Reflux Monitoring : Current recommendations and a look to the future

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GFNG
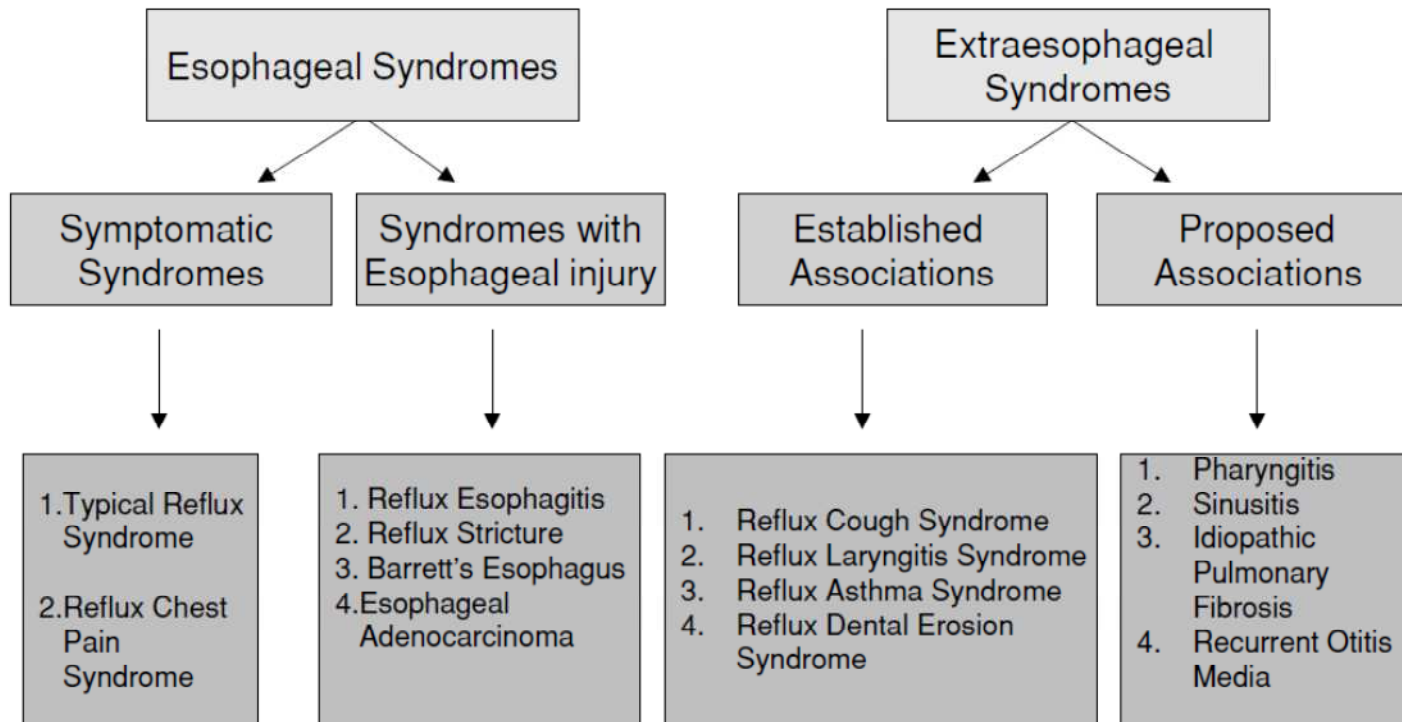Groupe Français
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Gastro-esophageal reflux disease

GERD is a condition which develops when the reflux of gastric content causes troublesome symptoms or complications

Esophageal Syndromes

- **Symptomatic Syndromes**
  1. Typical Reflux Syndrome
  2. Reflux Chest Pain Syndrome

- **Syndromes with Esophageal injury**
  1. Reflux Esophagitis
  2. Reflux Stricture
  3. Barrett's Esophagus
  4. Esophageal Adenocarcinoma

Extraesophageal Syndromes

- **Established Associations**
  1. Reflux Cough Syndrome
  2. Reflux Laryngitis Syndrome
  3. Reflux Asthma Syndrome
  4. Reflux Dental Erosion Syndrome

- **Proposed Associations**
  1. Pharyngitis
  2. Sinusitis
  3. Idiopathic Pulmonary Fibrosis
  4. Recurrent Otitis Media

The Montreal definition and classification, Am J Gastro 2006

Diagnosis of gastro-esophageal reflux disease

Symptoms Typical
Atypical/Extra-esophageal

Endoscopy Esophagitis
Complications
Rule out differential diagnosis (EoE)

Ambulatory reflux monitoring

Diagnosis of gastro-esophageal reflux disease

- **An adequate clinical evaluation is crucial**

  Heartburn ?

  Rumination ?

