

# Gastro-oesophageal Reflux Disease and PPI Therapy in 2022

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GATEWAYCENTRE  
FOR RESPIRATORY AND GASTROINTESTINAL DISEASE

# Overview

- **Epidemiology**
- **Pathophysiology**
- **Phenotypes**
- **Diagnostic Investigations**
- **Management**
- **PPI Refractory GERD**
- **New PPI Agent**



:k

Sunday 17th July  
Morning

# Definition

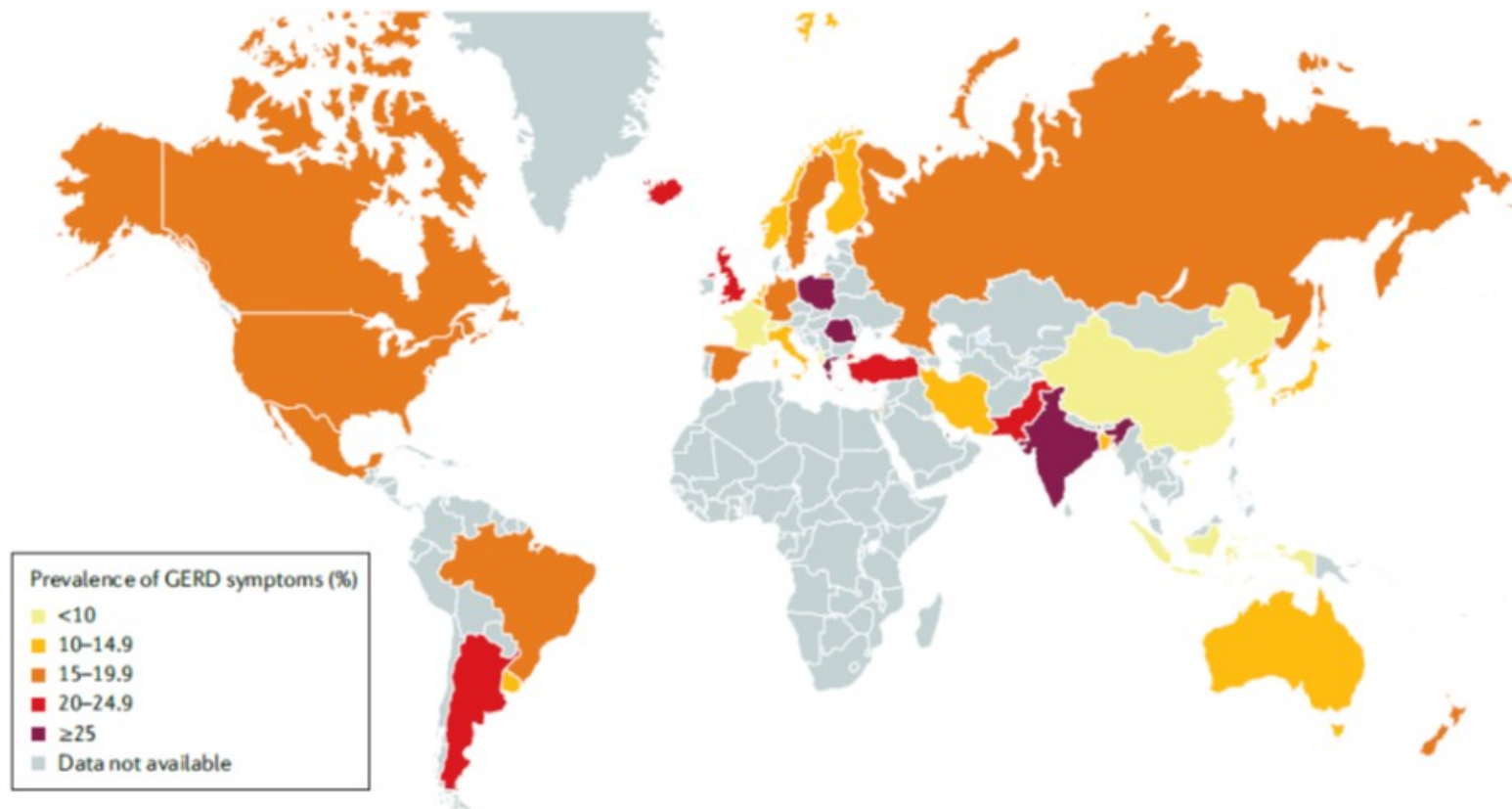
- **GERD is a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications.**

**The Montreal Definition and Classification of Gastroesophageal Reflux Disease: A Global Evidence-Based Consensus. AGA**

- **In clinical practice,**

**Symptoms of heartburn, mild symptoms occurring 2 or more days per week, or moderate to severe occurring 1 or more days per week, are considered as troublesome.**

# Epidemiology



- **Increasing Global prevalence.**
- **GERD Symptoms are common but vary geographically.**
- **The highest prevalence of GERD symptoms occurred in one Central American study (19.6%) whereas the lowest prevalence was observed in Asia (10.0%)**
- **No clear associations between GERD symptoms with race, age and sex.**

