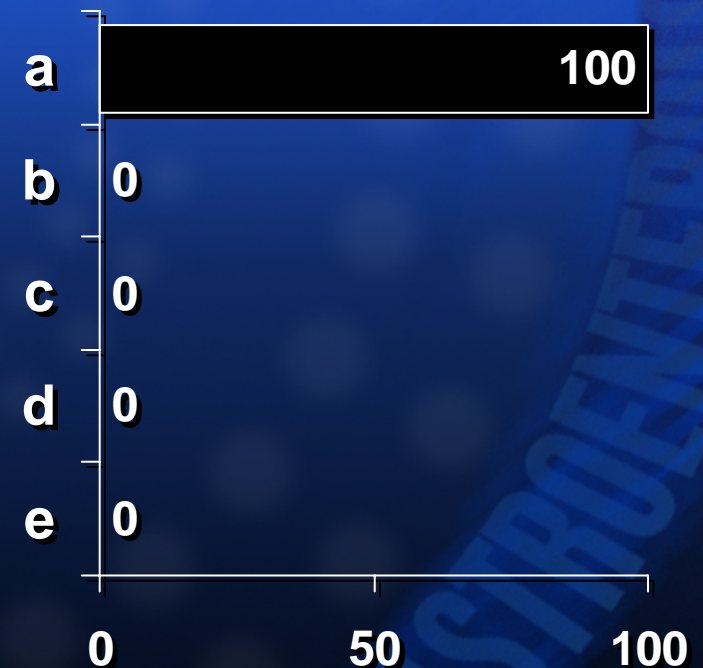
- ***PPIs are superior to H₂-RAs for the reduction of heartburn and healing of esophagitis.***
- **Meta-analysis – EE**
 - 43 trials in 7,635 patients
 - Healing: 83.6% (PPI) vs 51.9% (H₂RA) vs 28.2% (placebo)
(Chiba et al. *Gastroenterol* 1997;112:1798-810)
- **Meta-analysis – ENRD /HBDUD**
 - 13 trials in 5,953 patients
 - PPIs twice as effective as H₂-RAs for HBDUD
 - PPIs 20% more effective than H₂-RAs for ENRD (van Pinxteren B et al. *J Gen Intern Med* 2003;18:755-63)

Quality

- Level I

Classification

- Grade A



Initial therapy – Statement 24

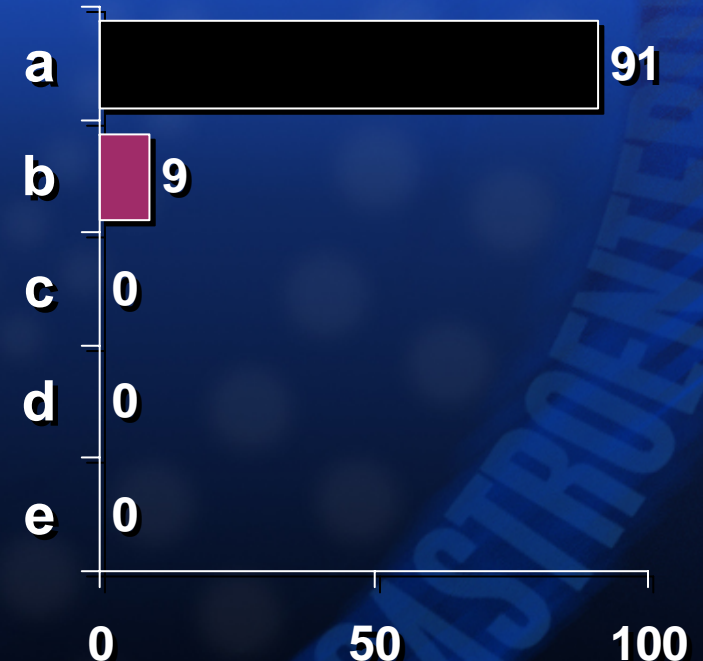
- *The effectiveness of PPIs and H₂-RAs for the healing of esophagitis is proportional to their ability to reduce intragastric acidity.*
- Prolonged gastric acid suppression is associated with:
 - Faster symptom relief, and
 - Higher healing rates.
- Proton pump inhibitors (PPIs)
 - Maintain intragastric pH above 4.0 more effectively than H₂-RAs
 - Produce greater healing and symptom relief than do H₂-RAs

Quality

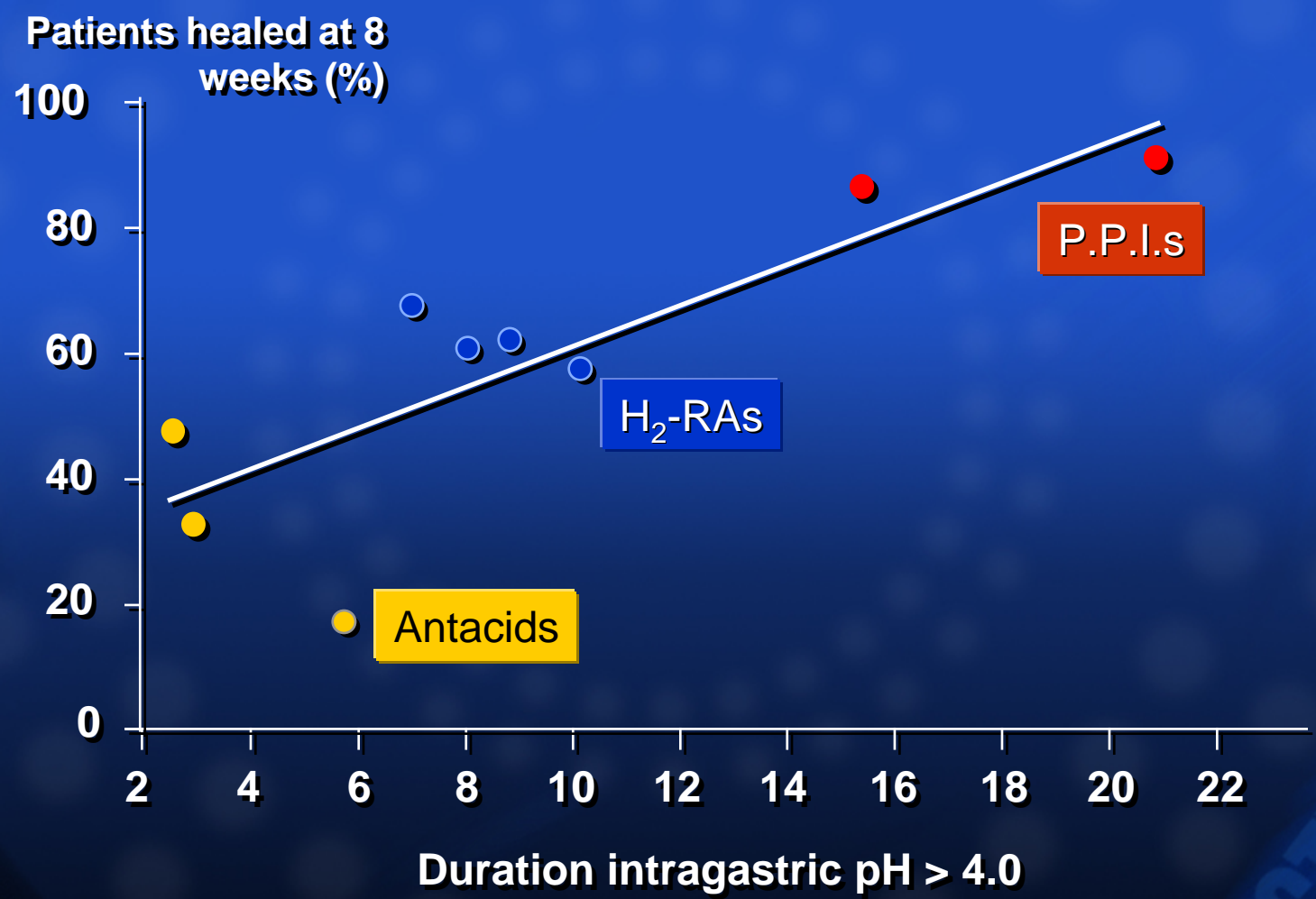
- Level I

Classification

- Grade A



Acid Inhibition & Esophagitis Healing



Initial therapy – Statement 25

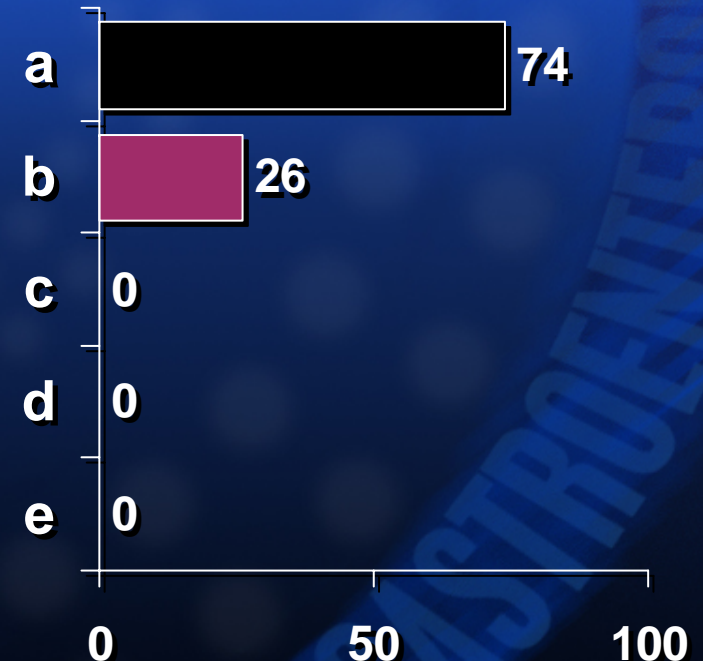
- ***Initial therapy for GERD symptoms should be a once-daily PPI unless symptoms are mild and infrequent (<3 times per week).***
- **PPIs have been evaluated primarily for GERD symptoms that occur ≥ 3 times per week**
- **PPIs are **not** required by all patients**

