Managing Oesophagogastric (O-G) Cancer in General Practice

Wednesday 18th October 2018
Presenters: Prof Jon Emery
Prof Alex Boussioutas

The education has been developed in partnership with Cancer Council Victoria, the University of Melbourne and supported by the Victorian Government.

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The Royal Australian College of General Practitioners

Cancer Council Victoria · THE UNIVERSITY OF MELBOURNE · VICTORIA State Government

Acknowledgement of Country

We recognise the traditional custodians of the land and sea on which we live and work.

We pay our respects to Elders past and present.

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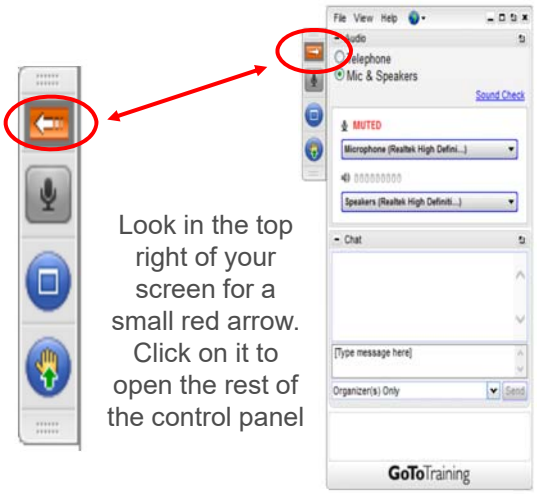
Where is my control panel?



Look in the top right of your screen for a small red arrow. Click on it to open the rest of the control panel

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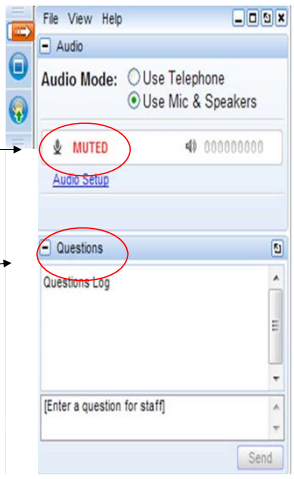
Listen only mode

You have been placed on “mute” to optimise the learning experience for you and your peers

Use the question box function to talk to us.



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Presenters

Presenter
Prof Jon Emery

Presenter
Prof Alex Boussioutas

Facilitator
Bobby Henry

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Learning Outcomes

By the end of this online QI & CPD activity you should be able to:

1. Describe the current evidence related to prevention, early detection, presentation, initial investigations and referral for oesophagogastric (O-G) cancer
2. Describe the current evidence about surveillance for Barrett's oesophagus
3. Use evidence-based tools and resources to determine patients risk of O-G cancer and to help the assessment of common symptoms associated with O-G cancer
4. Identify how to access local referral pathways for diagnostic imaging and specialist appointment for patients presenting with signs and symptoms of oesophagogastric cancers

RACGP | QI&CPD 2017–19 Accredited Activity Category 2 | 3 points

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Polling question

How would you rate your current awareness of the Optimal Care Pathways?

- Excellent
- Very good
- Good
- Fair
- Poor
- None

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Optimal Care Pathways

- Facilitate consistent care based on best evidence and practice
- Guides to optimal care across 15 tumour types for health professionals, including quick reference guides for GPs
- Have become recognised as a “standard of care”
- Encourage concept of an integrated pathway of care
- Emphasises the importance of communication across care sectors and at transition points for patients and carers
- Inform quality improvement projects by identifying gaps

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Oesophageal and Gastric Cancer

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Gastric cancer statistics

Estimated number of new cases in 2018

2,332 = 1,517 + 815

15th commonest cancer in Australia

Estimated number of deaths in 2018

1,078= 677 + 401

29% 5-year survival

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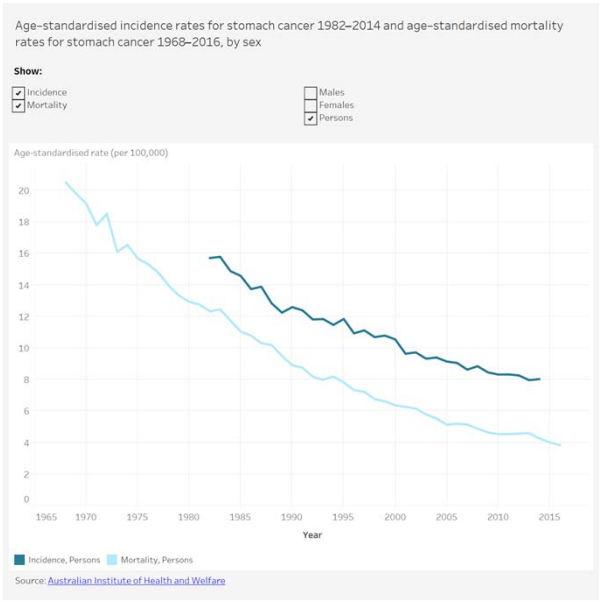
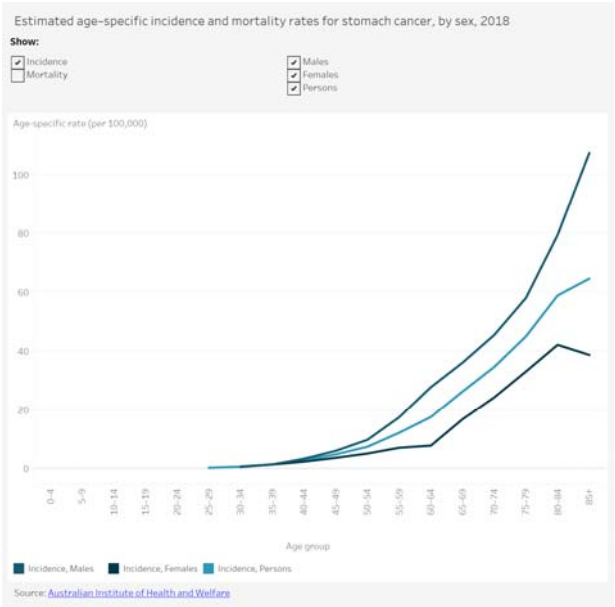
Gastric cancer statistics



Risk factors: age



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Risk factors

- Age – risk increases from 55 years
- Male
- Family history
- H pylori infection
- Smoking
- Race – Asian descent
- Pernicious anaemia
- Partial gastrectomy for ulcer disease