# Epidemiology

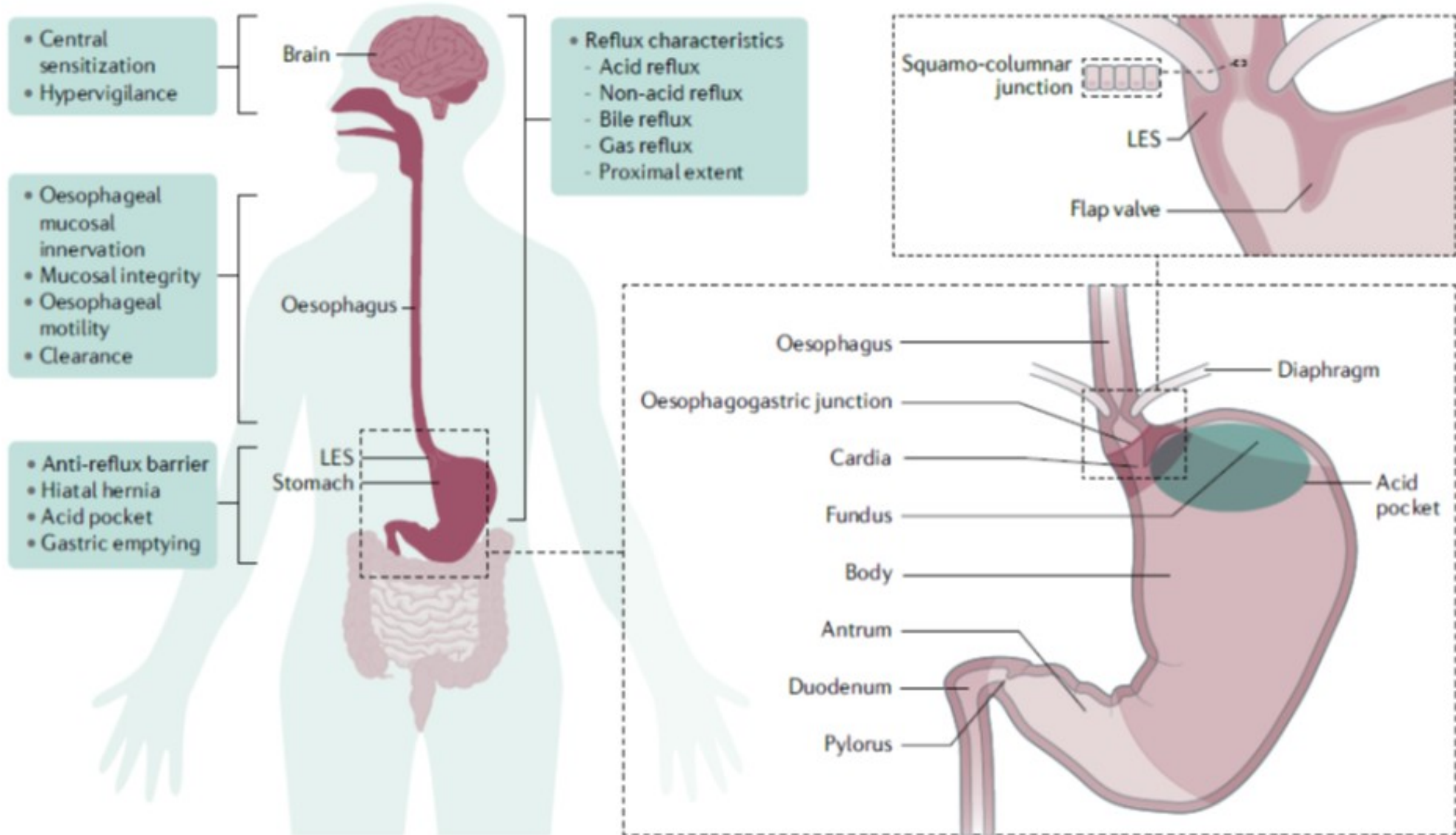
- **No consistent evidence for a genetic association with GERD symptoms.**
- **Smokers >> Non smokers**
- **Current drinkers > non drinkers**
- **NSAID users >>> non-users**
- **Positively associated with increased consumption of fat, sweets, chocolate, and salt & inversely associated with fruit and fibre.**



# Epidemiology

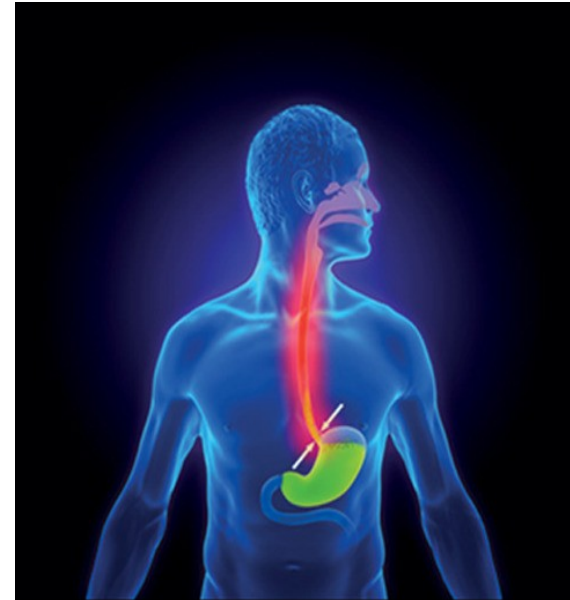
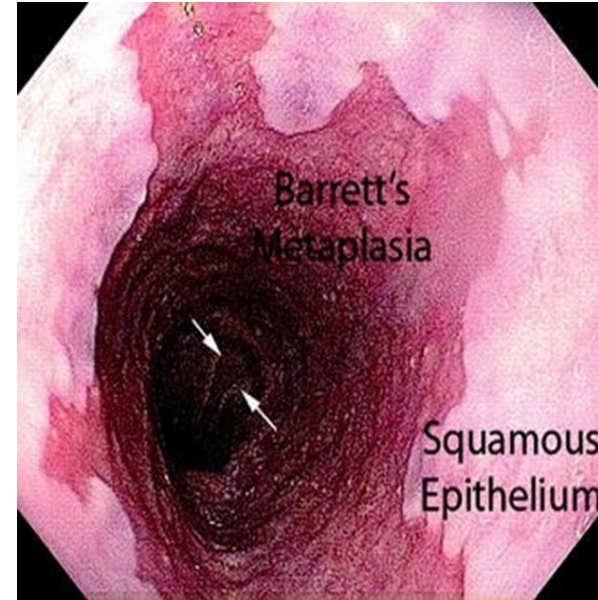
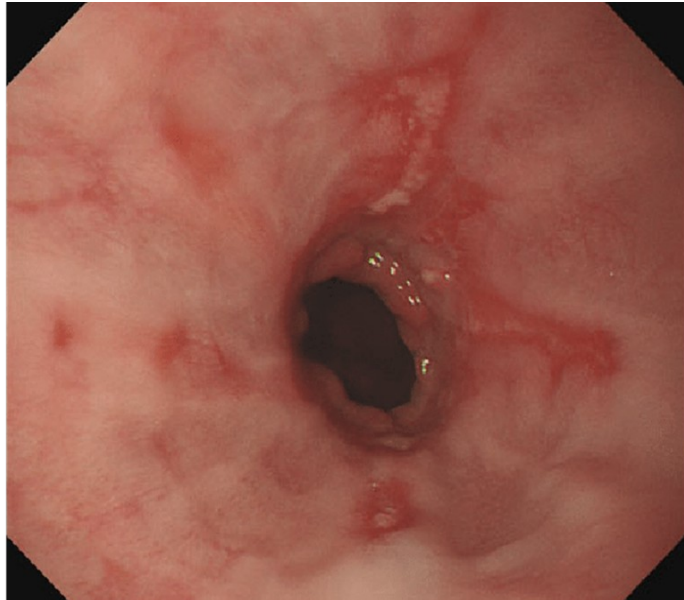
- **No evidence of carbonated beverages promoting GERD.**
- **More pH- verified supine reflux after a late evening meal.**
- **Moderate, regular aerobic exercise is inversely associated with GERD symptoms. By contrast, physical activity at work, for example, in a stooped posture, and strenuous exercise, such as weightlifting are positively associated with the presence of GERD symptoms.**
- **Obesity is a strong risk factor for GERD**
- **A meta- analysis of trials of *H. pylori* eradication found that the risk of GERD symptoms was not increased after eradication of *H. pylori***