- **Virtually all patients receive PPIs before being referred**

- **30 to 40% of patients don't achieve adequate symptom relief**

  Normal endoscopy

  Extra-esophageal symptoms

- **Refractory symptoms ≠ refractory GERD**

- **Endoscopy is mandatory despite a low diagnostic yield**

The roles of ambulatory reflux testing
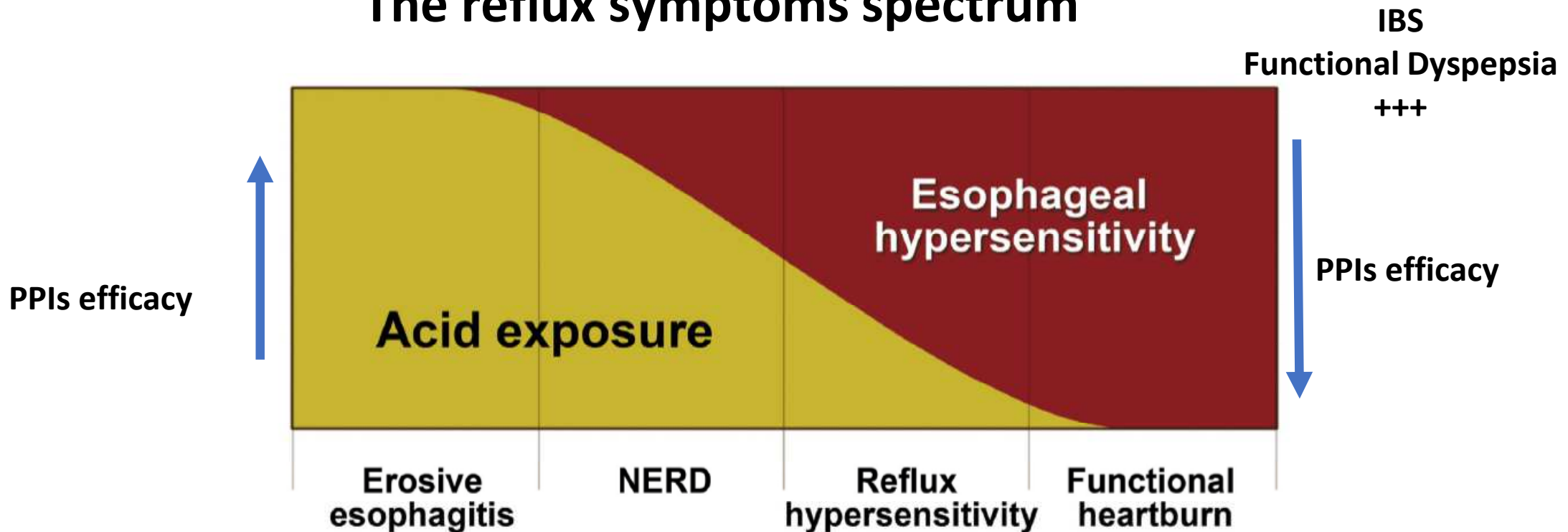
-> **Make a definite diagnosis of GERD**

  - **refractory symptoms**
  - **extra-esophageal symptoms**

-> **Select patients suitable for surgery**

Functional esophageal disorders – Rome IV

The reflux symptoms spectrum

IBS
Functional Dyspepsia
+++

PPIs efficacy

Esophageal
hypersensitivity

PPIs efficacy

Acid exposure

Erosive
esophagitis

NERD

Reflux
hypersensitivity

Functional
heartburn

The GERD spectrum
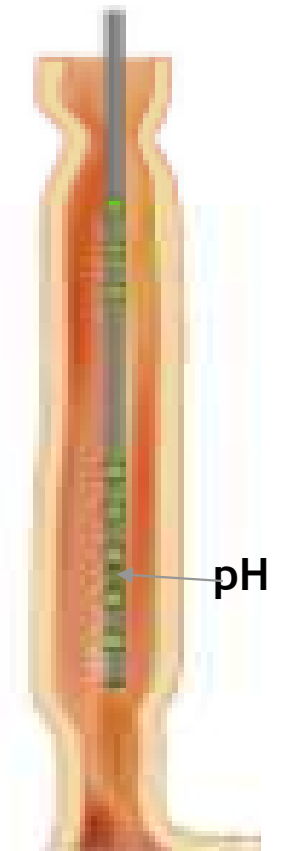
ROME
FOUNDATION
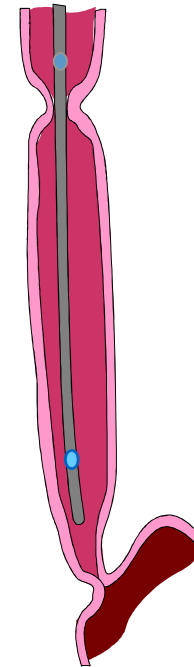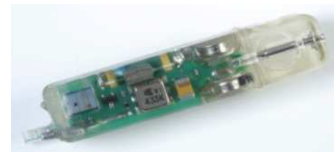
Types of Reflux Monitoring

1) pH only:

    A) Catheter-based

- Single channel pH-catheter
- Proximal and distal (multi channel) pH-catheter

    B) Wireless

- Bravo pH capsule

2) Catheter-based pH-Impedance

   - esophageal

   - pharyngeal and esophageal

pH

Ambulatory reflux monitoring for diagnosis of gastro-esophageal reflux disease: Update of the Porto consensus and recommendations from an international consensus group

Sabine Roman (1), C. Prakash Gyawali (2), Edoardo Savarino (3), Rena Yadlapati (4), Frank Zerbib (5), Justin Wu (6), Marcelo Vela (7), Radu Tutuian (8), Roger Tatum (9), Daniel Sifrim (10), Jutta Keller (11), Mark Fox (12), John E Pandolfino (4), Albert J Bredenoord (13) and the GERD consensus group

GERD consensus group
Fernando Azpiroz, Arash Babaei, Shobna Bhatia, Guy Boeckxstaens, Serhat Bor, Dustin Carlson, Donald Castell, Michele Cicala, John Clarke, Nicola De Bortoli, Vasile Drug, Marzio Frazzoni, Richard Holloway, Peter Kahrilas, Arne Kandulski, Phil Katz, David Katzka, Ravinder Mittal, Francois Mion, Luis Novais, Amit Patel, Roberto Penagini, Mentore Ribolsi, Joel Richter, Renato Salvador, Vincenzo Savarino, Jordi Serra, Felice Schnoll-Sussman, Andre Smout, Edy Soffer, Rami Sweis, Jan Tack, Salvatore Tolone, Michael Vaezi, Philip Woodland, Yinglian Xiao

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Quality of evidence	Definition
High quality	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality	Any estimate of effect is very uncertain.