Oesophageal cancer statistics

Estimated number of new cases in 2018

1,685 = 1,182 + 504

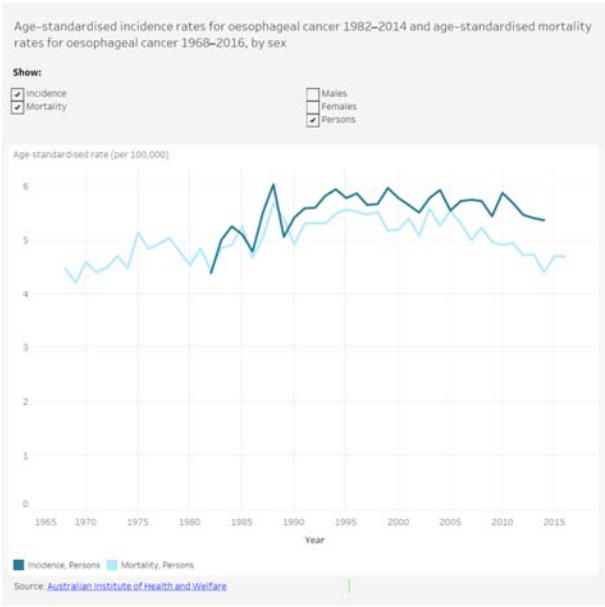
19th commonest cancer in Australia
12th commonest cause of cancer death

Estimated number of deaths in 2018

1,447= 1,045 + 403

21% 5-year survival

Oesophageal cancer statistics



Incidence of adeno-carcinoma increasing while squamous cell carcinoma is decreasing

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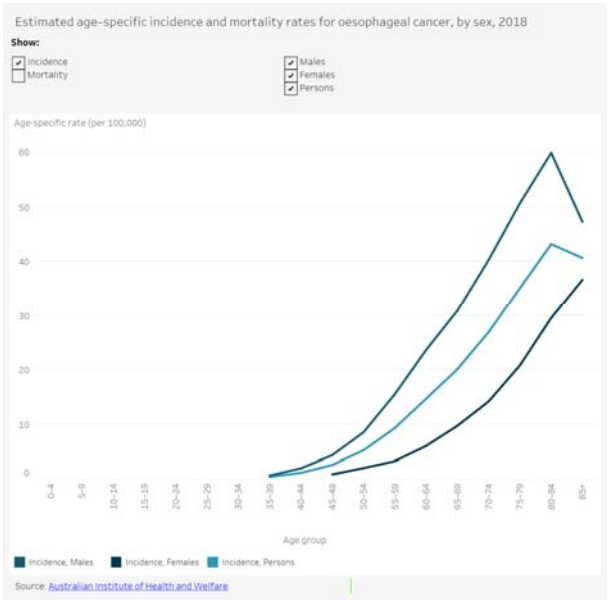
Risk factors: age



Risk factors

- Age – risk increases from >55 years
- Male
- Smoking
- Obesity
- Gastro-oesophageal reflux
- Alcohol
- Achalasia
- Barrett's oesophagus

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Polling question

Barrett's oesophagus can progress into:

Options:
Squamous cell carcinoma of the oesophagus
Adenocarcinoma of the oesophagus
Either type of oesophageal cancer

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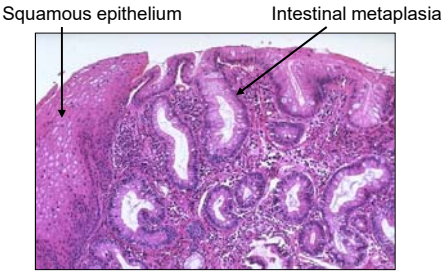
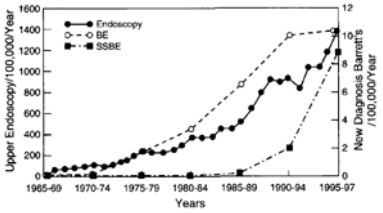
Defining Barrett's Oesophagus

- Replacement of Stratified squamous epithelium with intestinal metaplasia (columnar epithelium)
- Importance of Barrett's Oesophagus
  - Premalignant condition
    - Risk of Oesophageal adenocarcinoma
  - Increasing incidence
    - Australian detection rates for patients having endoscopy
      - 0.3% in 1990 to 1.9% 2002

(Kendall & Whiteman, *Am J Gastro*, 2006)



Incidence of Barrett's



(Falk, *Gastro*, 2002)

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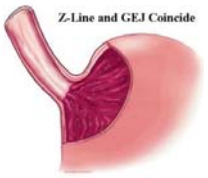
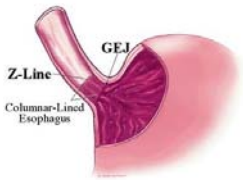
Changing definitions of Barrett's

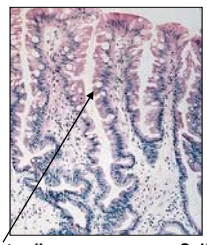
- Combined Endoscopic and Pathological
  - Endoscopy
    - proximal migration of Z-line
  - Pathology
    - Intestinal metaplasia (goblet cells)
    - Columnar epithelium

(Sharma, *Gastro*, 2004)
(Playford, *Gut*, 2006)
(Spechler, *Gastro*, 2011)

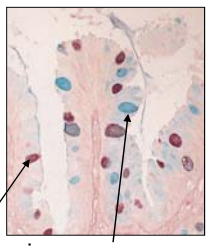




IM – Barrett's



Barrett's diamine stain



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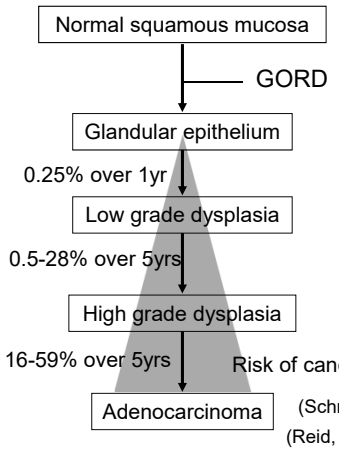
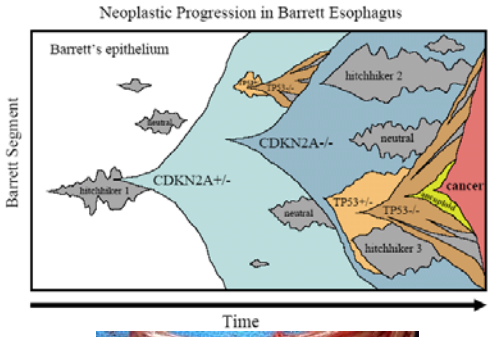
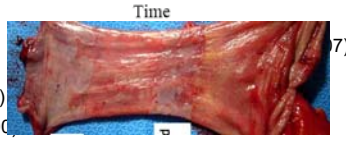
Barrett's a premalignant condition - progression to adenocarcinoma