# Pathophysiology





# GERD Phenotypes





# GERD : Extra-Oesophageal Manifestations

## **Laryngeal**

Cough, laryngitis, sub-glottic stenosis, globus, laryngeal cancer, vocal cord granuloma, vocal cord irritation, vocal cord polyps and post-nasal drip

## **Oropharyngeal**

Dental erosion, pharyngitis, sore or burning throat, gingivitis and halitosis

## **Ears and sinuses**

Earaches, otitis media and sinusitis

## **Pulmonary**

Chronic bronchitis, pneumonia, aspiration, bronchiectasis, asthma and idiopathic pulmonary fibrosis

## **Cardiac**

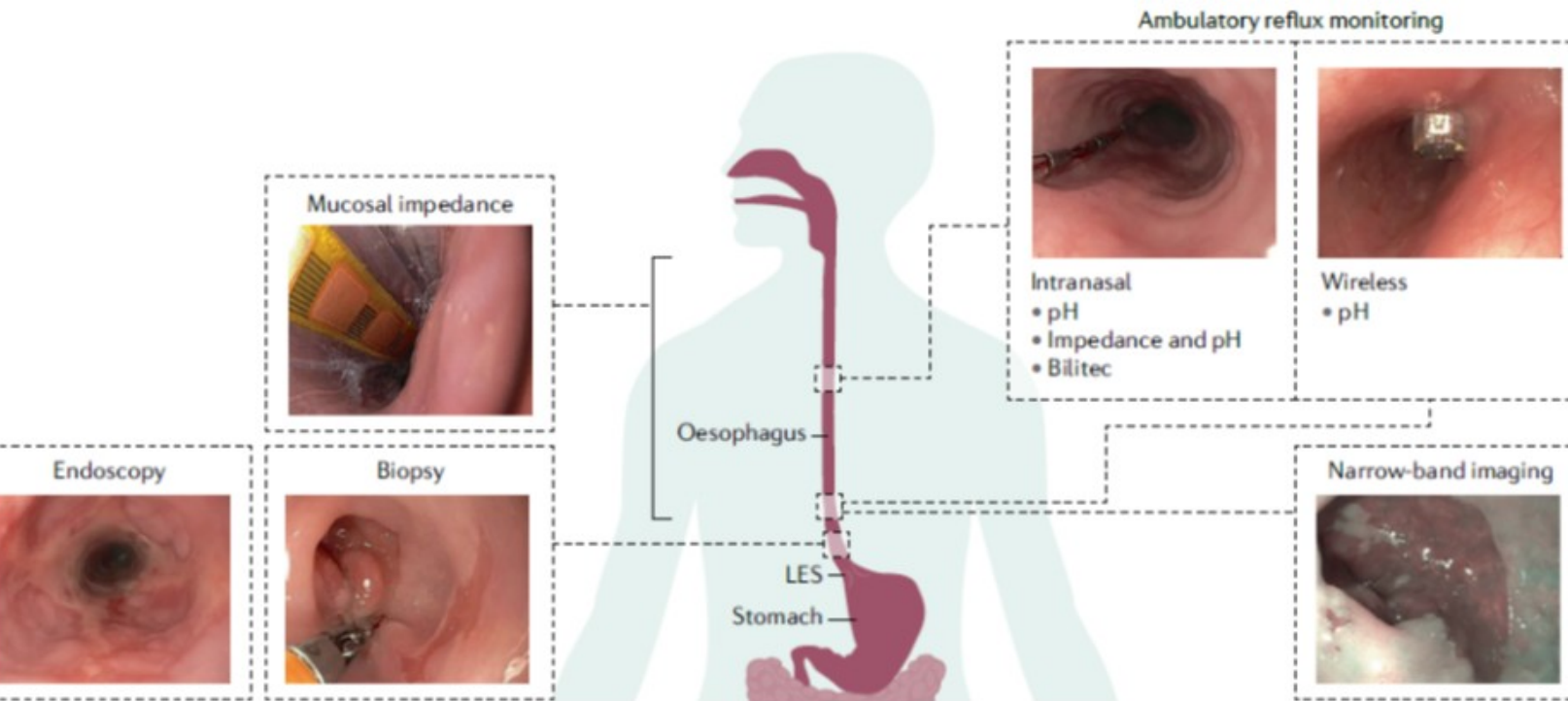
Arrhythmia, angina and myocardial infarction

## **Sleep**

Sleep apnoea, sleep deprivation, insomnia, snoring, nightmare and sleep disturbance

GERD, gastro-oesophageal reflux disease.