Indications and choice of GERD Testing

Esophageal pH impedance monitoring is the gold standard but availability, cost and patients preference may drive the choice between catheter based pH, impedance or wireless pH.

Esophageal pH impedance monitoring may be indicated for refractory symptoms despite PPI therapy prior to and/or following anti-reflux surgery, for symptoms of cough, frequent belching and rumination syndrome

Low

Wireless pH :

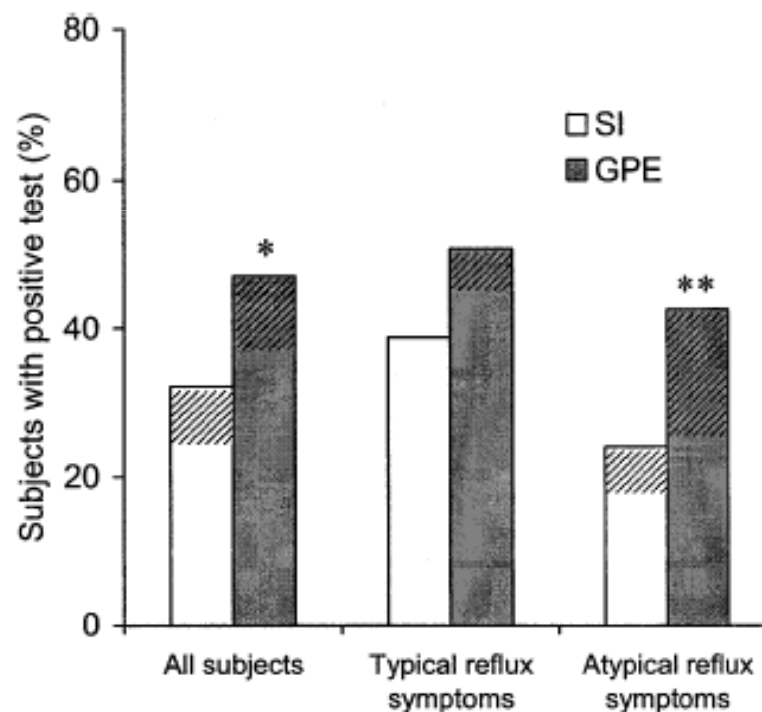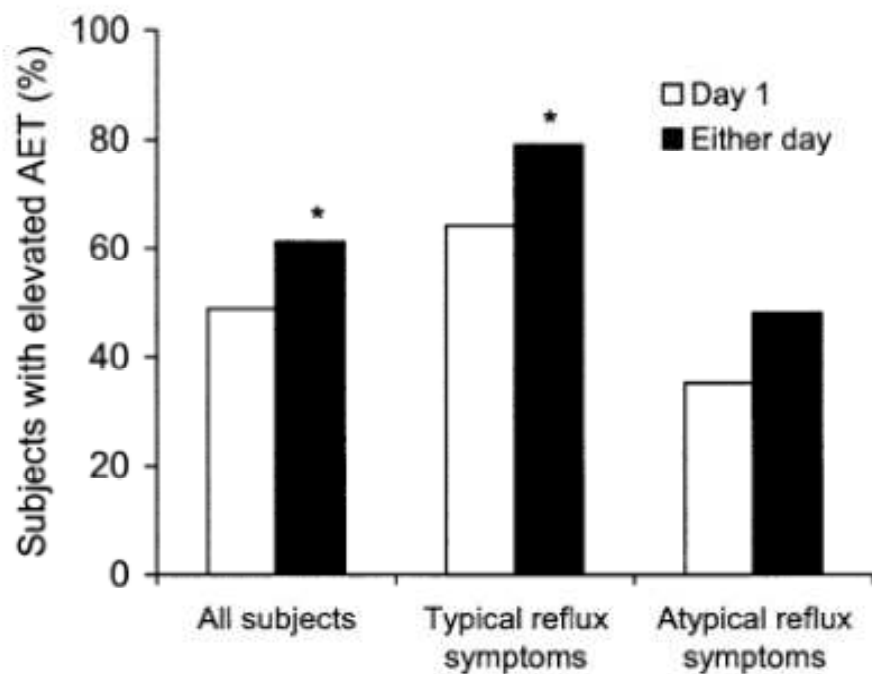   **patients intolerant of a pH or pH impedance catheter**

    patients with a negative catheter based pH study to elicit day to day variation in acid exposure and symptom association

Moderate

The Wireless pH monitoring (Bravo°)

Improved diagnostic yield related to prolonged recording duration

Prakash et al 2005

Indications and choice of GERD Testing
« off » or « on » PPIs ?