Quality

- Level I

Classification

- Grade A



See consensus paper for list of references

Initial therapy – Statement 26

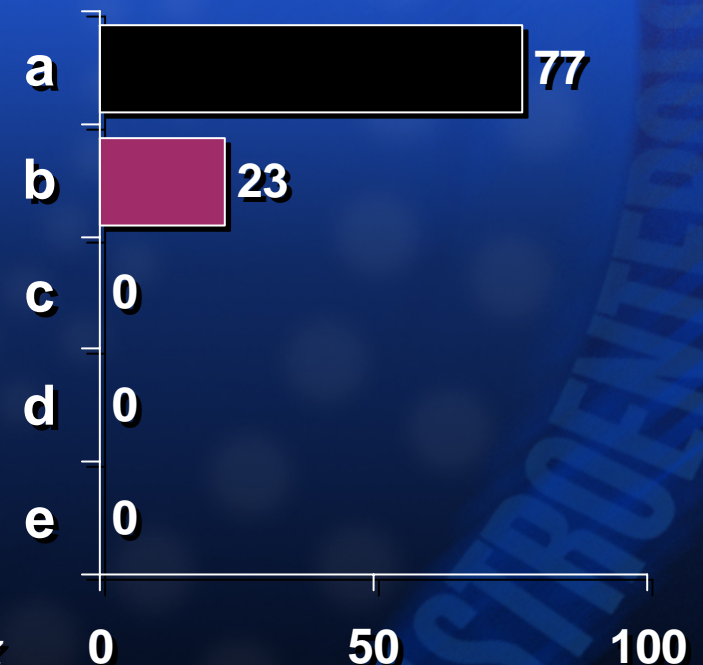
- ***The symptomatic response to an initial course of antisecretory therapy should be assessed at 4-8 weeks.***
- **For od vs bid PPI therapy, the response at 1 week was highly predictive (PPV 96.1% & 96.3%) of a good outcome at 4 weeks, but NPV were low (28.3% & 32.7%)**
 - ~ 15% of patients not responding at 1 week will respond at 4 weeks
Armstrong CJG 2004;18(Suppl A)
- **Further improvement occurs as therapy extends from 4 to 8 weeks in erosive esophagitis** (*Chiba Gastro 1997; Caro Clin Ther 2001; Klok APT 2003; Labenz CJG 2004;18(Suppl A); van Rensburg APT 1996*)

Quality

- Level II-1

Classification

- Grade B



Initial therapy – Statements 27-29

Statement 27

- *Twice-daily PPI therapy is not generally required as initial therapy for typical GERD symptoms.*

Statement 28

- *Twice-daily, standard-dose PPI therapy may be used for patients who have severe symptoms despite standard once-daily PPI therapy. (Level II-3, B; **Vote: a 91%, b 9%**)*

Statement 29

- *Twice-daily, standard-dose PPI therapy may be used for patients who have severe esophagitis (LA Grade C/D or stricture). (Level I, B; **Vote: a 96%, b 4%**)*