# Diagnostic Investigations



GERD is commonly diagnosed based on the response to empiric acid suppressive therapy or on objective findings

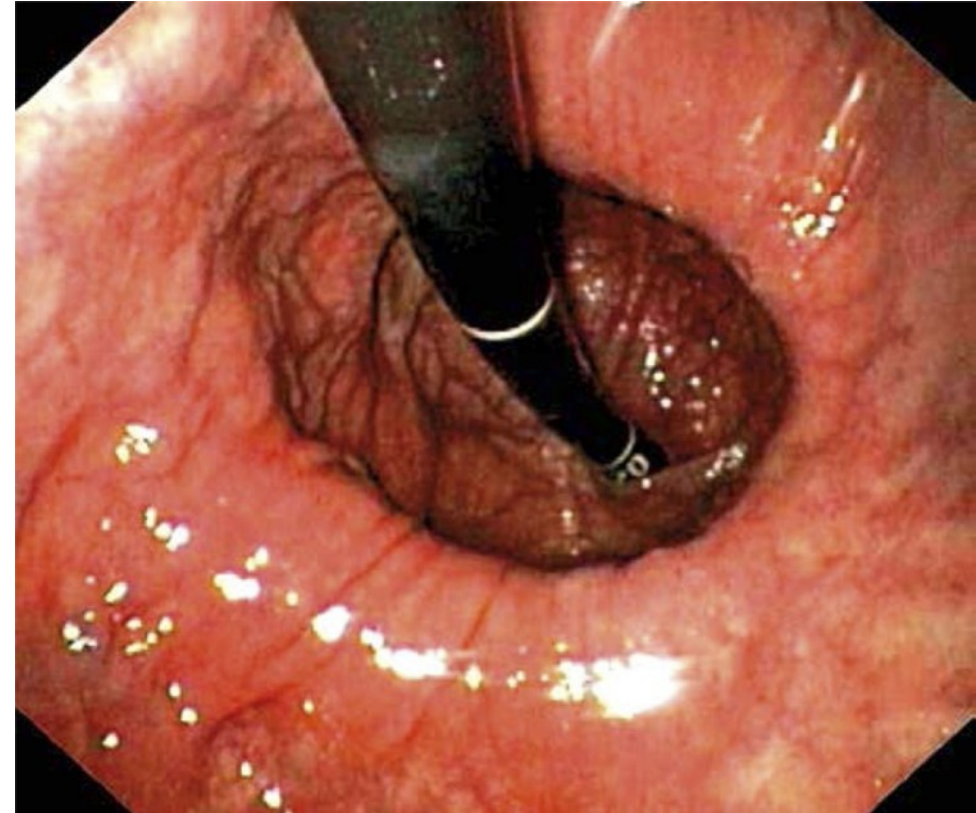
- **Diagnostic tests are reserved for patients that continue to be symptomatic or need surgery.**

- **Visual alterations, or device to determine presence and extent**

# Diagnostic Investigations

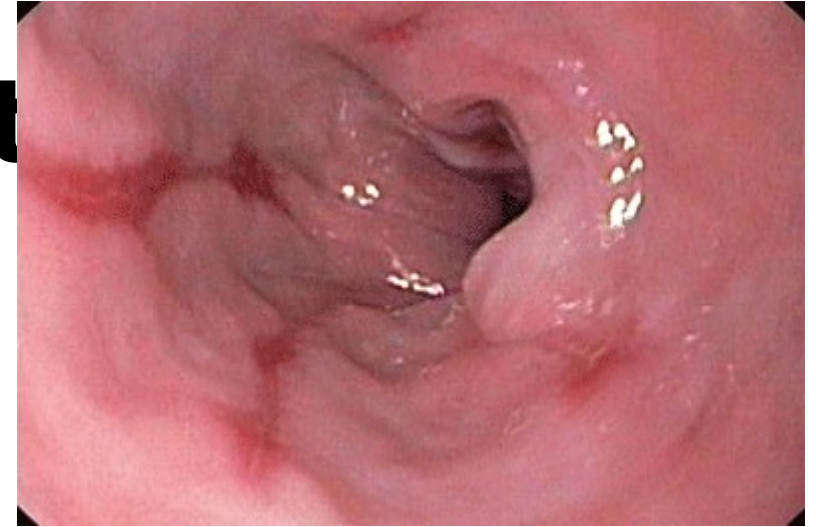
## Endoscopy

- **Warning symptoms( dysphagia, weight loss, haematemesis, vomiting?)**
- **Chronic GERD at risk of Barretts**
- **Suspect disorders: EOE, infection, pill injury...**
- **Poor response to therapy.**
- **Require Surgery**



# Diagnostic Investigation

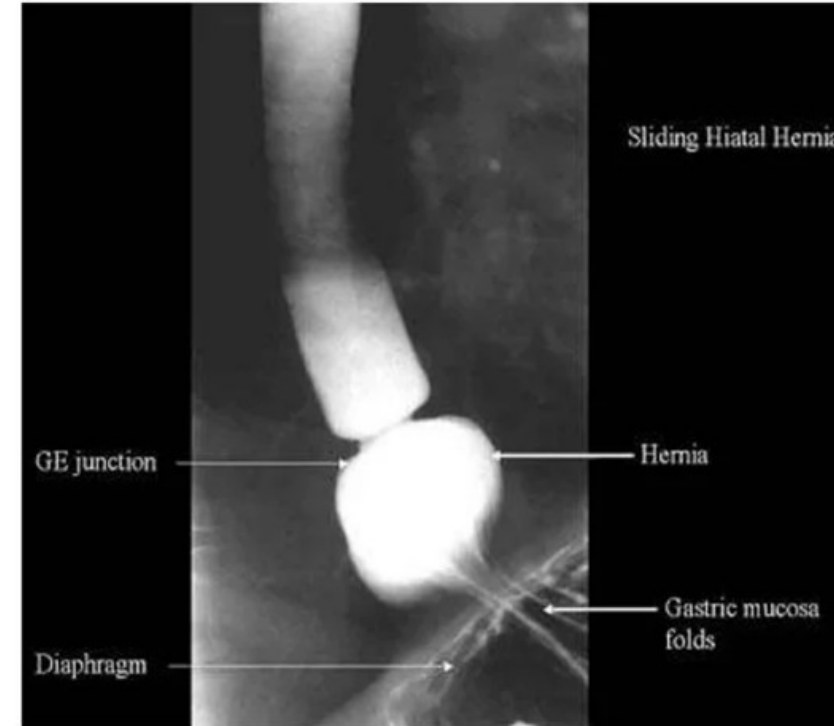
- **For GERD Diagnosis: Visual Alterations to confirm GERD**
- **Presence of oesophagitis is a strong indicator for GERD.**
- **Gastroscopy is normal in 2/3 patients**