Model of Barrett's progression



Clonal evolution theory of progression





(Schnell, *Gastro*, 2001)
(Reid, *Am J Gastro*, 200
(Skacel, *Am J Gastro*, 2000)

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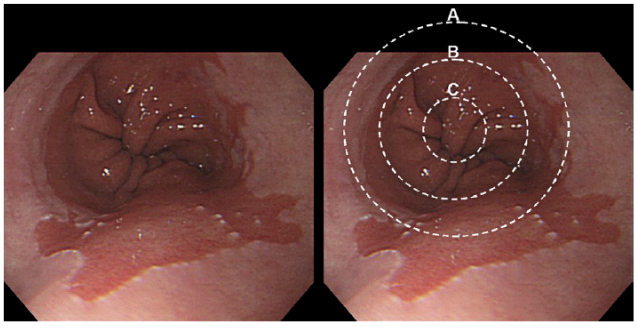
Challenges in diagnosis

Endoscopic landmarks

- Where does oesophagus end and stomach begin?
  - Gastric folds best landmark to begin measure



(Amano, *Gastrointestinal Endo*, 2005)

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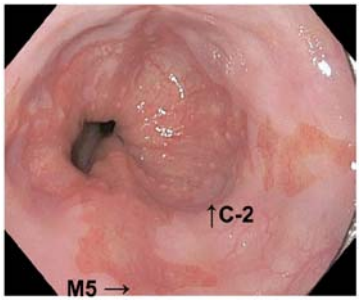
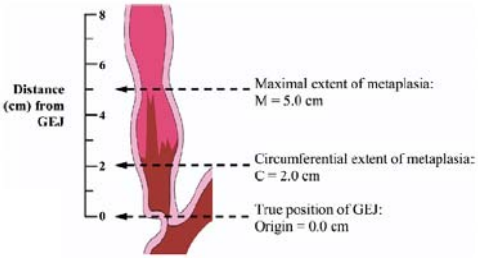
Challenges in diagnosis

How long is my Barrett's?

- Measurement from GOJ
- Prague criteria
  - Measure maximal extent of IM
  - Measure circumferential IM
- Length is one factor that determines risk for OA





(Sharma, *Gastro*, 2006)

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Defining Barrett's - summary

- Barrett's defined - endoscopy and pathology
- Barrett's oesophagus increasing prevalence
- Oesophageal adenocarcinoma increasing prevalence exponentially
- Barrett's is a premalignant condition
- Risk of progression associated with:
  - ✓ Length of Barrett's oesophagus
  - ✓ Presence and degree of dysplasia
  - ✓ Degree of molecular changes

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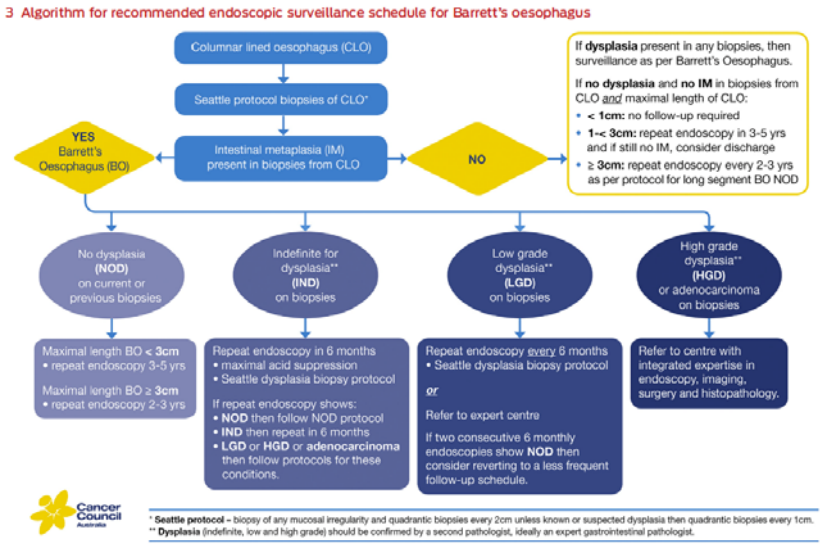
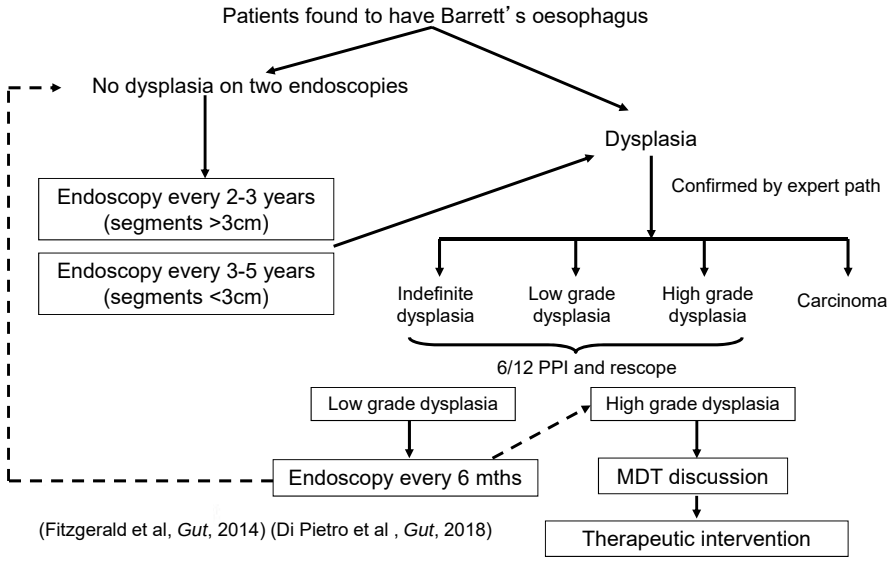
Endoscopic surveillance for Barrett's oesophagus



(Whiteman and Kendall, *MJA*, 2016) (http://wiki.cancer.org.au/australia/Guidelines:Barrett%27s)

BSG guidelines for Barrett's surveillance

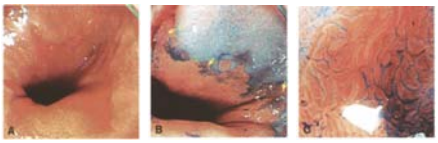


(Fitzgerald et al, *Gut*, 2014) (Di Pietro et al , *Gut*, 2018)