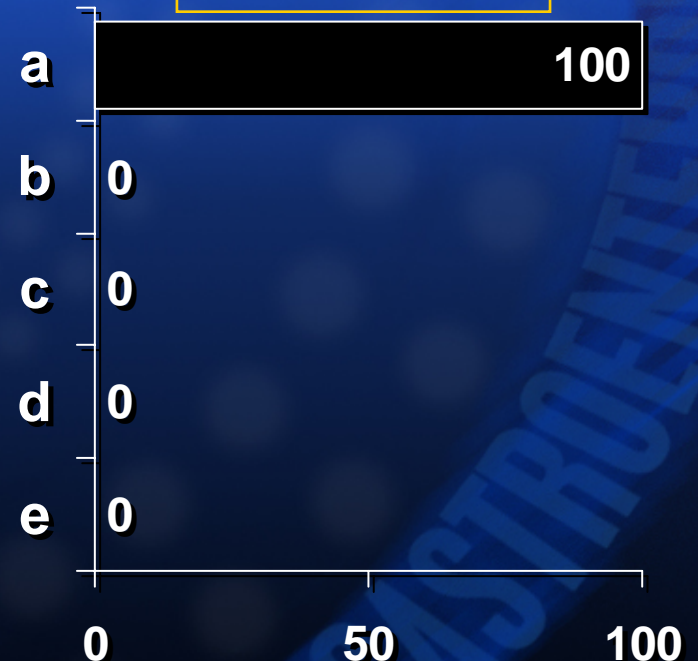
Quality

- Level I

Classification

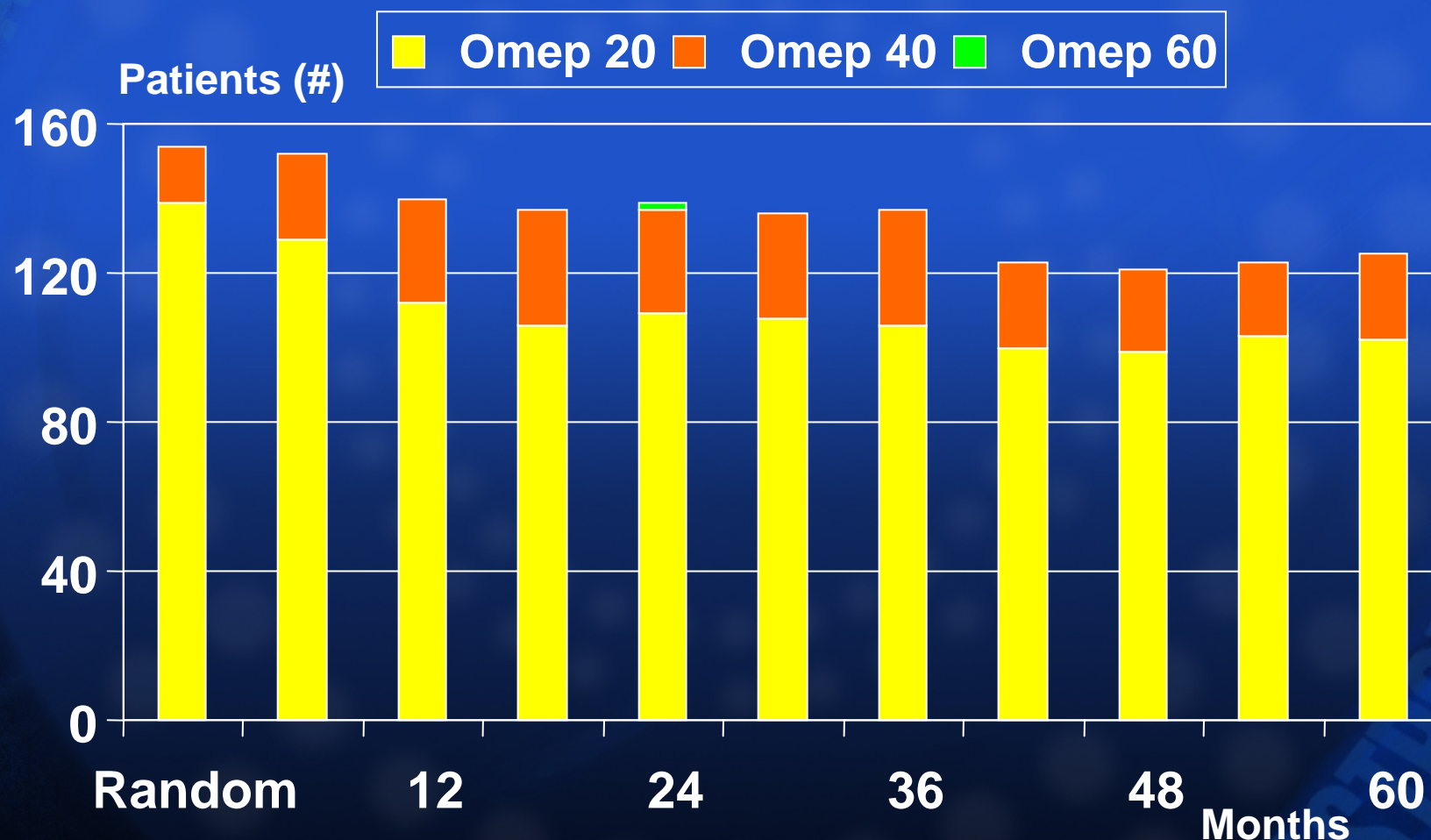
- Grade A

Statement 27



GERD – Medical vs Surgical Therapy

Omeprazole Dosing



Initial therapy – Statement 30

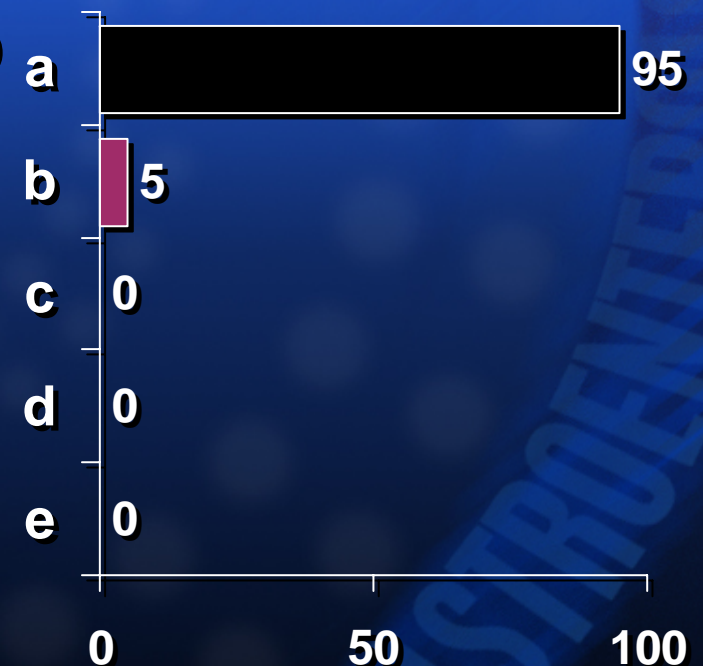
- ***Prokinetic or promotility agents are not recommended, either alone or in conjunction with antisecretory agents, for the routine initial treatment of GERD.***
- **A systematic review: cisapride is effective for mild-to-moderate GERD in adults but not for GERD in children** (*Armstrong D in: Guidelines for Management of Symptomatic GORD, Science Press 1998; Augood C Cochrane Library 2004*)
- **As empiric therapy for GERD, cisapride was not superior to placebo, and for ENRD, PPIs were superior to cisapride** (*van Pinxteren B Cochrane Library 2004*)

Quality

- Level II-1

Classification

- Grade C



Therapy Definitions – Statements 31-32

Statement 31

- **‘Continuous’** medical maintenance therapy is defined as the daily intake of a medication for an indefinite period to prevent or minimize recurrent reflux-related symptoms or injury to the esophagus.

Statement 32

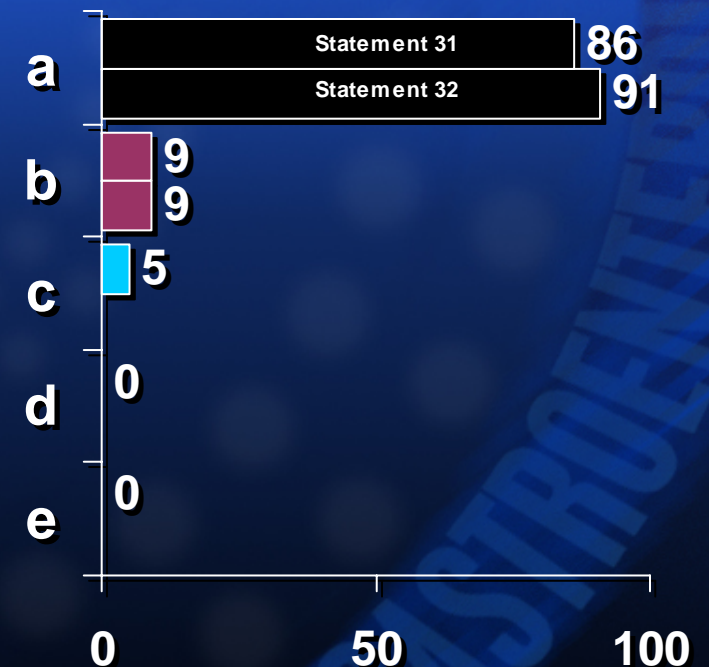
- **‘Intermittent’** medical maintenance therapy is defined as the daily intake of a medication for a predetermined, finite period (usually 2 to 8 weeks) to produce resolution of reflux-related symptoms or healing of esophageal lesions following relapse of the individual’s condition.

Quality

- N/A

Classification

- N/A



Therapy Definitions – Statement 33

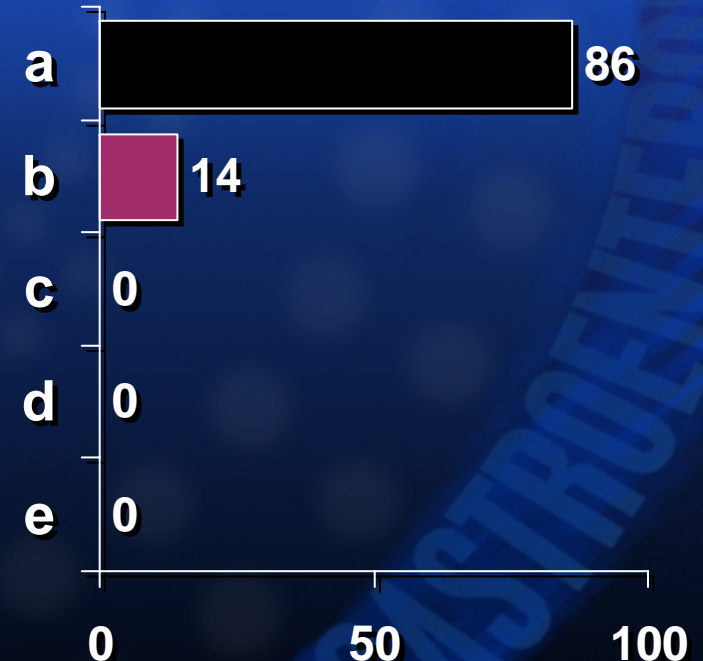
- ***'On-demand'*** medical therapy is defined as the daily intake of a medication for a period sufficient to achieve resolution of the individual's reflux-related symptoms; **following** symptom resolution, the medication is discontinued until the individual's symptoms recur, at which point, medication is again taken daily until the symptoms resolve.
- There are no standardized definitions but Statements 31-33 ('Continuous', 'Intermittent' & 'On Demand') are consistent with clinical trial definitions.
- One may consider:
 - 'On demand' therapy is 'patient-driven'
 - 'Intermittent' therapy is 'physician-driven'

Quality

- N/A

Classification

- N/A



Long-term therapy – Statement 34

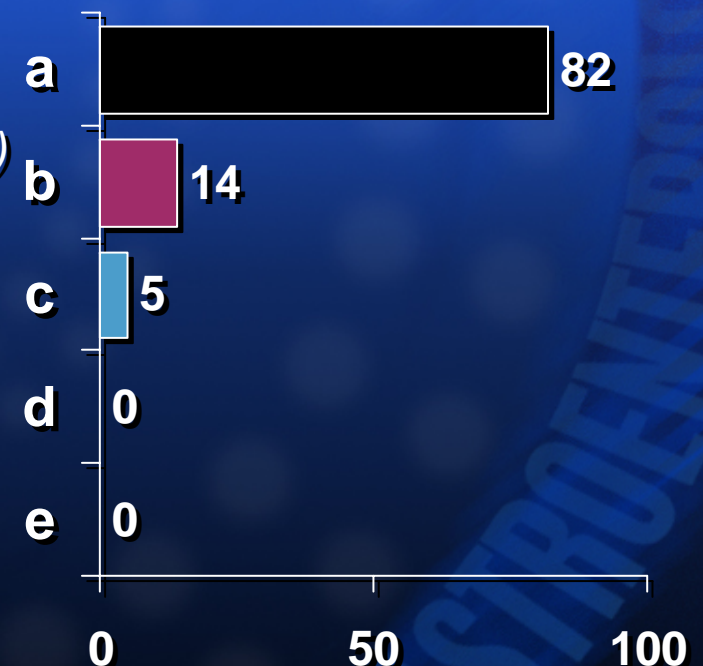
- **The prime aim of long-term GERD therapy is symptom abolition or control sufficient to normalize the individual's health-related quality of life.**
- **Long-term therapy is generally recommended for erosive esophagitis** (*Dent APT 2003; Pohle Arch Surg 2000; Freston APT 2004; Richter AJG 1997*)
- **Additional aim: to prevent complications (e.g. stricture, ulcer, hemorrhage or Barrett's epithelium)** (*Barbezat APT 1999; Stal CJG 1998; Smith Gastro 1994; Marks Gastro 1994; Swarbrick Eur J Gastro Hepatol 1996*)
- **BUT: data are limited for regression of Barrett's epithelium.**

Quality

- Level III

Classification

- Grade A



Initial therapy – Statements 35-37

Statement 35

- *An individual, whose reflux symptoms have responded well to standard-dose PPI therapy, may discontinue medication to confirm the need for ongoing therapy.*

Statement 36

- *Long-term maintenance therapy should be given at the lowest dose and frequency that is sufficient to achieve optimal control of the patient's symptoms. (Level III, B; **Vote: a 71%, b 10%, c 10%, d 5%, e 5%**)*