# Diagnostic Investigations

## Barium

- **Sensitivity: 67% and specificity 47%**
- **Should not be done for the diagnosis**





# Management :

## Lifestyle and Dietary Changes

- **Patient with mild symptoms.**
- **Evidence :Weight loss, elevation of head of the bed, and avoid eating at least 3 hrs before bedtime.**
- **There is limited/no evidence for other lifestyle recommendations.**



# Management : Pharmacological

## Antacids

- Not shown to heal EE or prevent complications of GERD.
- Safe (E.g: Al-hydroxide, Mag-hydroxide, Calcium carbonate, Sodium bicarbonate.
- Alginate : More likely to resolve GERD symptoms than placebo or other antacid
- Sulcralfate : Better than placebo in NERD, Limited in healing EE
- Consider Adding to once daily PPI, helped to control breakthrough symptoms



# Management : Pharmacological

## H2 Receptor Antagonists

- Could be consider in NERD, or those low grade EE, on demand therapy for patient with mild disease due to rapid action.
- Consider in patients that are poorly responsive to double dose PPI
- H2RA are commonly added at bedtime to suppressive the effect of night time histamine driven surge of gastric acid secretion.
- It can relieve postprandial heartburn for up to 12 hrs.
- Tachyphylaxis is common and develop with chronic use.
- **Other: Potassium Acid Blockers, Baclofen, Prokinetics**

# Management: Pharmacological

- Proton Pump Inhibitors

Numerous studies: PPI are superior to H2RA in symptom control, mucosal healing and prevention of relapse of GERD

**Gold Standard For GERD!**

# Simple Algorithm of GERD Therapy

- Lifestyle Modifications and On Demand Antacids



- Intermittent PPI



- PPI Daily (and Optimise)



- PPI BD (and consider further tests - Refer)



- Refractory PPI

- 6 Mistakes with PPI Use...

# Management: PPI Therapy

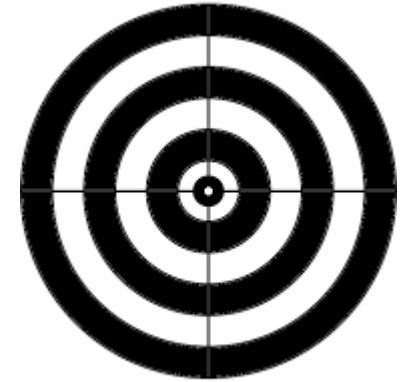
## Mistake 1



## Prescribing a PPI without instructions for use

- PPI can only bind and inhibit active proton-pumps – H/K ATPase
- Proton-pumps become active during eating, and not all pumps become active at once
  - PPI need to be in plasma when pumps become active- during eating
  - Ingestion 30min before meals

# Management: PPI Therapy

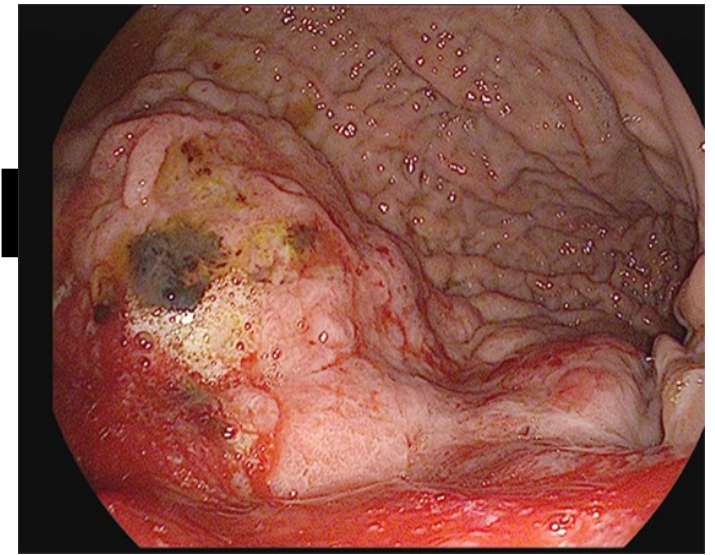


## Mistake 2

### Considering the PPI test to be accurate for GERD diagnosis

- Consider 24hr Ph measurement as the gold standard for GERD, PPI test is not ideal in studies. Low sensitivity and sensitivity.
- NB: other conditions can respond to PPI e.g gastric ulcer – low specificity

# Management: PPI Therapy



## Mistake 3

### Increasing PPI for persistent heartburn when there is no evidence for GERD

- PPI non-responders often do not have GERD
- ? is the diagnosis of GERD correct
- Symptoms are poor predictors of GERD.

NB sensitivity of clinical history in the diagnosis of GERD – 55%





# Management: PPI Therapy

## Mistake 4

### Withholding PPI Rx due to fear of complications

? Pneumonia, Fracture, C.Diff diarrhea , Clopidogrel interactions, CKD, Dementia, Gastric Cancer, Mortality..

- Compass trail – NEMJ: No significant in mortality with pantoprazole Vs placebo.
- Moayyedi Gastro 2019, Slightly higher chance of enteric infections..