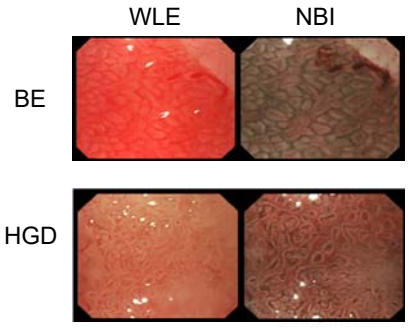
Developments in detection

Technology used to detect BE

- Chromoendoscopy
  - Use of vital stains to visualise metaplasia/dysplasia
    - Methylene Blue; Toluidine Blue
    - Indigo carmine
    - Lugols Iodine
- Narrow Band Imaging
  - Use of blue bandwidth of light to illuminate oesophagus
  - Blue light allows visualisation of mucosal vasculature
- *Confocal Endomicroscopy*
- *Optical Coherence Tomography*



WLE Chromo X10 Chromo X100



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Therapeutic technologies

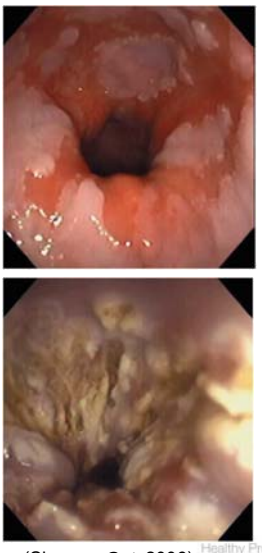
Thermal and Photothermal

- Electrocoagulation (MPEC)
- APC (Argon Plasma Coagulation)
- Nd-YAG laser
- Photodynamic therapy (PDT)
  - Use oral photosensitizer (5-ALA)
  - 530nm light

Radiofrequency Ablation

Mucosal resection

- EMR (Endoscopic mucosal resection)
- ESD (Endoscopic Submucosal Dissection)



(Sharma, *Gut*, 2006)

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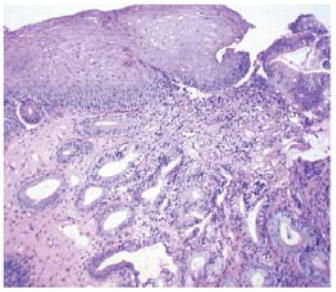
Complications of Ablation

Stricture	10-50%
Chest pain	30-50%
Dysphagia	<20%
Odynophagia	30-60%

Photosensitivity in PDT

Subsquamous Barrett's

- 5-90%
- Progression rate to OA unknown



Subsquamous Barrett's

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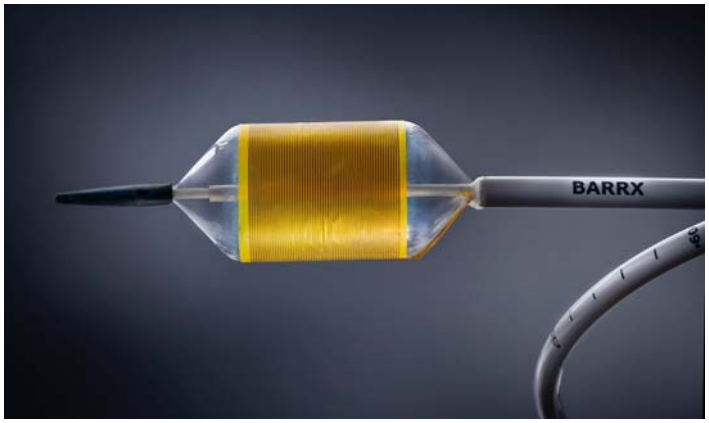
HALO^{360} Ablation Catheter