Statement 37

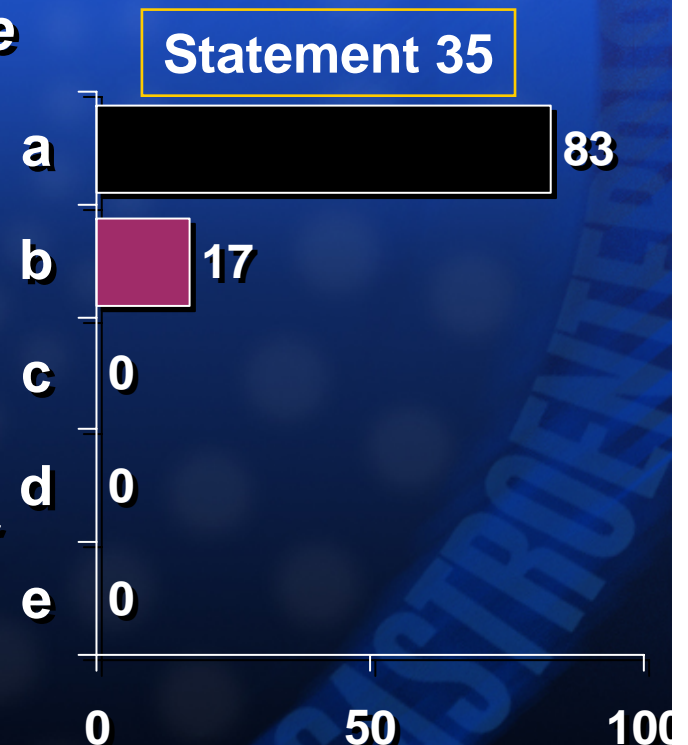
- *On-demand acid suppression therapy is a reasonable long-term medical strategy for selected patients with GERD. (Level I, B; **Vote a 55%, b 45%**)*

Quality

- Level II-3

Classification

- Grade C



See consensus paper for list of references

Long-term therapy – Statement 38

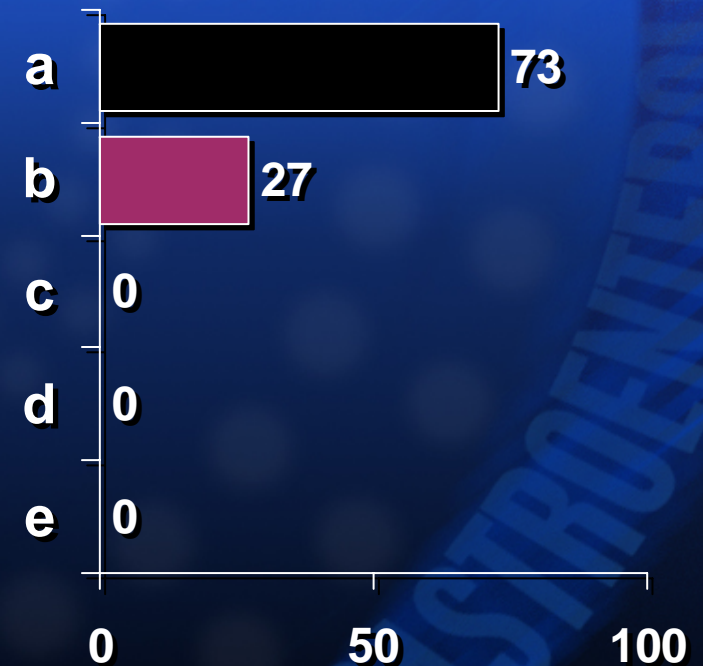
- *Long-term PPI therapy has not been associated with any clinically significant adverse events.*
- Experience with long-term PPI use extends over millions of patient-years of therapy.
- Data are available for all currently-available PPIs.
- Adverse events or significant drug interactions are rare.
- Concerns over hypergastrinemia, ECL- hyperplasia and carcinoids have not been substantiated

Quality

- Level II-2

Classification

- Grade A



See consensus paper for list of references

Long-term therapy – Statement 39

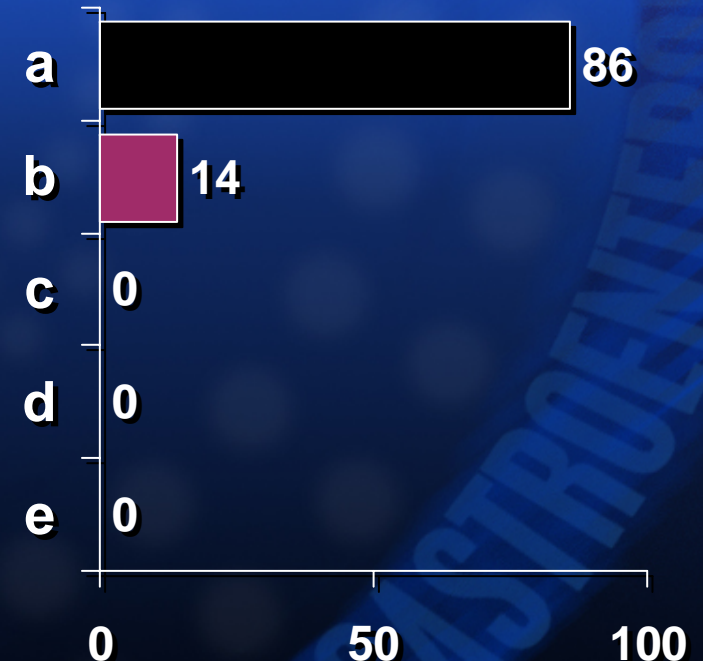
- *Prokinetic or promotility agents are not recommended, either alone or in conjunction with antisecretory agents, for the routine long-term treatment of GERD.*
- **Cisapride is effective but no longer generally available.**
- **Insufficient data to support use of other prokinetics for monotherapy**
- **Addition of a prokinetic produces no significant added benefit compared with PPI monotherapy.**

Quality

- Level I

Classification

- Grade A



Long-term therapy – Statement 40

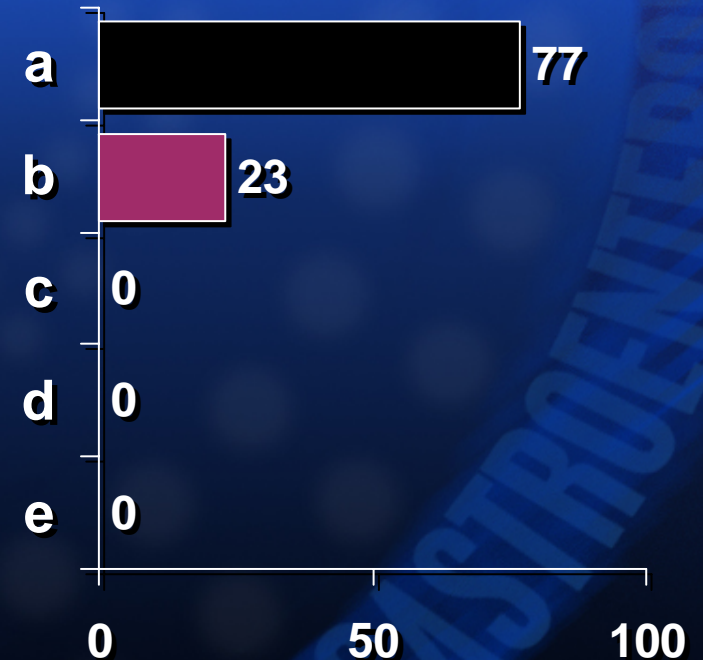
- *Supplementary night-time H₂-RA therapy is not generally recommended for individuals who have responded incompletely or have failed to respond to standard-dose or double-dose PPI therapy of adequate duration.*
- “NAB” – night-time periods with gastric pH <4.0 for > 1 hour on bid PPI – but, no data to show that this is clinically significant or that suppression of nocturnal acid breakthrough is beneficial.

Quality

- Level I

Classification

- Grade A



Long-term therapy – Statement 41

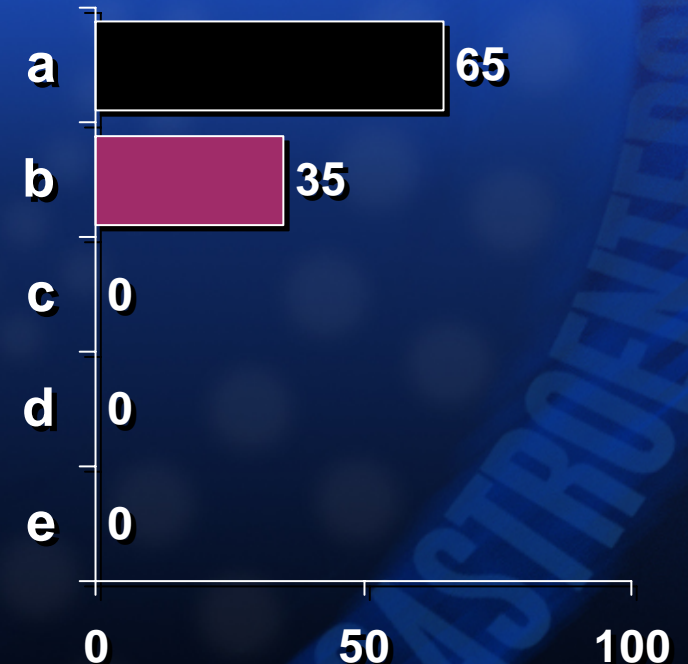
- ***Surgical antireflux therapy is an alternative to medical therapy for the long-term management of selected patients with GERD.***
- **Surgery is effective, but:**
 - Little long-term advantage over medical therapy
 - May not eliminate the need for medication
- **Surgery was superior to PPI therapy at 3 and 5 years, only if PPI dose was not increased**