*AGA statement. “Much of the evidence linking PPI use to serious long term adverse consequence is weak and insubstantial. It should not deter prescribers from using appropriate doses of PPI for the appropriate indication*

# Management: PPI Therapy



## Mistake 5

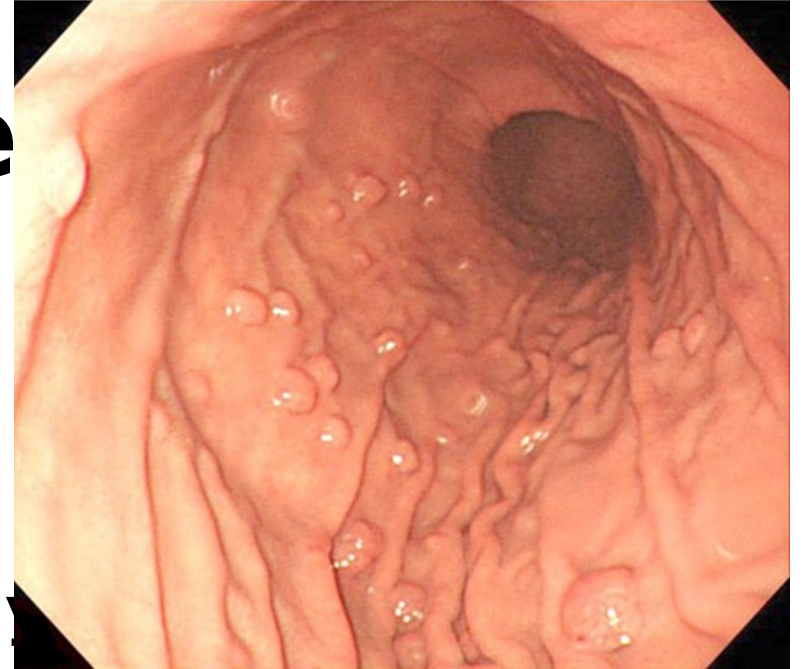
Not taking hypomagnesemia seriously in PPI users

- Severe -  $< 0.5$  (Rare  $< 0.01$ )
- Mechanism - unclear
- Class affect.
- Stop PPI - H2 antagonist, surgery

# Management: PPI The

## Mistake 6

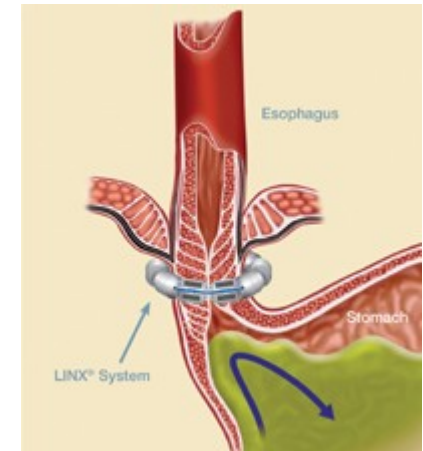
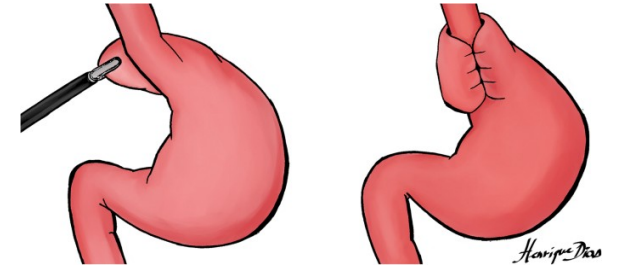
### Stopping PPI Rx due to fundic gland poly



- 2% pop - common
- Can be associated with syndromes/ Mostly sporadic
- 4x risk in chronic PPI users
- No risk of dysplasia/cancer

# Management: Surgery ?

- Medical therapy -unsatisfactory or undesirable.
- Side effects to therapy
- Poor compliance to therapy
- Large hiatal hernia
- Regurgitation as a predominant symptom
- EE despite max PPIs



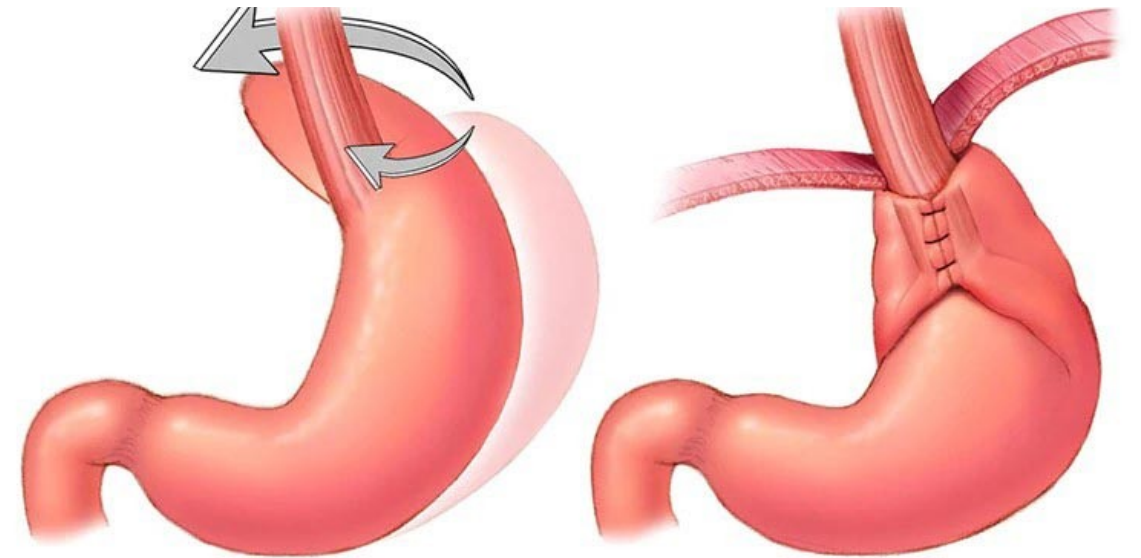
- Types: Fundoplication, Magnetic sphincter augmentation device – LINX, Roux and Y :Morbid obese patients and GERD

# Management: Surgery

- As effective as medical therapy, ? studies superior in controlling GERD symptoms.
- More effective than adding medical therapy - (Baclofen to PPI bd. In patient with GERD with true PPI refractory heartburn)
- **Side Effects: Bloating, dysphagia, re-operation.**