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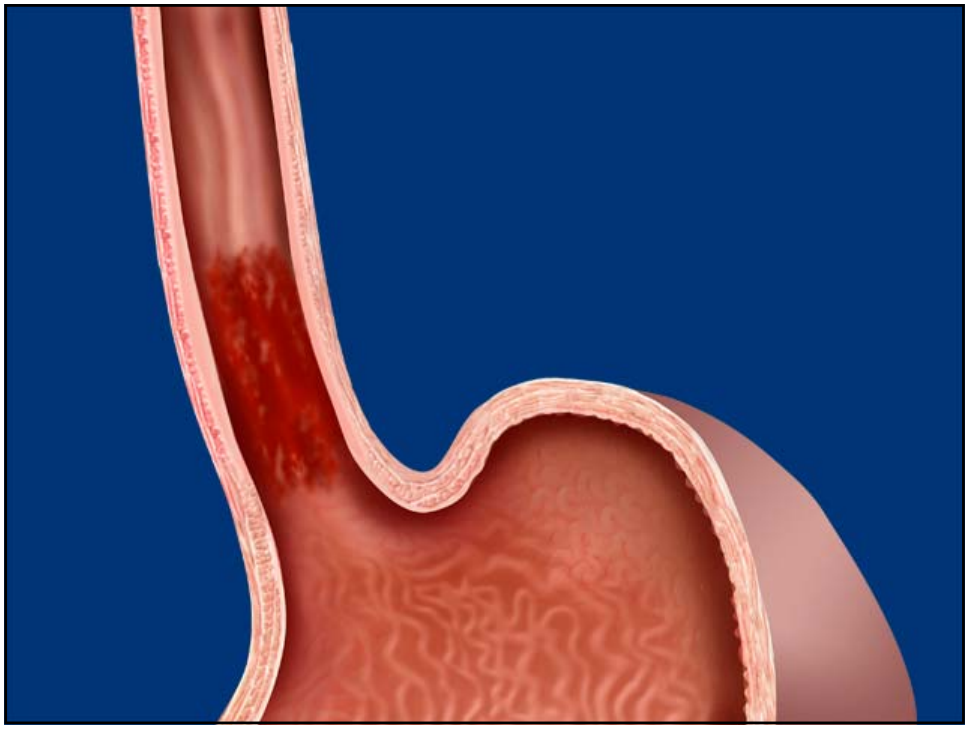
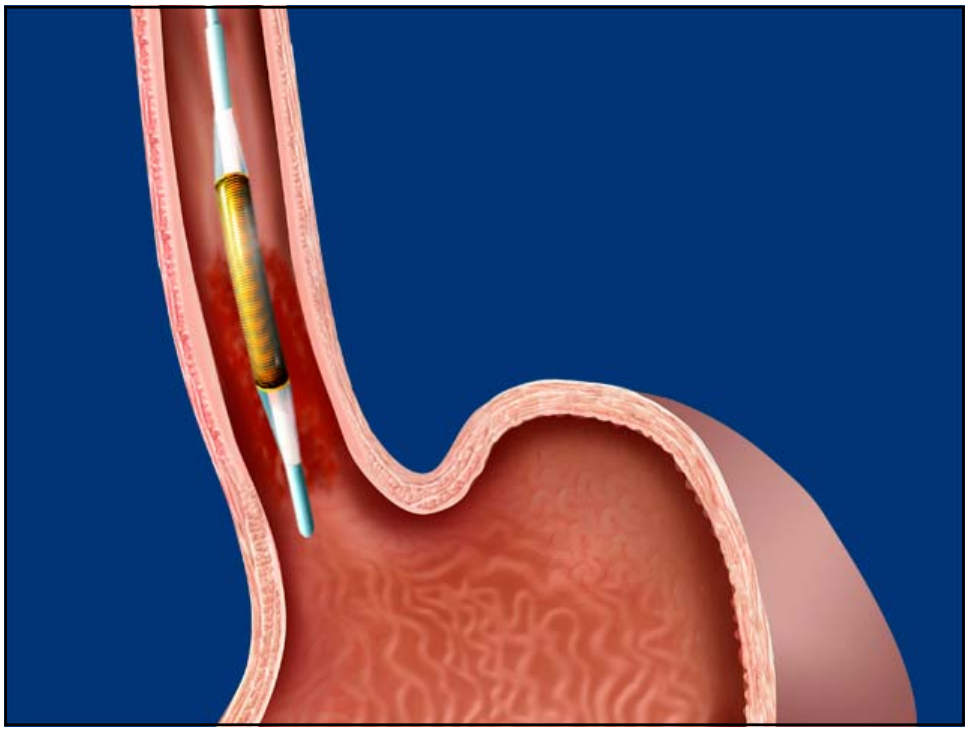
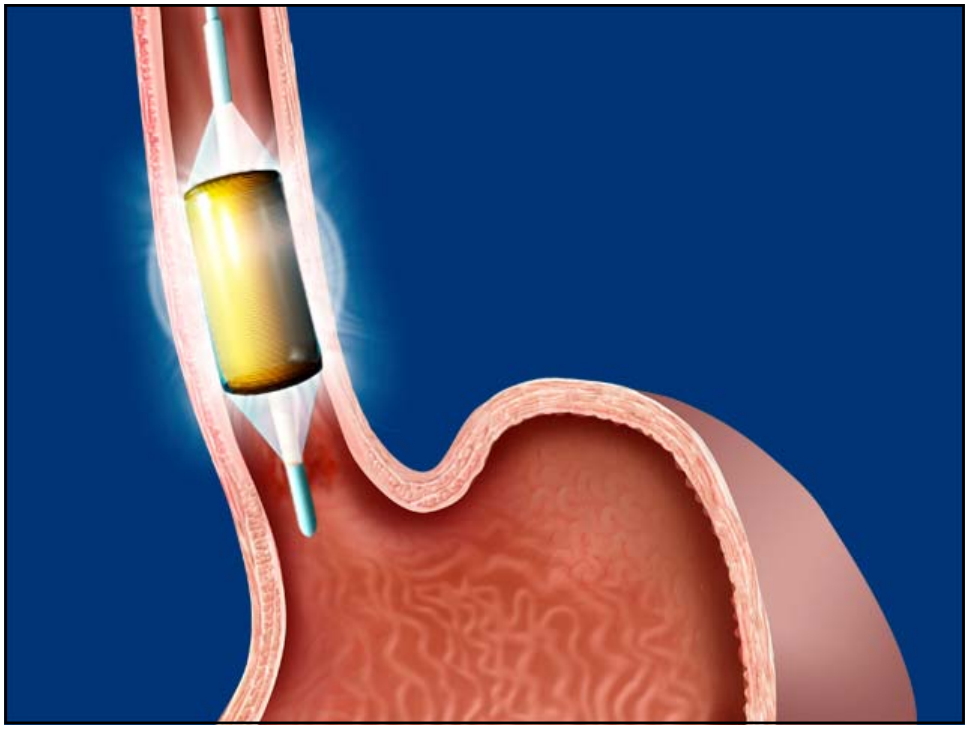
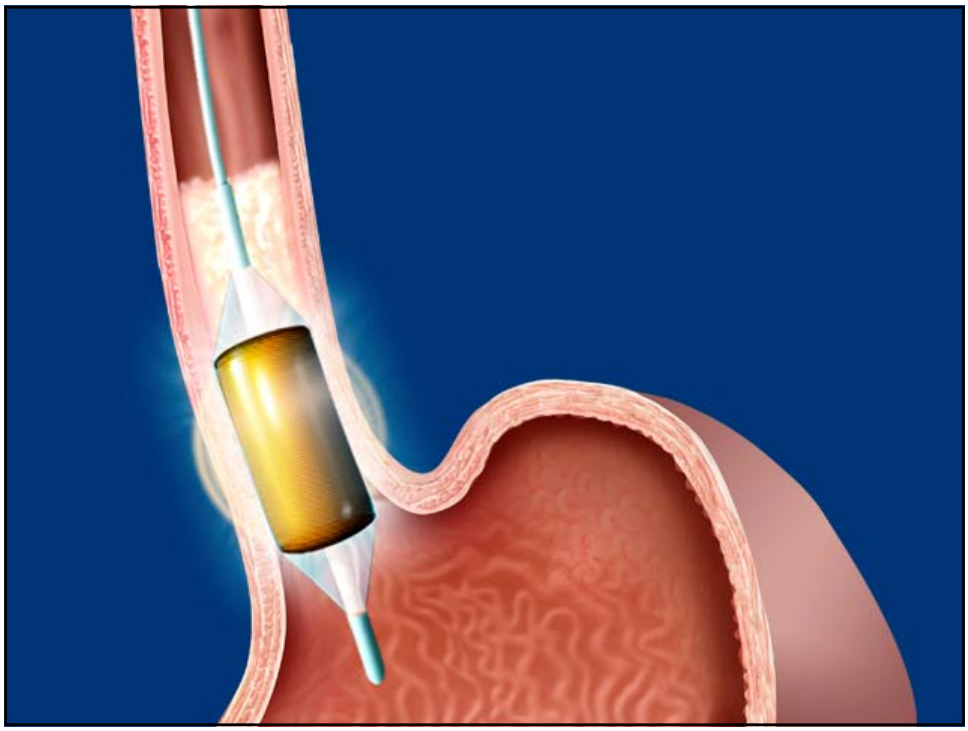
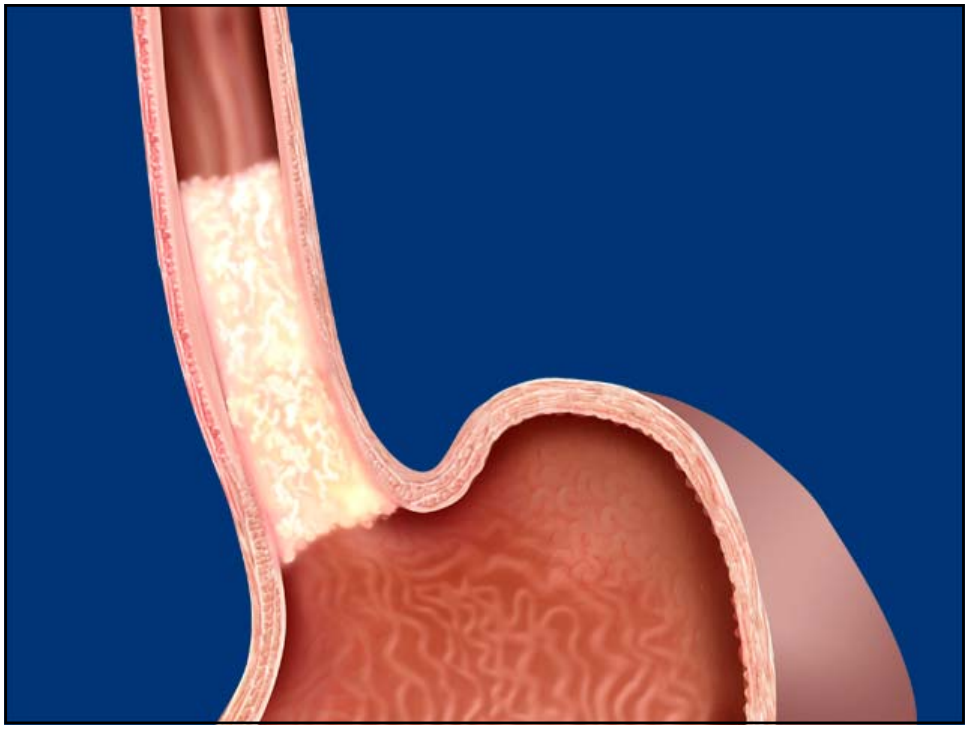