Quality

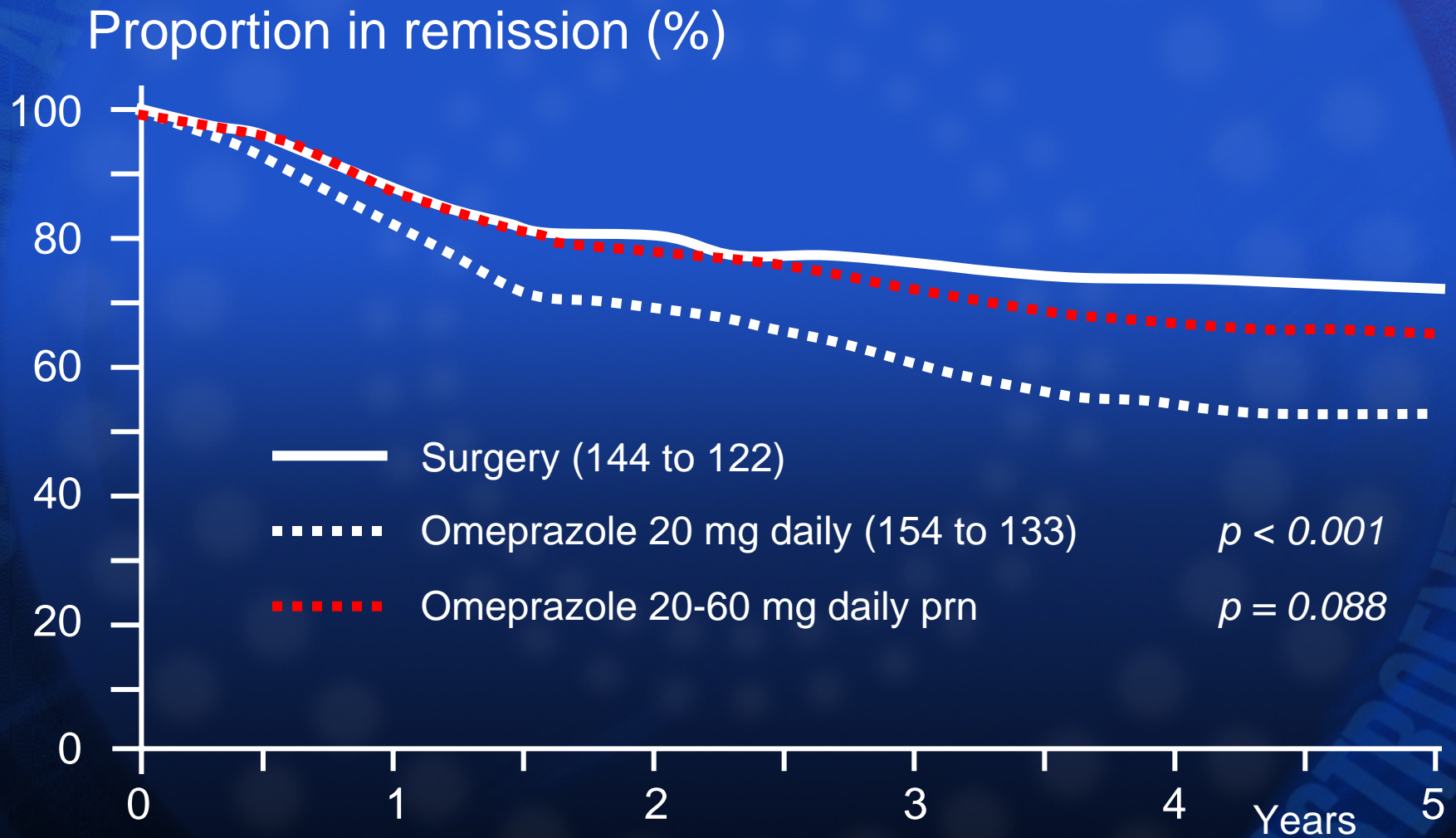
- Level I

Classification

- Grade A



GERD – Medical vs Surgical Therapy



Lundell L et al. J Am Coll Surg 2001;192:172–181.

Long-term therapy – Statement 42

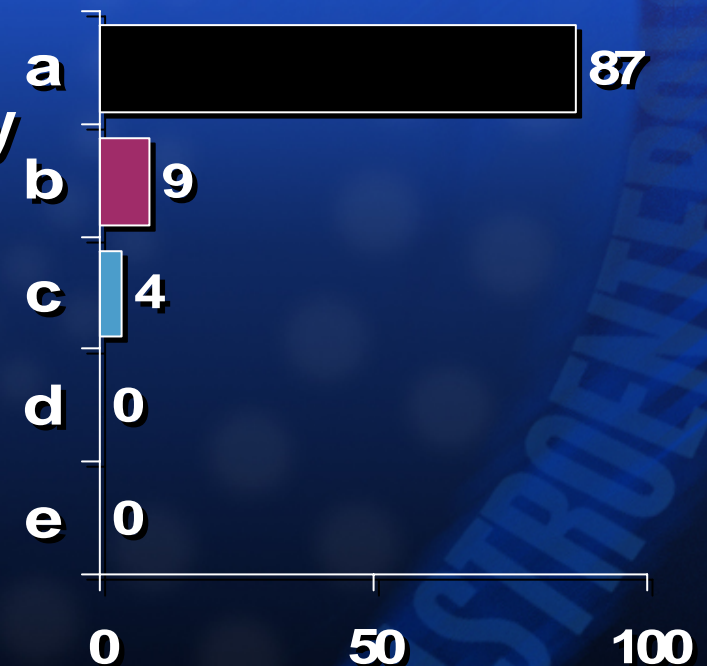
- *The role of endoscopic antireflux procedures for the management of GERD in clinical practice has not been adequately defined.*
- **Fair evidence that these procedures should not be used**
- Improvements in acid exposure are limited, and published trials have only entered patients with mild to moderate GERD
- Thus, the outcomes of endoscopic therapy cannot be compared directly to those of surgery or standard medical therapy

Quality

- Level II-3

Classification

- Grade D



See consensus references 212-222, 153

***Helicobacter pylori* – Statement 43-46**

- ***Statement 43*: Testing for *H. pylori* infection is not necessary before starting treatment for typical symptoms of GERD. (Level I, B; **Vote: a 82%, b 9%, c 9%**)***
- ***Statement 44*: The presence of erosive esophagitis at endoscopy does not preclude testing for *H. pylori*. (Level II-2, A; **Vote: a 64%, b 32%, c 5%**)***
- ***Statement 45: It is not necessary to test routinely for *H. pylori* in a patient taking long-term PPI therapy for GERD symptoms. (Level II-3, C; **Vote: a 74%, b 26%**)***
- ***Statement 46: Eradication of *H. pylori* has no clinically relevant, adverse effect on the long-term outcome of GERD. (Level I, A; **Vote a 87%, b 13%**)***

See consensus references 223-242

Barrett's Epithelium – Statement 47

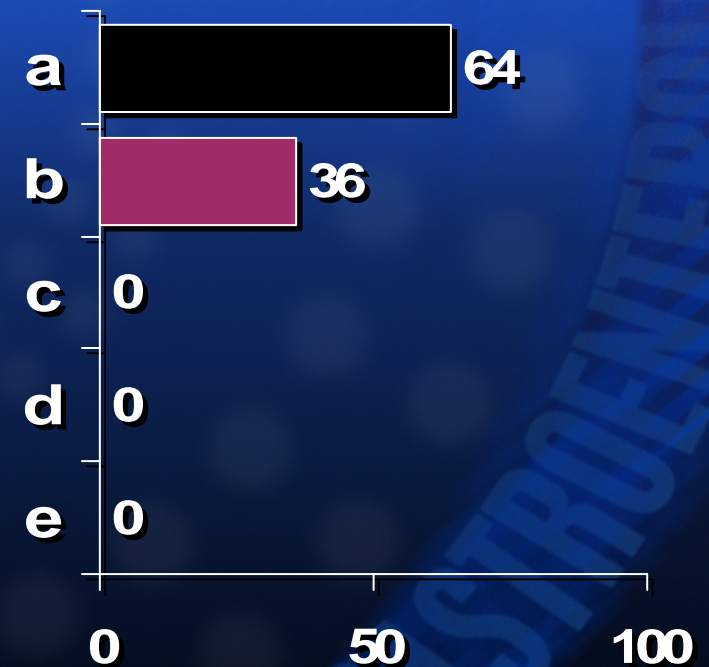
- ***The presence and extent of reflux-related columnar metaplasia in the distal esophagus should be recorded in a standardized manner as “endoscopic suspicion of Barrett’s epithelium”; a formal diagnosis of “Barrett’s epithelium” requires histological confirmation.***
- **ACG – “A change in the esophageal epithelium of any length that can be recognized at endoscopy and is confirmed to have intestinal metaplasia by biopsy of the tubular esophagus and excludes intestinal metaplasia of the cardia”**