## Predictors of Successful Surgery:

- Typical GERD
- Symptomatic response to PPI
- Abnormal PH and Normal Scope



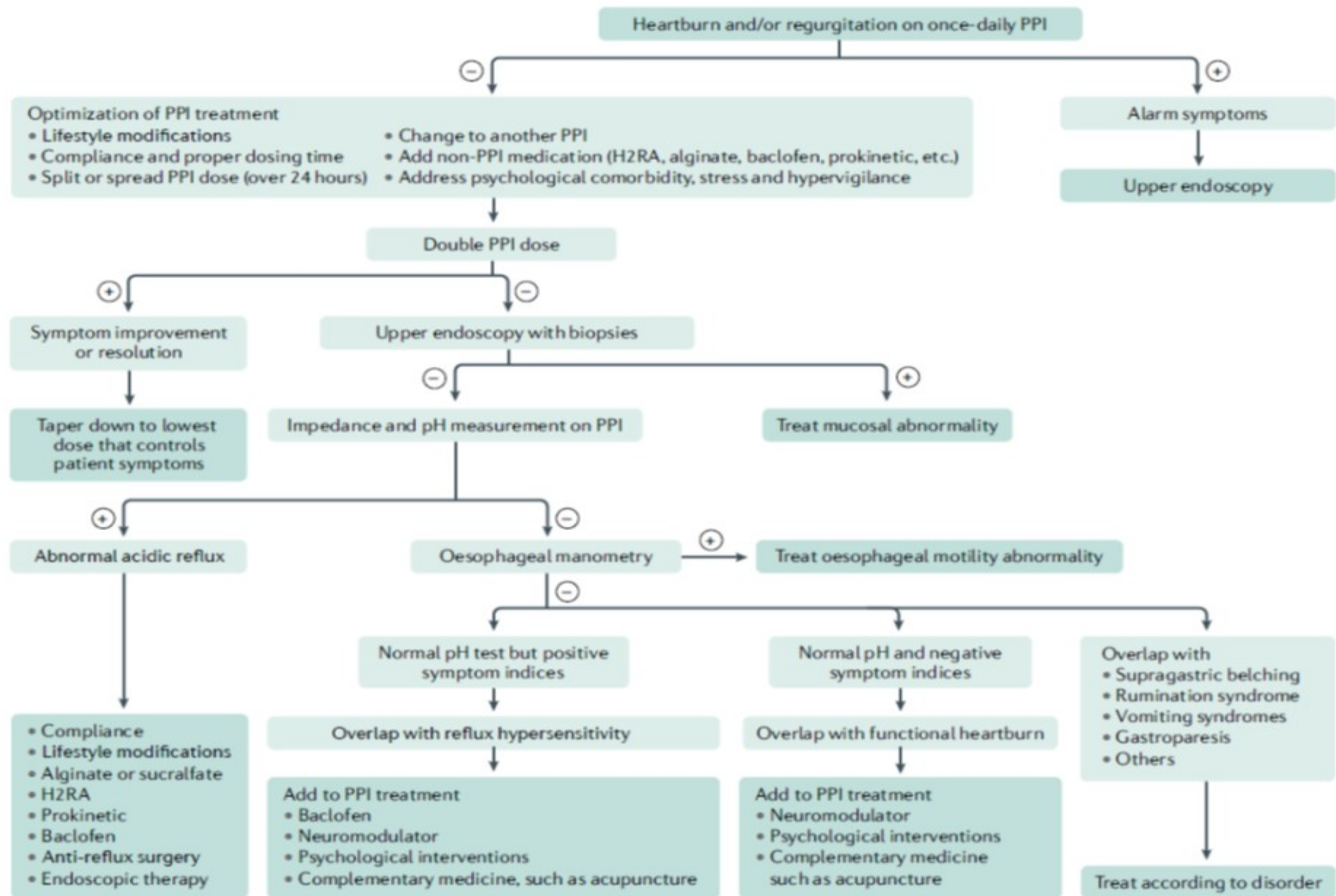
A. The fundus is wrapped around the back side of the esophagus

B. The wrap is secured with sutures to anchor lower esophagus below diaphragm

# Management: Endoscopic

## Alternatives to Surgery

- Stretta procedure: low power, temperature-controlled radiofrequency energy at OGJ.
- Transoral incisionless fundoplication
- Medigus Ultrasonic Surgical Endostapler