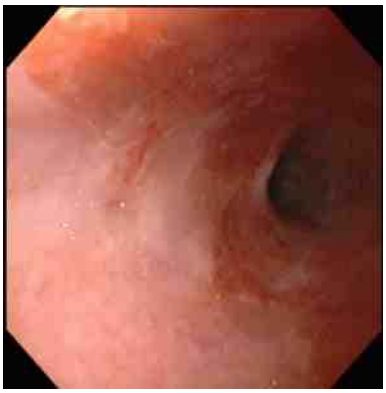




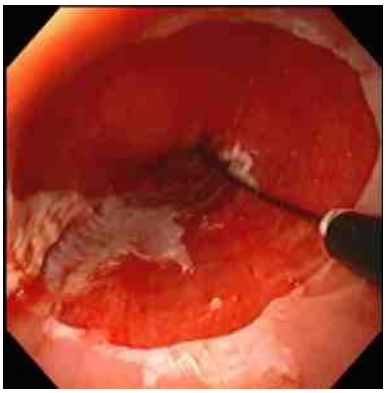




Endoscopic Appearance- post ablation



Baseline, 4 cm IM



Immediate Slough

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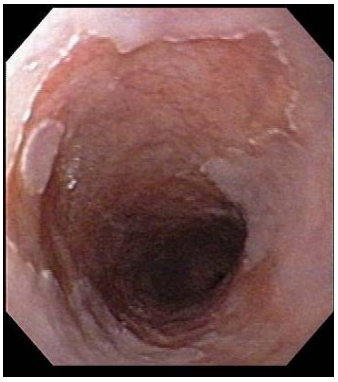
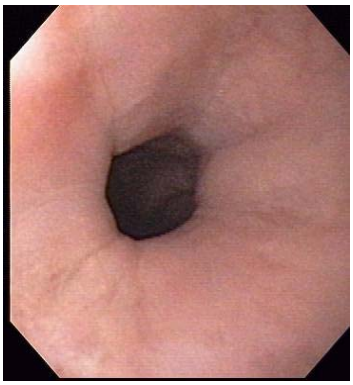
Complete Response after ablation





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The NEW ENGLAND JOURNAL of MEDICINE

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Radiofrequency Ablation in Barrett's Esophagus with Dysplasia

Nicholas J. Shaheen, M.D., M.P.H., Prateek Sharma, M.D., Bergein F. Overholt, M.D., Herbert C. Wolfsen, M.D., Richard E. Sampliner, M.D., Kenneth K. Wang, M.D., Joseph A. Galanko, Ph.D., Mary P. Bronner, M.D., John R. Goldblum, M.D., Ana E. Bennett, M.D., Blair A. Jobe, M.D., Glenn M. Eisen, M.D., M.P.H., M. Brian Fennerty, M.D., John G. Hunter, M.D., David E. Fleischer, M.D., Virender K. Sharma, M.D., Robert H. Hawes, M.D., Brenda J. Hoffman, M.D., Richard I. Rothstein, M.D., Stuart R. Gordon, M.D., Hiroshi Mashimo, M.D., Ph.D., Kenneth J. Chang, M.D., V. Raman Muthusamy, M.D., Steven A. Edmundowicz, M.D., Stuart J. Spechler, M.D., Ali A. Siddiqui, M.D., Rhonda F. Souza, M.D., Anthony Infantolino, M.D., Gary W. Falk, M.D., Michael B. Kimmey, M.D., Ryan D. Madanick, M.D., Amitabh Chak, M.D., and Charles J. Lightdale, M.D.