Surgery may provide good results in refractory patients with

- **Abnormal esophageal acid exposure (true NERD)**

- **Hypersensitive esophagus**

Khajanchee, 2004, Broeders 2009, Broeders 2011

Group 1 = HE or SAP+,pH- (n=28)
Group 2 = Reflux patients with abnormal AET or SAP+, pH+ (n=126)

At 5 Year follow-up

Broeders JA et al. *British Journal of Surgery 2009*; 96: 1023–1030
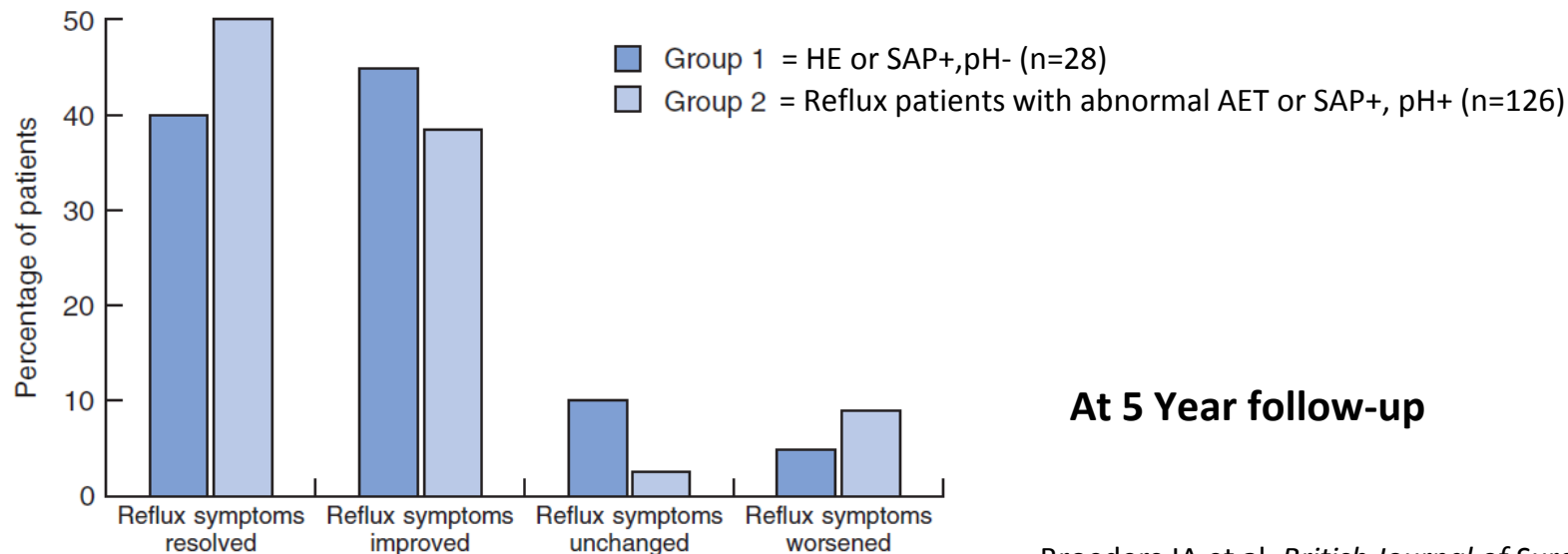
Indications and choice of GERD Testing
« off » or « on » PPIs ?

Abnormal oesophageal acid exposure and Symptom index

Typical symptoms

Extraesophageal symptoms

%

60

50

40

30 — 33 — 31

20

10 — 9

2

0

QD   BID   QD   BID

Charbel et al, AJG 2005

Indications and choice of GERD Testing
« off » or « on » PPIs ?

Off PPI (n =79)

On PPI (n = 71)