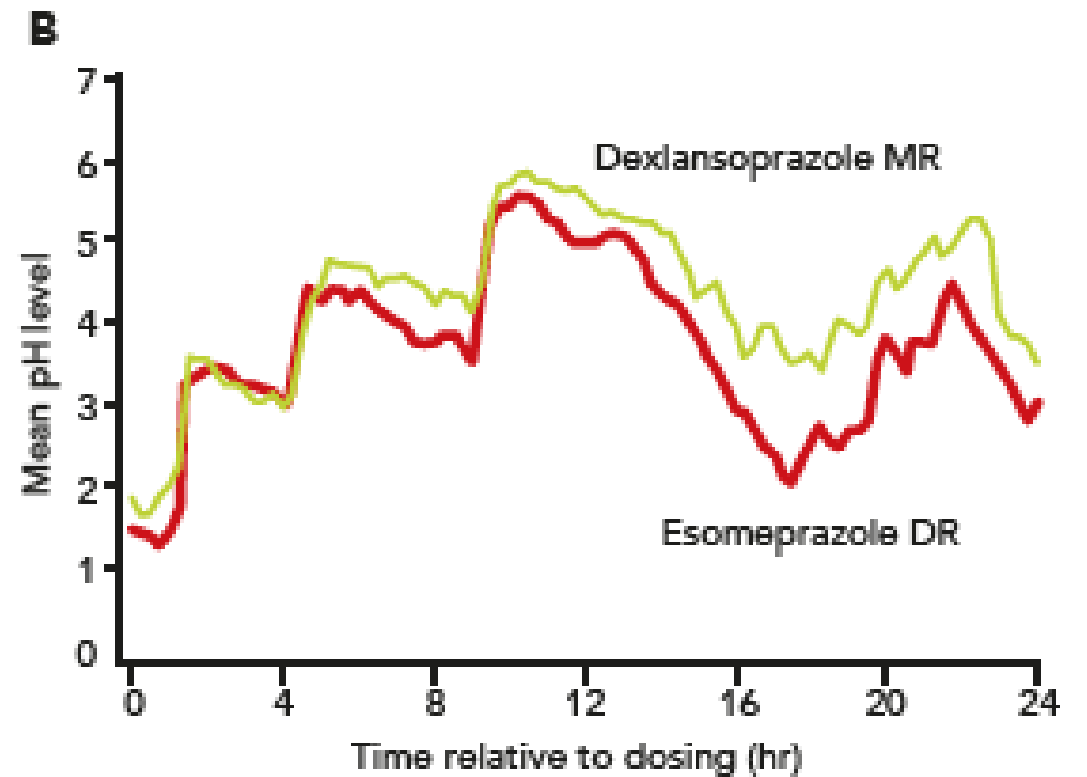
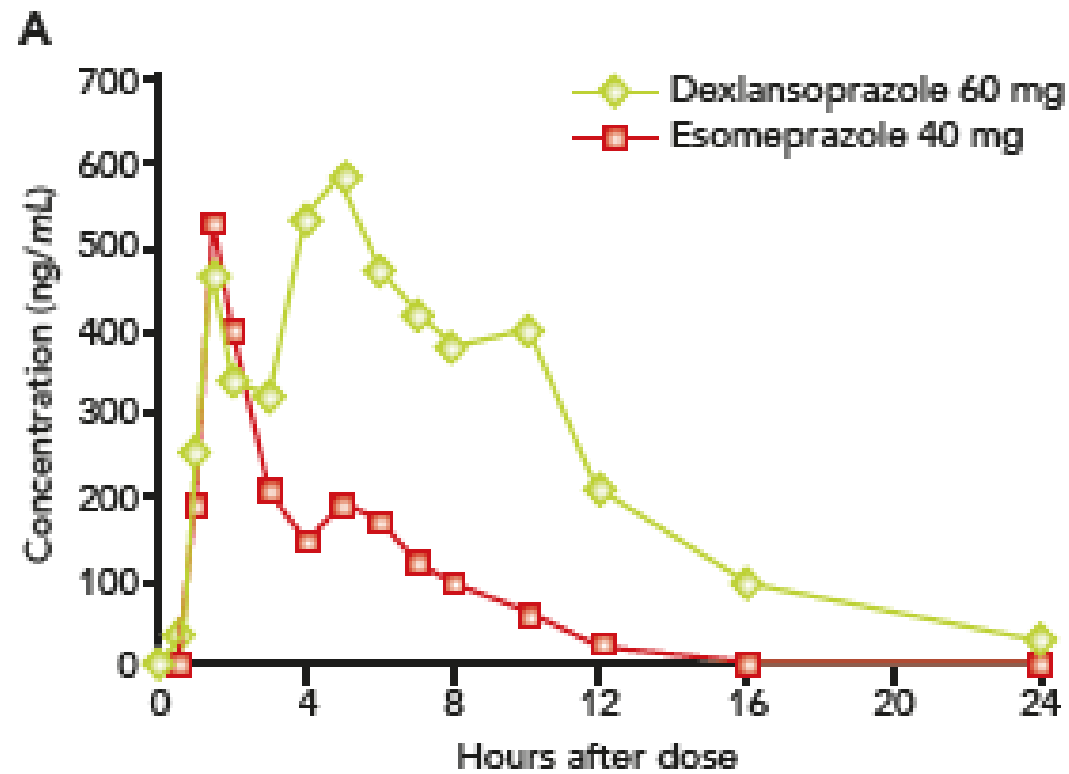




# New PPI Agent : Dexilant

- DEXILANT® (dexlansoprazole modified-release capsules) is the first new Proton Pump inhibitor to be launched in South Africa since the launch of esomeprazole.
- It has a unique delivery system allows dual release of the active ingredient – in the duodenum and the small intestine.
- It achieves two peak concentrations at various times, within two and five hours of administration.
- Ensures the longest maintenance of drug concentration in the plasma of all known proton pump inhibitors
- Dexlansoprazole modified-release inhibits both basal and stimulated gastric acid secretion.

# New PPI Agent : Dexilant



# New PPI Agent : Dexilant vs Esomeprazole

- A comparison of esomeprazole 40 mg and dexlansoprazole modified-release capsule 60 mg, the average 24-hour intragastric pH following a single dose of dexlansoprazole modified-release capsule was higher compared to a single dose of esomeprazole (58 % versus 48 %;  $P=0.0003$  )
- NERD – Significantly better symptom control
- GERD – 24 weeks – Similar

# New PPI Agent : Dexilant

- Better optimal dosing, providing 24-hour symptom control for most patients
- With convenience and flexibility regardless of food or timing of food/dose
- Consistently higher EE healing rates compared with lansoprazole
- High rates of healing are seen across all grades of EE, including moderate-to-severe EE
- Dexlansoprazole is well tolerated
- Safety and tolerability profile similar to lansoprazole

# New PPI Agent : Dexilant

- DEXILANT® is available in two dosage strengths, 30 and 60 mg, and is currently approved for 3 clinical indications: in adults and adolescents,
- Treatment of erosive reflux oesophagitis;
- Maintenance of healed erosive oesophagitis and maintenance of relief of heartburn
- Short-term treatment of heartburn and acid regurgitation associated with symptomatic NERD.

NEW  
**DEXILANT**  
dexlansoprazole  
30 MG | 60 MG MODIFIED-RELEASE CAPSULES

## Indications and Dosage Frequency Extended symptom control<sup>1,2,3</sup>

Indication <sup>1</sup> (indicated in patients 12 years of age and older)	Recommended Dose	Frequency
Healing of all grades of erosive oesophagitis (EO)	60 mg	Once-daily for up to 8 weeks
Maintain healing of EO and relief of heartburn	30 mg	Once-daily <sup>†</sup>
Treating heartburn associated with symptomatic non-erosive gastro-oesophageal reflux disease (GORD)	30 mg	Once-daily for 4 weeks

The first  
once-a-day PPI  
with novel dual  
delayed release  
technology<sup>1,3</sup>

- Greater 24 hours acid control than esomeprazole<sup>4</sup>
- Can be administered with clopidogrel<sup>1</sup>
- Once-daily, taken with or without food<sup>1</sup>



# Take Home Message

- Personalise Therapy and Advice
- Red Flags
- Have a Therapeutic Approach
- Optimise PPI Therapy --- Refer Refractory Cases
- New PPI Agent: Novel Option

# Thank You !

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