Quality

- Level III

Classification

- Grade B



Barrett's Epithelium – Statement 48

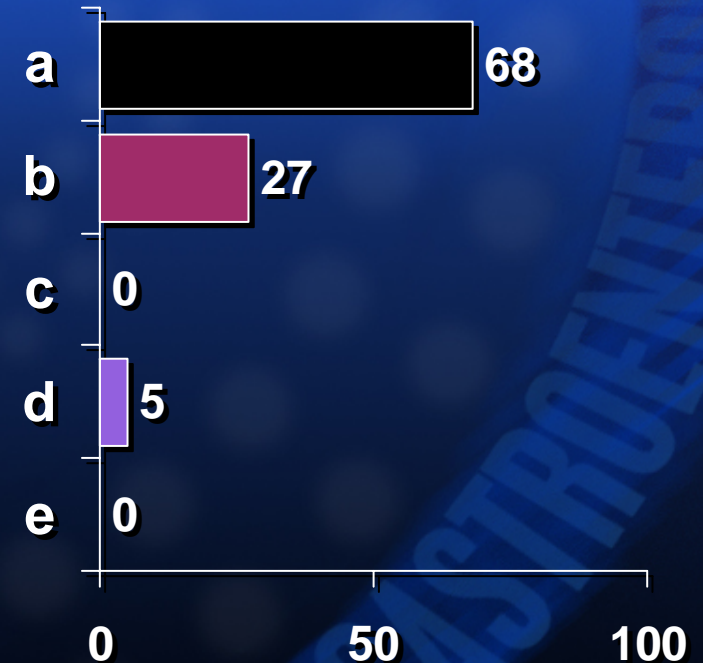
- Barrett's epithelium is defined as the presence of abnormal epithelium ("endoscopic suspicion of Barrett's epithelium"), of any extent, extending proximally beyond the limit of the gastroesophageal junction, that demonstrates specialized intestinal metaplasia ("esophageal columnar epithelium; intestinal metaplasia positive") on histological examination of the endoscopic biopsies.***

Quality

- N/A

Classification

- N/A



Barrett's Epithelium – Statement 49

- **Barrett's epithelium is associated with the development of esophageal adenocarcinoma.**
- **Progression from specialized intestinal metaplasia, via low- and high-grade dysplasia, to malignancy**
- **Publication bias in many studies**
- **Estimated risk of adenocarcinoma:**
 - **Barrett's** ~0.4% p.a.
 - **No Barrett's** <0.07% p.a.
- **Also heartburn associated with esophageal adenocarcinoma**

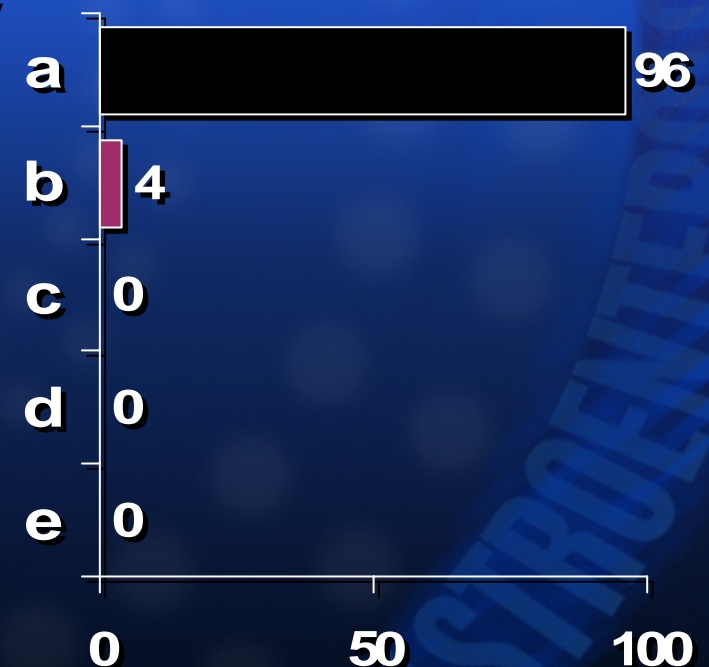
Shaheen NJ et al. *Gastroenterology* 2000; 119: 333-338
Lagergren J et al. *NEJM* 1999; 340: 825-831

Quality

- Level II-3

Classification

- Grade B



Esophageal Cancer – Statement 50

- *The risk of esophageal adenocarcinoma increases with the severity, frequency and duration of GERD symptoms.*
- **Odds ratios for adenocarcinoma vs. asymptomatic individual:**
 - **Recurrent symptoms 7.7**
 - **Prolonged (> 20y), severe 43.5**
 - *(Lagergren J et al. N Engl J Med 1999;340:825)*
- **Other risk factors include:**
 - **White male**
 - **Size of hiatus hernia**
 - **Extent of Barrett's epithelium**
 - **Obesity, Diet, Smoking**

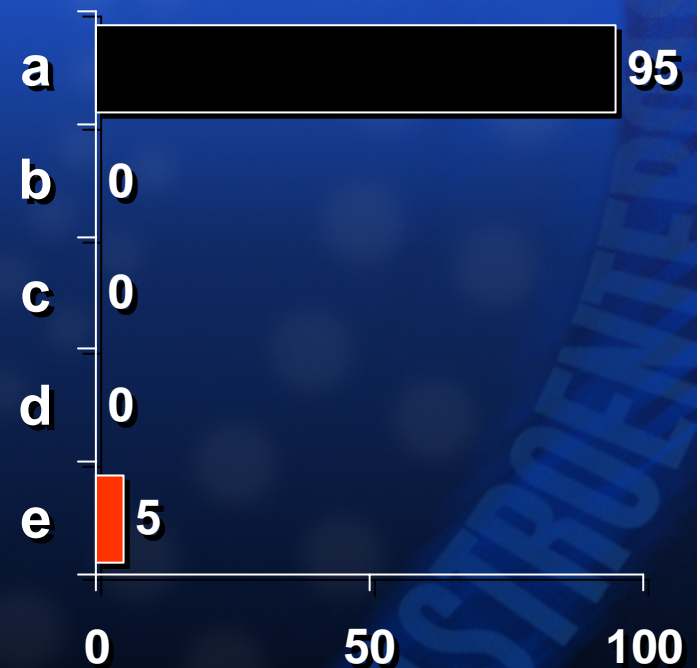
(Fallone C et al in: Evidence-based Gastroenterology BMA House 2004)

Quality

- **Level II-2**

Classification

- **Grade A**



Barrett's Epithelium – Statement 51

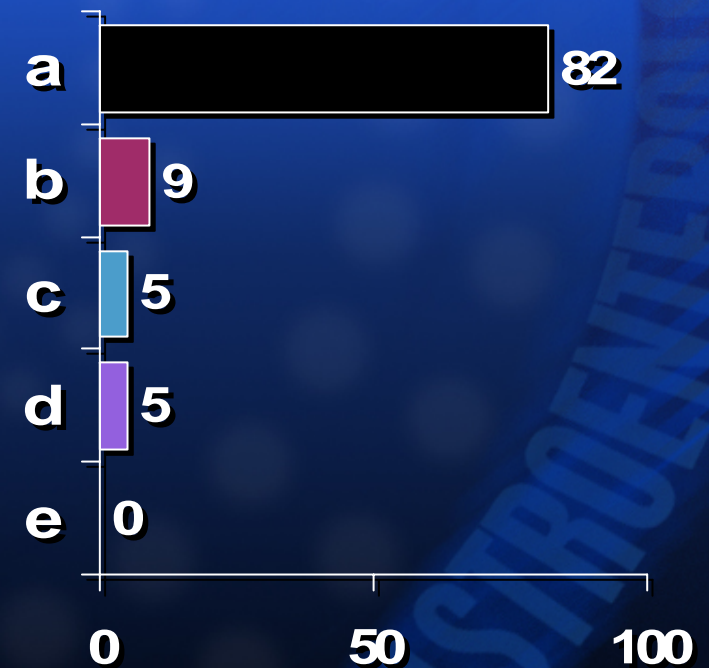
- *Neither medical nor surgical therapy has been proven to prevent the development or progression of Barrett's epithelium or the subsequent development of esophageal adenocarcinoma.*
- **Fair evidence that these strategies should not be used for prevention**
- **Four RCTs**
 - Acid suppression: symptom control but no disappearance of Barrett's epithelium despite regression.
 - Antireflux surgery: in 161 patients, at 7-21 years post-op:
 - Dysplasia in 10.5%
 - Adenocarcinoma in 2.5%

Quality

- Level I

Classification

- Grade D



(Spechler JAMA 2001; Peters Gut 1999; Ortiz Br J Surg 1996; Parrilla Ann Surg 2003)

Barrett's Screening – Statements 52-53

- *Endoscopy to detect Barrett's esophagus with dysplasia may be considered in adults with GERD symptoms for more than 10 years.*
- Statement 52: *Endoscopic screening for Barrett's esophagus in patients with longstanding GERD has not been shown to reduce mortality from esophageal adenocarcinoma.*
(Level III, C; **Vote: a 39%, b 44%, c 9%, d 4%, e 4%**)