% of patients

pH-Impedance
pH alone

SAP (+) SI (+)   SAP (+) SI (+)
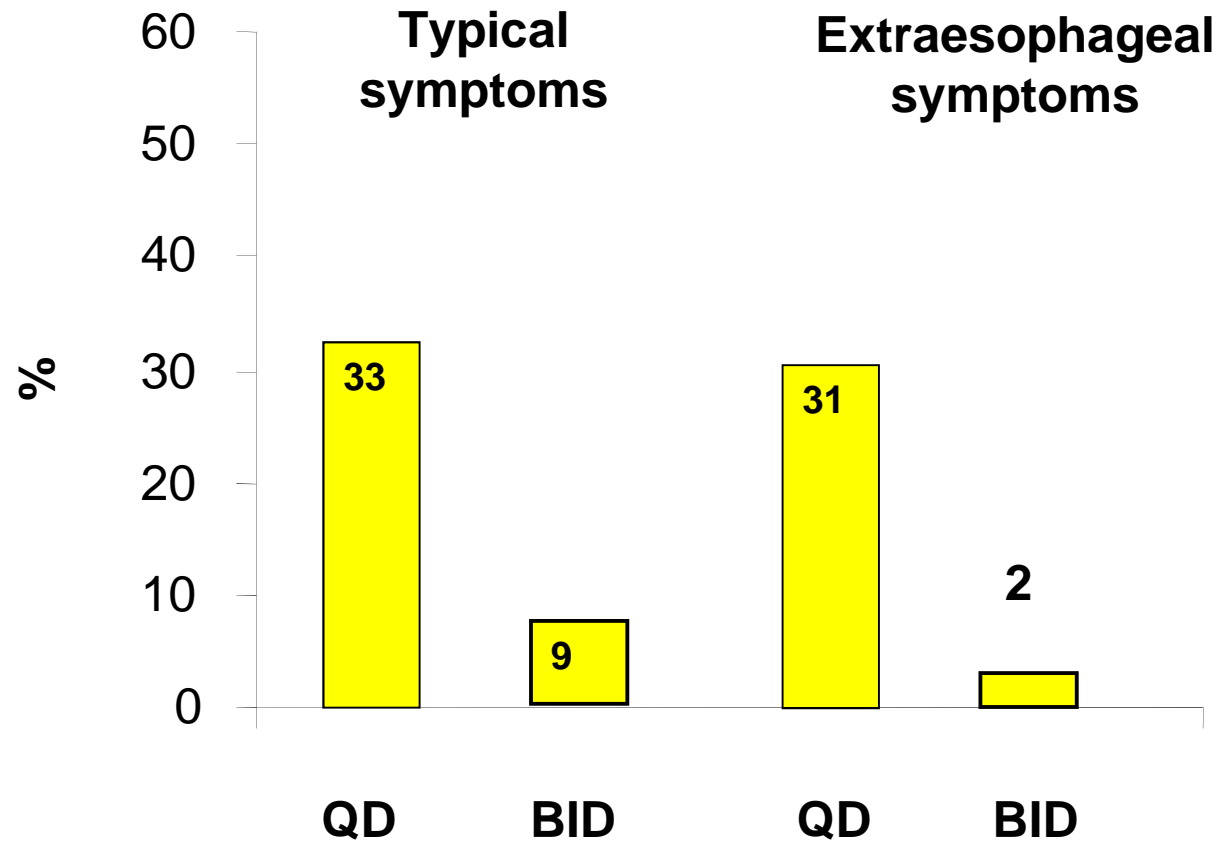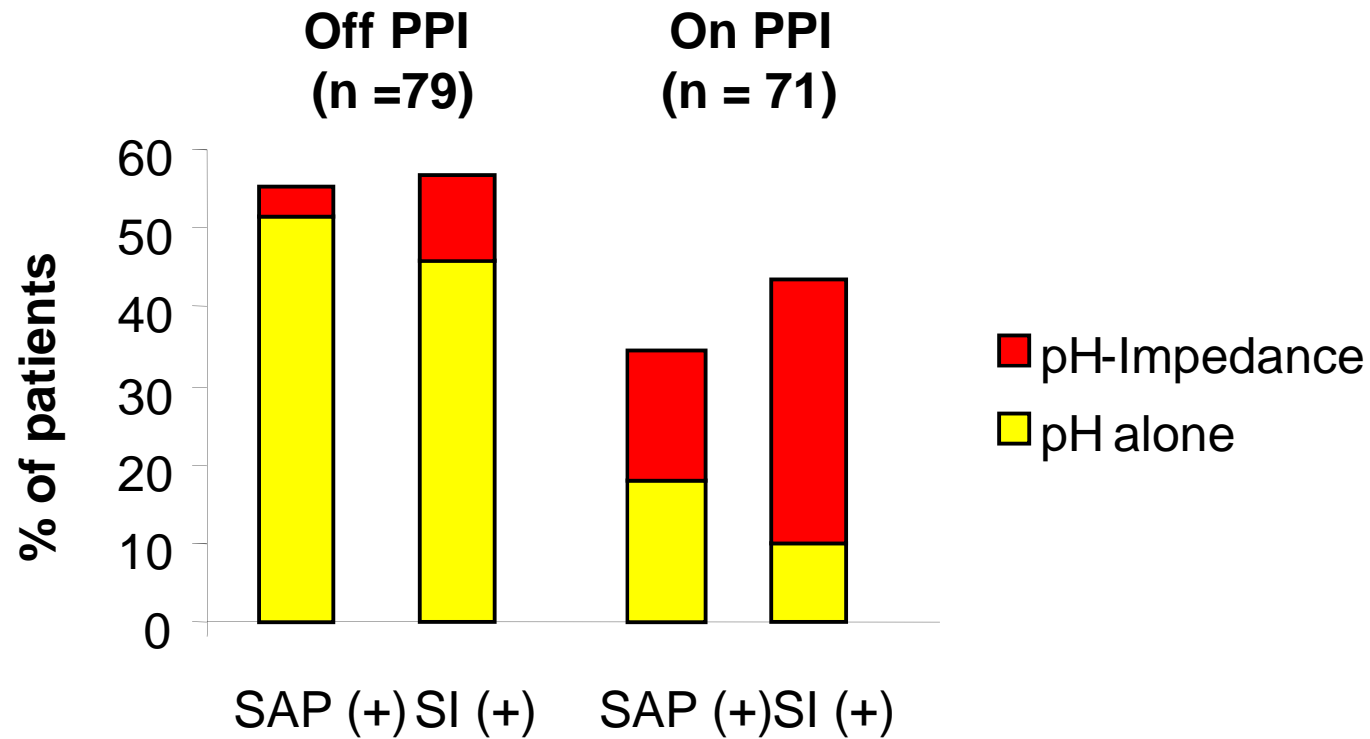
SAP: Symptom Association Probability
SI: Symptom Index

Zerbib et al, Am J Gastro 2006

Reflux monitoring ON therapy
Combined pH-impedance

- **Acid not controlled**   **10%**

- **Symptoms due to "non-acid" reflux**   **30-40%**

- **Symptoms <u>not</u> due to reflux**   **50-60%**

Indications and choice of GERD Testing
« off » or « on » PPIs ?

Reflux monitoring (catheter based pH, wireless pH, or pH impedance) should be performed off of PPI to demonstrate abnormal reflux prior to antireflux surgery	Very low
Reflux monitoring (catheter based pH, wireless pH, or pH impedance) should be performed off of PPI to demonstrate abnormal reflux in the setting of PPI non response	Very low
Reflux monitoring in the form of pH impedance should be performed on PPI in settings with prior evidence for reflux	Moderate

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                    ┌─────────────────────────────────────────┐
                    │  Persistent symptoms suggestive of GERD   │
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| Upper GI endoscopy without esophagitis grade C or D, Barrett's mucosa or peptic stricture | Esophagitis grade C or D, Barrett's mucosa or peptic stricture |

or

| Atypical symptoms |

or

| Prior to anti-reflux surgery |

or

or

| Recurrent/persistent symptom on PPI and/or after surgery | Prior positive pH testing |

| **Catheter based or wireless pH monitoring or 24-h pH-impedance monitoring off PPI** | **24-h pH-impedance monitoring on double dose PPI** |