127 patients dysplastic BE

Randomised sham control

- PPI therapy/Sham vs PPI/HALO ablation

Endpoints

- Primary: Eradication of dysplasia; Eradication of Metaplasia
- Secondary: Progression of disease

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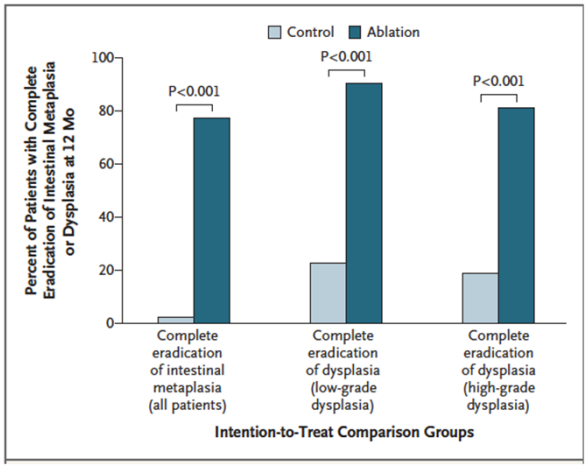
High rates of dysplasia eradication at 12m



(Shaheen et al, *NEJM*, 2009)

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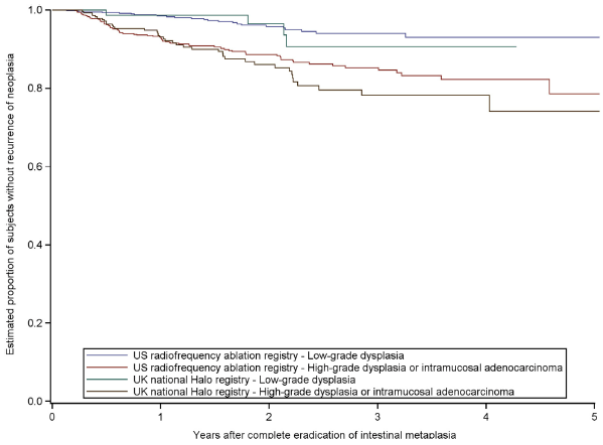
Durability of response to ablation



(Cotton et al, *Gastro*, 2018)

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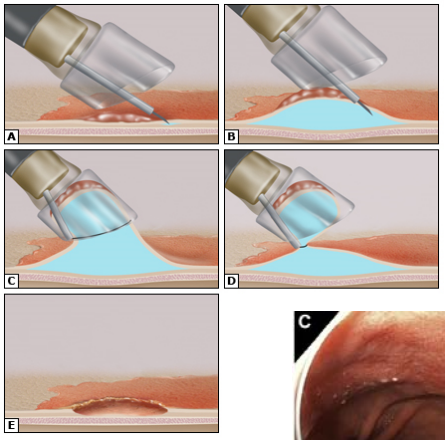
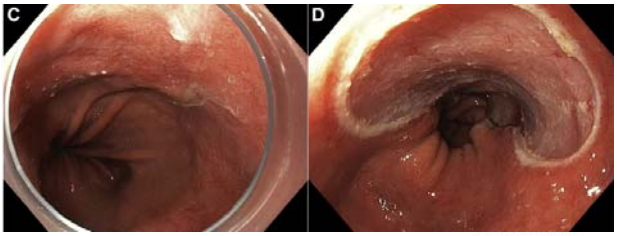
Endoscopic resection





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Take homes

- Barrett's oesophagus is a premalignant condition
- Screening to find Barrett's oesophagus not cost effective but perhaps in select populations
- Surveillance programs have altered to reflect local incidence rates
- Active research into endoscopic imaging to target bx
- Ablation and resection technologies have improved but not yet advocated for non-dysplastic Barrett's oesophagus*

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Polling question

Collin is a 59 year old man with a history of reflux controlled with intermittent PPIs. He sees you for a repeat prescription and says that he has started feeling food sticking in his chest. He has no other symptoms. What is the probability that he has oesophageal cancer?

2%
5%
15%
33%

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Symptoms of O-G cancer in primary care

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Symptoms of O-G cancer in primary care

Symptoms of O-G cancer in primary care

Dysphagia

43% of patients with O-G cancer had at least 3 visits to GP before referral

Research

Presentations to general practice before a cancer diagnosis in Victoria: a cross-sectional survey

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Symptoms of OG cancer in primary care

Low haemoglobin <12 g/dL for women <13 g/dL for men	Raised platelets >400 x10⁹/L	Constipation	Chest pain	Abdominal pain	Nausea or vomiting	Dyspepsia	Epigastric pain	Reflux	Weight loss	Dysphagia	PPV = Positive predictive value (%) or probability of Ca if Sx present
0.2	0.5	0.2	0.2	0.3	0.6	0.7	0.9	0.6	0.9	4.8	PPV as a single symptom
	0.6	0.4	0.3	0.5	0.9	1.0	1.6	0.9	1.0	4.6	Low haemoglobin
		0.9	0.8	0.8	1.4	1.4	1.9	1.6	1.8	6.1	Raised platelets
			0.4	0.4	0.6	0.8	1.4	0.7	1.1	4.2	Constipation
				0.3	0.6	0.7	0.9	0.6	1.1	5.8	Chest pain
					0.7	1.0	0.9	0.6	1.4	6.5	Abdominal pain
					1.0	1.3	1.3	2.3	2.8	7.3	Nausea or vomiting
						1.2	1.4	0.9	2.1	9.8	Dyspepsia
								1.5	4.2	9.3	Epigastric pain
									3.1	5.0	Reflux
										9.2	Weight loss
										5.5*	Dysphagia

Probability of cancer
≤1% 1-2% 2-5% >5%
* second presentation

Figure 1 shows the probability of oesophageal or gastric cancer for individual symptoms and pairs of symptoms, including second presentation* of same symptom **in people over 55 years.**[1]

Probabilities highlighted in red are >5% and urgent referral should be considered.

Reference: 1. Stapley, S et al. The risk of oesophagogastric cancer in symptomatic patients in primary care: a large case-control study using electronic records. British Journal of Cancer. 2013;108, 25-31.