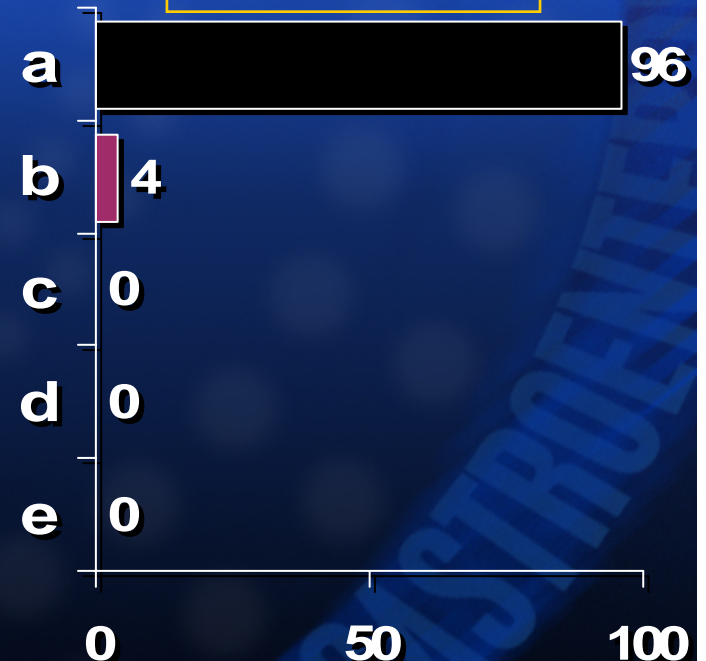
Quality

- Level III

Classification

- Grade C

Statement 53



Barrett's Surveillance – Statement 54

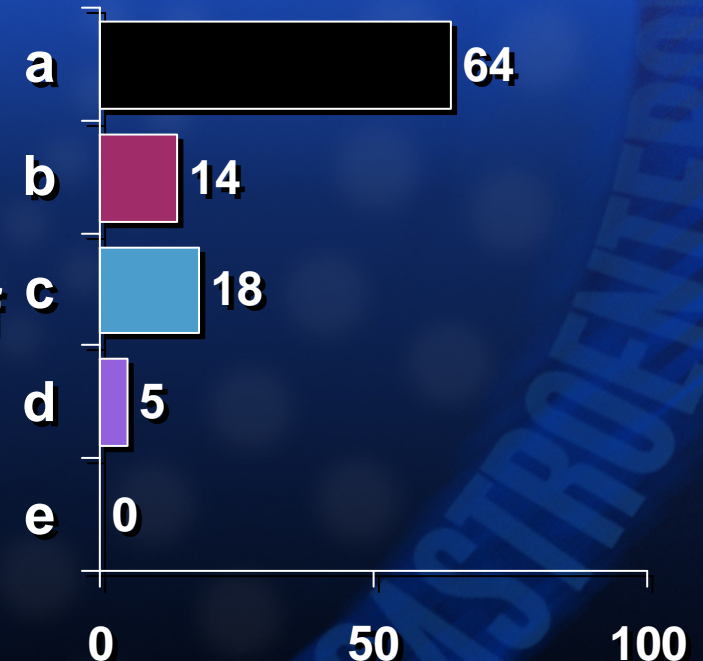
- ***Endoscopic surveillance in patients with Barrett's epithelium should include a standard biopsy protocol and should be performed while the patient continues to take therapy sufficient to optimize symptom relief.***
- **Based on risk of adenocarcinoma in the presence of Barrett's epithelium**
- **Effective therapy minimizes effect of inflammation and repair in producing histological appearances suggestive of dysplasia**

Quality

- Level III

Classification

- Grade C



Barrett's Surveillance – Statement 55

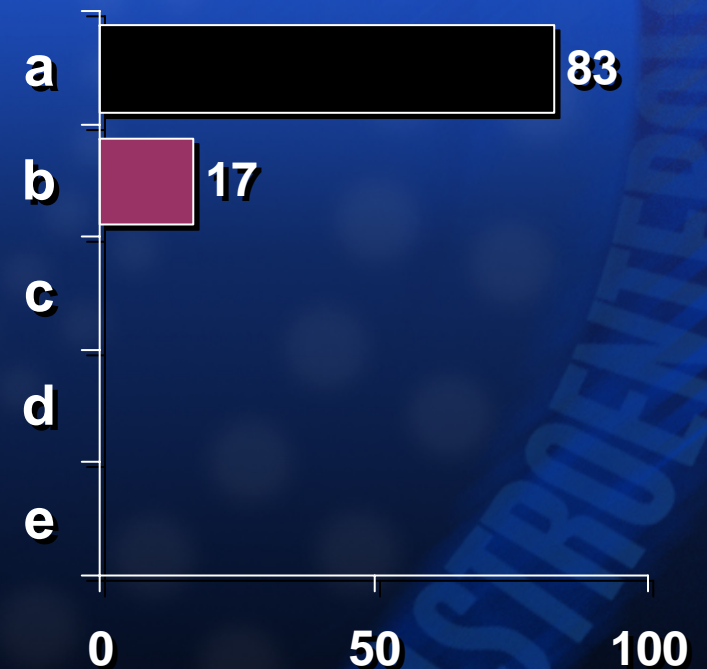
- ***Patients with Barrett's epithelium and dysplasia should generally undergo surveillance.***
- **Dysplasia is associated with an increased risk of malignancy compared with Barrett's epithelium alone**
 - Risk of progression is greater for high-grade dysplasia (HGD) than for low-grade dysplasia (LGD)
- **There is significant interobserver variability in dysplasia grading**
 - Agreement on classification of LGD is less than 50%

Quality

- Level III

Classification

- Grade C



Barrett's Surveillance – Statement 56

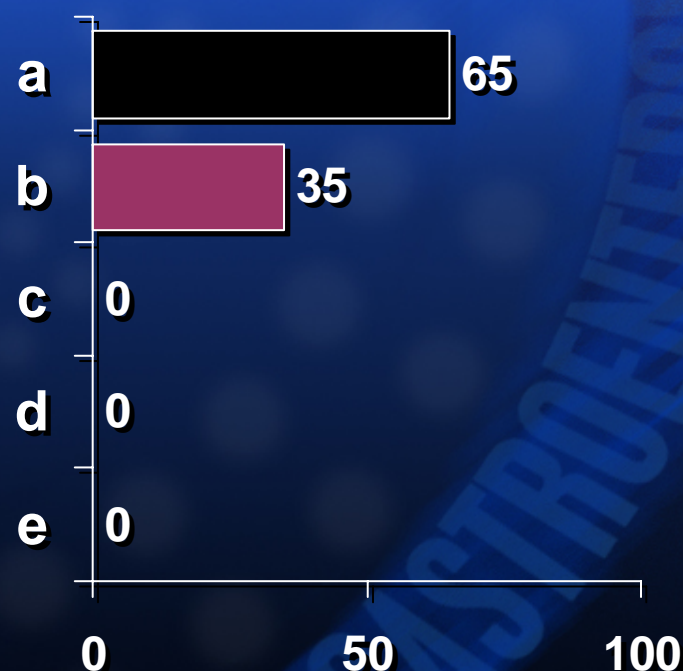
- *In the presence of low-grade dysplasia, surveillance endoscopy should be repeated within 12 months with a concentrated biopsy protocol and repeated annually until there is no dysplasia.*
- Risk of progression from low- to high-grade dysplasia or cancer – 10% to 28% over 5 years
- Risk of progression from high-grade dysplasia to cancer – 16% to 59% over 5-7 years

Quality

- Level II-3

Classification

- Grade B



Barrett's Screening – Statement 57

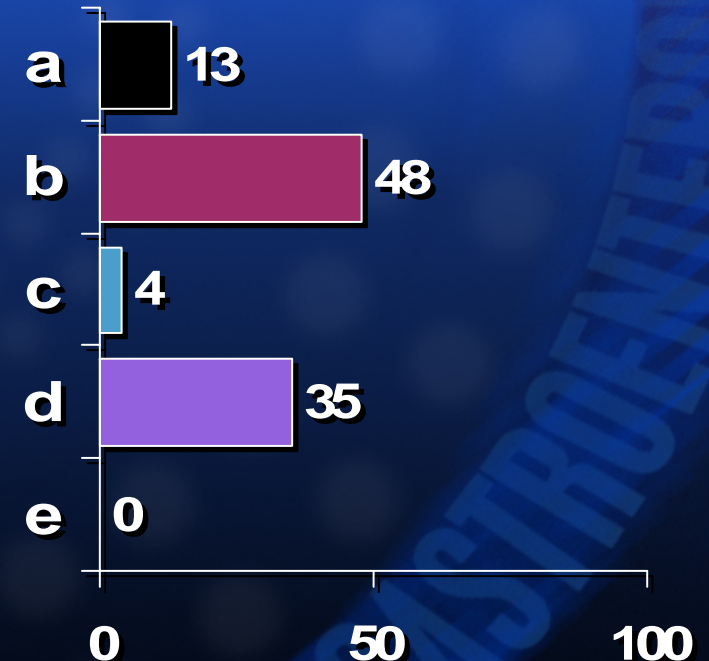
- *Patients with Barrett's epithelium in the absence of dysplasia should generally undergo surveillance.*
- Surveillance has major implications for health care resource utilization
- **Pro** – Consistent with standard of care endorsed by American College of Gastroenterology
- **Con** – Significant costs with limited documented benefit
- However, surveillance is **not** endorsed for patients who are not eligible for surgical / endoscopic therapy