Interpretation of pH and pH-impedance monitoring

A total AET value of <4% is consistently normal	Moderate

A total AET value of >6 % is consistently abnormal	High

Automated analysis of pH impedance studies is **adequate for acid RE** Automated analysis of pH impedance **overestimates non-acidic RE** **Manual review of the 2 minutes preceding each symptom** event in pH impedance studies is necessary	Very low

Upper gastro-intestinal endoscopy

24-h esophageal pH ± impedance monitoring (off or on therapy)

Pathological GERD

Grade C or D esophagitis and/or Peptic stricture and/or Barrett's esophagus

or

AET > 6%

Normal
Grade A or B esophagitis

or

AET 4-6 %

No pathological GERD

AET < 4 %

Considering additional testing:
total number of reflux, baseline impedance, evaluation of microscopic esophagitis
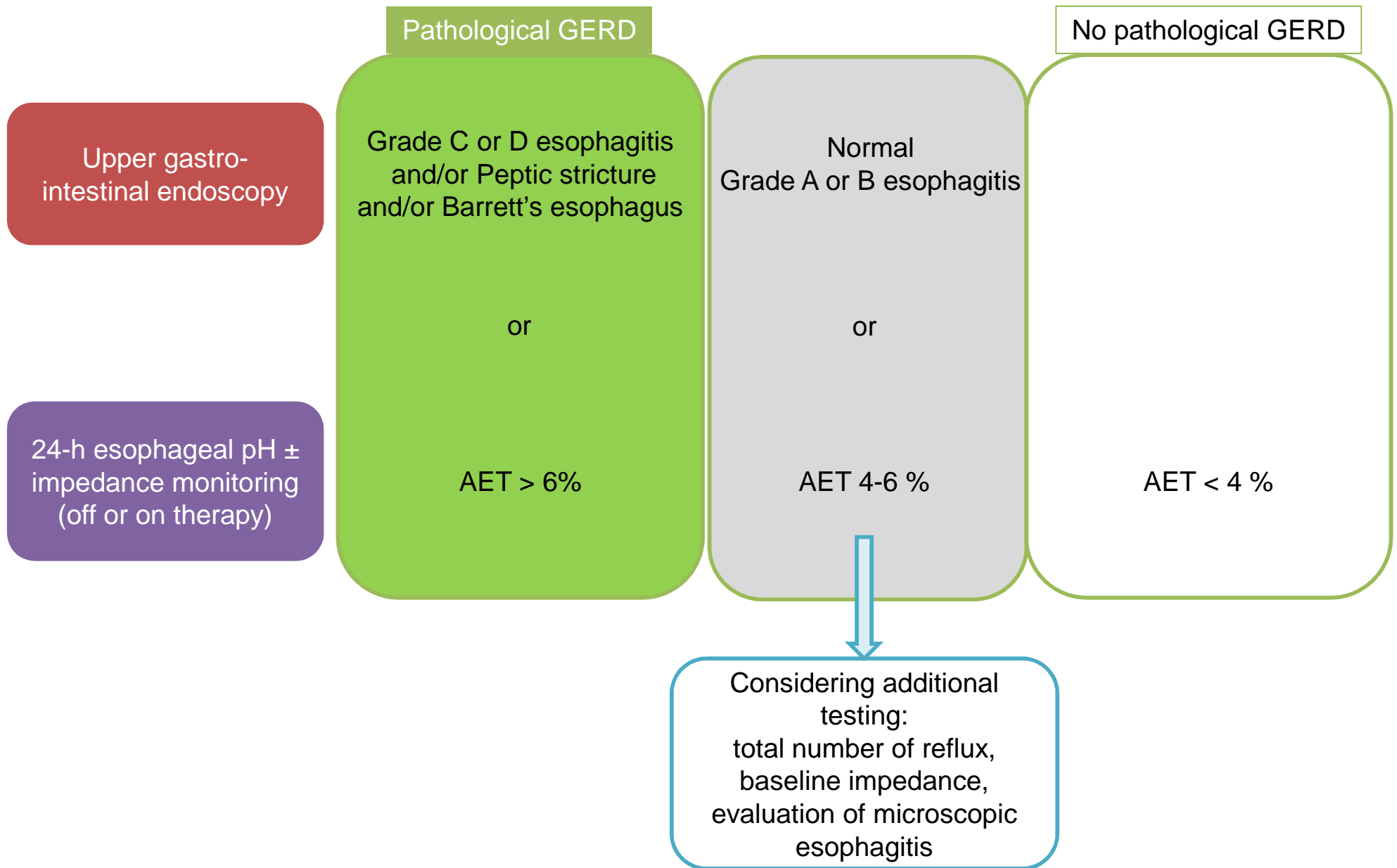
Interpretation of pH and pH-impedance monitoring
Symptom reflux association