Quality

- Level III

Classification

- Grade C



See consensus references 247, 277-283

Barrett's Screening – Statement 58

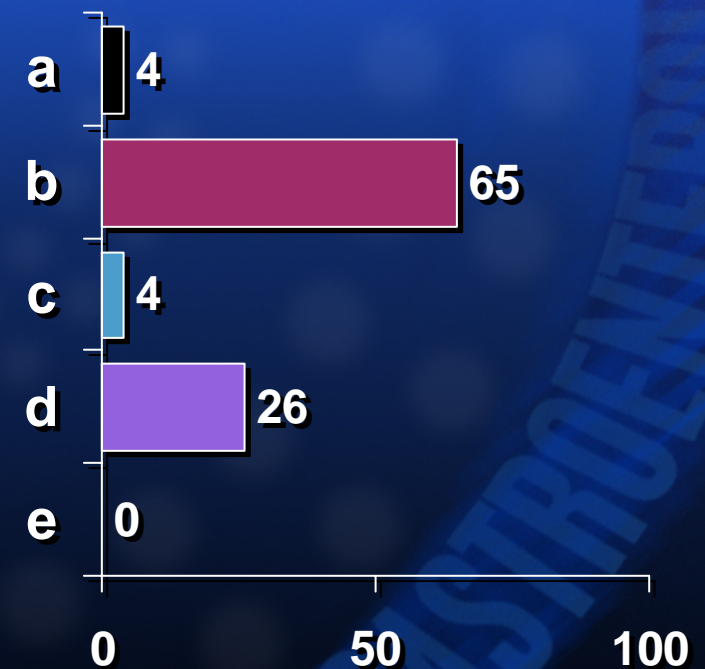
- *For patients with Barrett's epithelium, in the absence of dysplasia, enrolled in a surveillance programme, endoscopy should be repeated every 2 to 5 years.*
- **Recommendations on surveillance intervals are based largely on cost-effectiveness modelling studies**
 - Assuming cancer rate of 0.4% p.a., **only** 5-yearly surveillance was cost effective in the United States (*Provenzale AJG 1999*)
 - Relevant studies based on Canadian data are not available

Quality

- Level III

Classification

- Grade C



Dysplasia Management – Statement 59

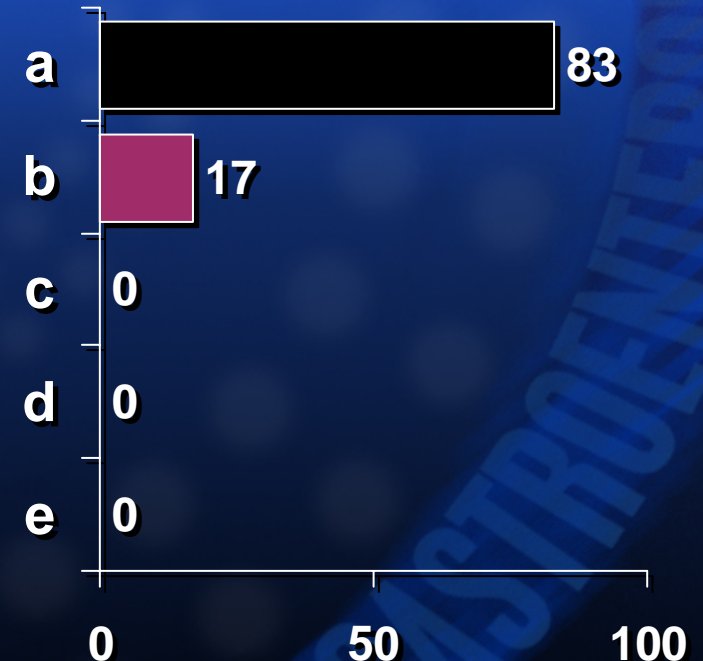
- *When high-grade dysplasia is detected for the first time, endoscopy should be repeated within three months with a concentrated biopsy protocol and expert pathologist review of all biopsies.*
- **Double-dose PPI therapy recommended prior to re-biopsy to minimize inflammatory changes**
- **There may be localized areas of malignancy**

Quality

- Level II-3

Classification

- Grade B



Dysplasia Management – Statement 60

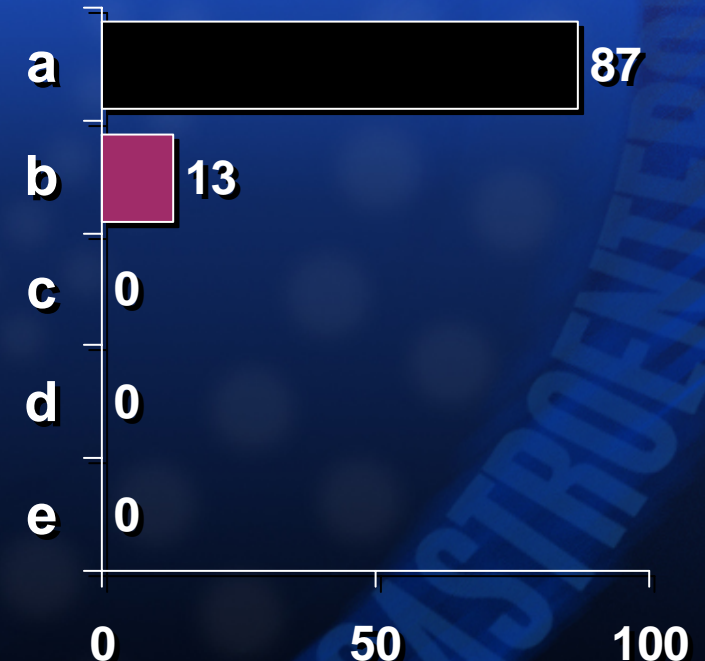
- *In the presence of confirmed high-grade dysplasia or malignancy, expert consultations should be obtained to ascertain the optimal endoscopic or surgical management strategy.*
- Multifocal high grade dysplasia can trigger referral for therapy without repeat, confirmatory endoscopy
- Limited availability of endoscopic mucosal resection and ablation
- Surgery, in experienced centres, is recommended generally
- Areas of expertise: gastroenterology, oncology, GI pathology & thoracic surgery

Quality

- Level III

Classification

- Grade B



Dysplasia Management – Statement 61

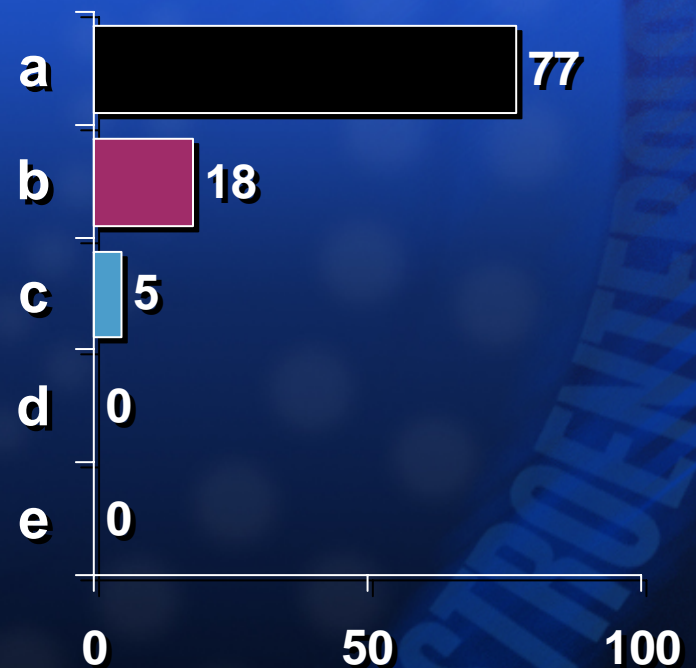
- ***Ablation therapy should be considered for individuals with high-grade dysplasia or esophageal adenocarcinoma who are unfit for or unwilling to undergo surgery.***
- **Suitable for patients ineligible for surgery due to major comorbidity**
- **Ablation therapies include:**
 - Photodynamic therapy (PDT)
 - Endoscopic mucosal resection (EMR)
 - Thermal destruction
 - Nd:YAG laser ablation
 - Injection therapy
 - Argon plasma coagulation (APC)
 - Bipolar electrocoagulation

Quality

- Level I

Classification

- Grade A



See consensus references 284-290, 296, 297

Economics of GERD Therapy

- **GERD is a costly illness,**
 - **US \$9.3 billion p.a. in the USA**
 - **US \$5.89 billion p.a. – drugs**
 - **Can \$670 million p.a. – PPI and H₂RA In Canada**
- **PPI is a cost-effective alternative to H₂RA therapy for the long-term medical management of GERD.**
- **The higher acquisition costs for PPIs are partially offset by gains in health status.**
- **Treatment with PPIs resolves symptoms more rapidly and prevents symptomatic recurrence more effectively.**
- **Decision analysis shows that initial PPI therapy followed by on-demand therapy is a cost-effective approach.**

See consensus references 200, 270, 298-308

Future Requirements

Prospective studies are needed to investigate

- 1.** Clinically-relevant risk factors for the development of GERD and its complications,
- 2.** GERD progression, on and off therapy,
- 3.** Optimal management strategies for typical GERD symptoms in primary care patients, and
- 4.** Optimal management strategies for:
 - i.** Atypical GERD symptoms,
 - ii.** Barrett's epithelium and
 - iii.** Esophageal adenocarcinoma

Participants

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Represented Societies:

Canadian Association of Gastroenterology (CAG),
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Pediatrics Committee,
Canadian Association of General Surgeons (CAGS),
Canadian Association of Primary Care
Gastroenterology (CanGut),
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