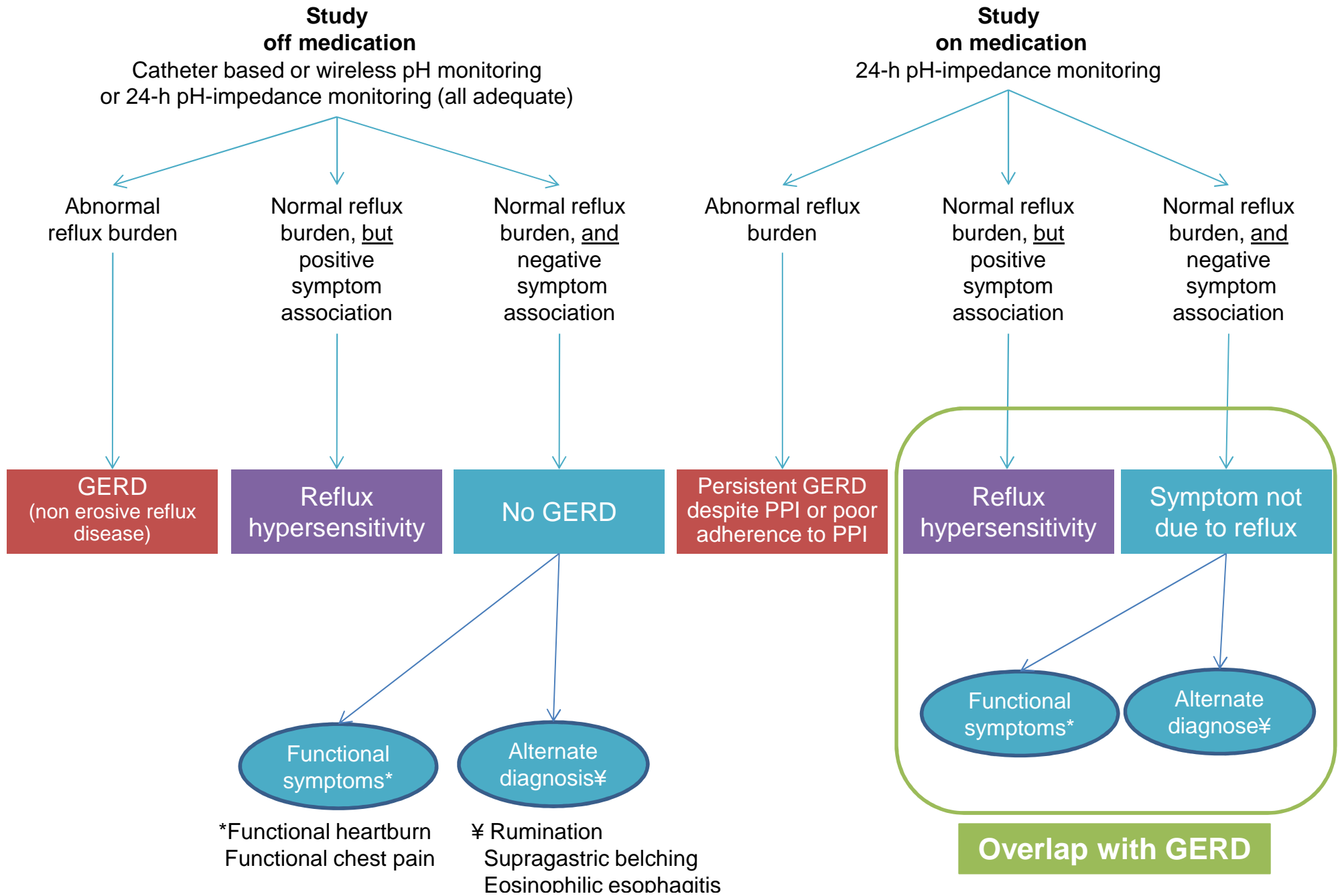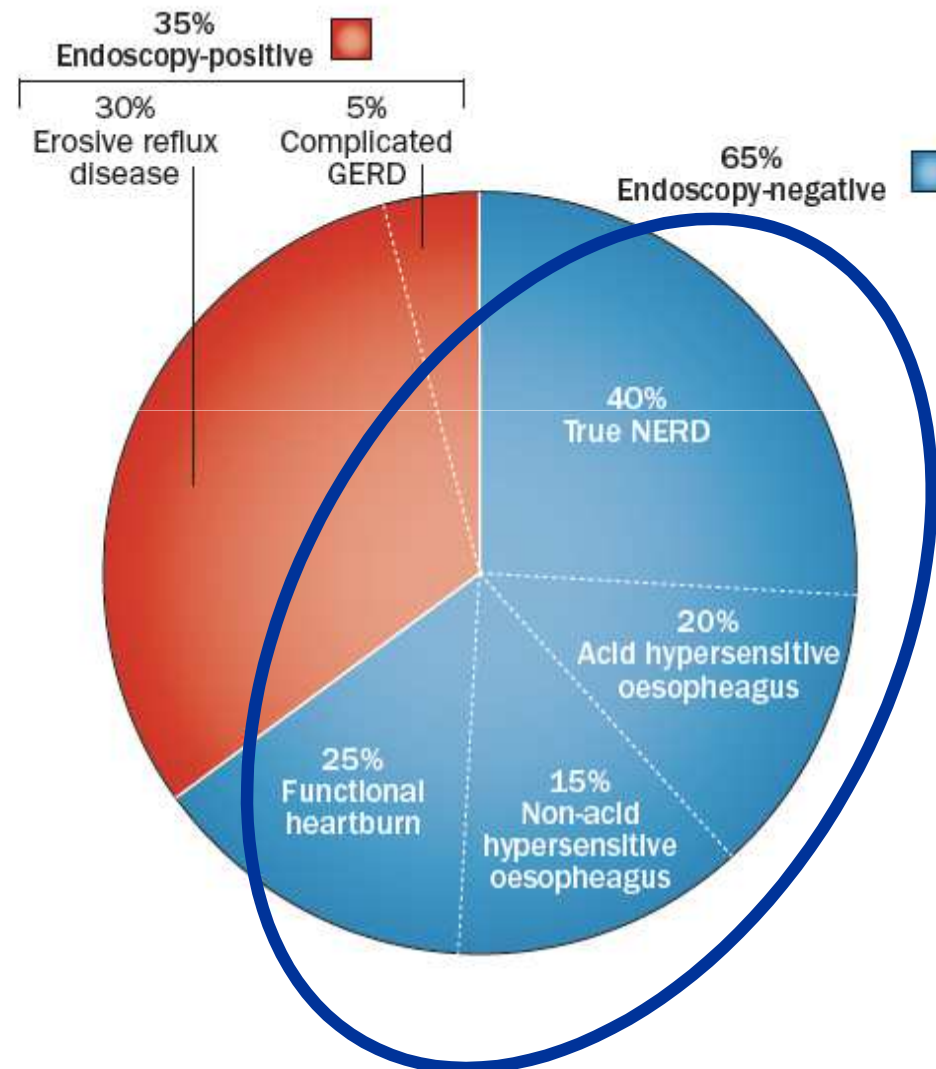|	
The only time window for symptoms following a reflux event is 2 minutes	Moderate
All reflux events detected by impedance are used in calculation of RE	High
Symptom index (SI) and Symptom Association Probability (SAP) have value in pH and pH-impedance monitoring	High
SI and SAP are complementary and cannot be directly compared to each other	Very low
The 2 minute period prior to each symptom event and 2 minute period following each reflux episode should be evaluated prior to calculating the SI	Moderate
Abnormal AET with both SAP and SI positive represents the strongest evidence for reflux	Moderate

The GER phenotypes

Study off medication
Catheter based or wireless pH monitoring
or 24-h pH-impedance monitoring (all adequate)

Study on medication
24-h pH-impedance monitoring

Abnormal reflux burden

Normal reflux burden, but positive symptom association

Normal reflux burden, and negative symptom association

Abnormal reflux burden

Normal reflux burden, but positive symptom association

Normal reflux burden, and negative symptom association

GERD (non erosive reflux disease)

Reflux hypersensitivity

No GERD

Persistent GERD despite PPI or poor adherence to PPI

Reflux hypersensitivity

Symptom not due to reflux

Functional symptoms*

Alternate diagnosis¥

Functional symptoms*

Alternate diagnose¥

*Functional heartburn
Functional chest pain

¥ Rumination
Supragastric belching
Eosinophilic esophagitis

Overlap with GERD

Stratification of Patients with Typical Reflux Symptoms

35%
Endoscopy-positive

30%
Erosive reflux disease

5%
Complicated GERD

65%
Endoscopy-negative

40%
True NERD

20%
Acid hypersensitive oesopheagus

25%
Functional heartburn

15%
Non-acid hypersensitive oesopheagus

Savarino E, et al. Nat Rev Gastroenterol Hepatol. 2013;10(6):371-80

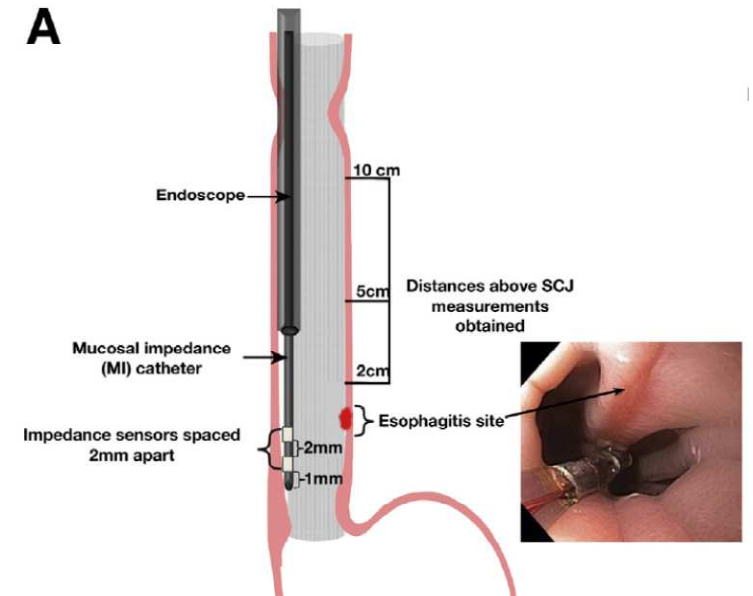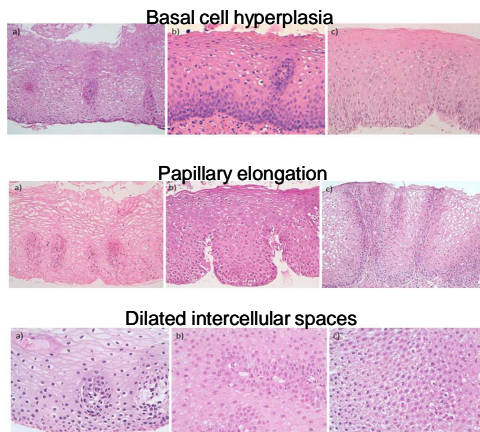# What is not in the consensus
What could have been in
What may be in the future

Pharyngeal reflux /Dual probe pH monitoring have no value to guide clinical management

The total number of reflux episodes alone, **baseline impedance, histological assessment**

> ➤ not sufficient to confirm the diagnosis of GERD

> ➤ should be considered as an exploratory tool.

Basal cell hyperplasia

Papillary elongation

Dilated intercellular spaces

A

Endoscope

10 cm

5cm — Distances above SCJ measurements obtained

Mucosal impedance (MI) catheter

2cm

Esophagitis site

Impedance sensors spaced 2mm apart — 2mm — 1mm

What is not in the consensus
What could have been in
What may be in the future

Validation of additional parameters   Number of reflux events
Bolus exposure
Baseline impedance

Validation of new tools   Microscopic esophagitis
Salivary pepsin
Direct measurements of MI
Combined HRM-impedance studies
Automatic analysis of impedance recordings

Outcome prospective studies +++