Upper gastrointestinal endoscopy categorisation guidelines for adults 2018

	Category 1 (<30 days)	Category 2 (<60 days)	Category 3 (<180 days)	Comments/Not Indicated
Indication A: Symptoms and investigations				
➢ **Dysphagia** alone is an automatic Category 1 ➢ **Additional symptom:** dyspepsia, GORD, upper abdominal pain, persistent nausea/vomiting, early satiety or unexplained loss of appetite ➢ **Abnormal blood test:** low Hb, low ferritin, microcytosis, hypochromia, raised platelets				
1.	**Dysphagia** • any age			
2.	**Haematemesis/Melaena** • any age (see Comments)			Delayed presentation of symptoms; assume haemodynamically stable and no ongoing acute bleed requiring immediate admission.
3.	**Anaemia and/or Iron deficiency**, *and:* • age ≥ 55 years	**Anaemia and/or iron deficiency**, *and:* • age < 55 years		Refer to investigation of iron-deficiency anaemia in Explanatory notes.
4.	**Abnormal imaging**, likely oesophageal or gastric cancer • any age			Upper gastrointestinal endoscopy is not indicated for metastatic adenocarcinoma of unknown origin when results will not alter management.
5.	**Weight loss, unexplained**, *and:* • age ≥ 55 years, *plus* – any **additional symptom** *or* – **abnormal blood test** or imaging	**Weight loss, unexplained**, *and:* • age < 55 years, *plus* – any **additional symptom** *or* – **abnormal blood test** or imaging		
6.	**Dyspepsia**, *and:* • age ≥ 55 years, *plus* – any **additional symptom** *or* – **abnormal blood test** or imaging *or* – atrophic gastritis *or* – FHx of upper GI cancer in 1st degree relative	**Dyspepsia**, *and:* • age < 55 years, *plus* – any **additional symptom** *or* – **abnormal blood test** or imaging *or* – atrophic gastritis *or* – FHx of upper GI cancer in 1st degree relative **Dyspepsia**, *and:* • any age, *plus* – non-responsive to PPI and/or *H. pylori* therapy or *H. pylori*-negative		Refer to test and treat policy for *H. pylori* in Explanatory notes. Upper gastrointestinal endoscopy is not indicated if symptoms resolved after test and treatment for *H. pylori*.

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Upper gastrointestinal endoscopy categorisation guidelines for adults 2018

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Combinations of symptoms, age and abnormal test results

https://www2.health.vic.gov.au/about/publications/policiesandguidelines/gastrointestinal-endoscopy-categorisation-guidelines-adults-2018

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Urgent upper GI endoscopy

- Dysphagia at any age
- Haematemesis or melaena at any age
  - Assume delayed presentation and haemodynamically stable
  - Not requiring immediate admission

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Polling question

Mary is a 57 year old woman who came to see you after being found to be anaemic when she went to donate blood. She has no relevant symptoms. Her last period was 5 years ago. She is a non-smoker, drinks 10 units per week and is vegetarian. Her Hb is 111 g/l and MCV 78. Her serum ferritin is low and total iron binding capacity increased. What will you do next?

Refer for colonoscopy
Refer for colonoscopy and gastroscopy
Order immunochemical FOBT and coeliac screen
Prescribe 3 months of iron supplements and repeat FBC and iron studies

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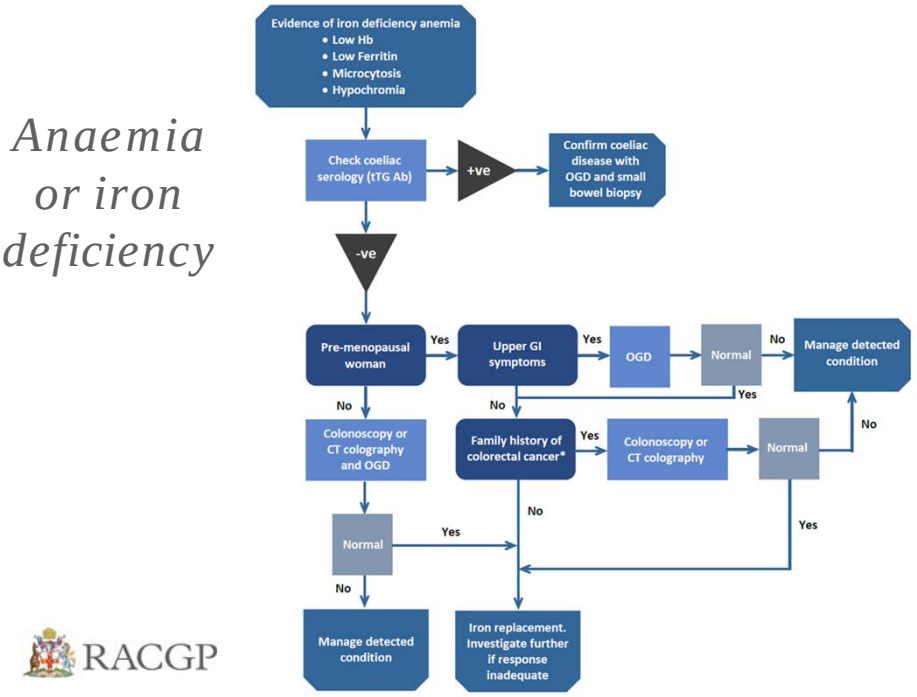
Anaemia or iron deficiency



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Gastro-oesophageal reflux (GORD)

CATEGORY 1 (<30 days)	**CATEGORY 2** (<60 days)
GORD, recent onset, *and:* • age ≥ 55 years, with • any **additional symptom** or • **abnormal blood test** or imaging	**GORD**, recent onset, *and:* • age < 55 years, with • any **additional symptom** or • **abnormal blood test** or imaging

Additional symptom: dyspepsia, upper abdominal pain, persistent nausea/vomiting, weight loss

Abnormal blood test: low Hb, low ferritin, raised platelets

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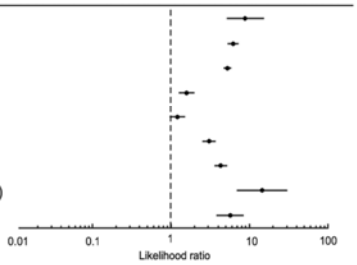
How useful is thrombocytosis in predicting an underlying cancer in primary care? a systematic review

Sarah E R Bailey[a,*], Obi C Ukoumunne[b], Elizabeth Shephard[a] and Willie Hamilton[a]

Ref	Cancer site	Cases		Controls		LR (95% CI)
		n	Total	n	Total	
[5]	Lung	34	247	19	1235	8.9 (5.19-15.41)
[30]	Kidney	348	3183	251	15707	6.20 (5.3-7.3)
[7]	Oesophago-gastric	707	7657	568	37699	5.28 (4.73-5.90)
[8]	Uterine	110	3166	207	9537	1.60 (1.27-2.01)
[34]	Breast	91	4407	369	21755	1.22 (0.97-1.53)
[33]	Bladder	156	4935	247	24098	3.08 (2.53-3.76)
[10]	Pancreatic	214	3635	222	16459	4.36 (3.63-5.25)
[31]	Ovarian	26	212	9	1060	14.61 (6.94-30.73)
[11]	Colorectal	48	349	42	1744	5.71 (3.84-8.50)



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Dyspepsia, *and:* • age ≥ 55 years, with • any **additional symptom** or • **abnormal blood test** or imaging	**Dyspepsia,** *and:* • age ≥ 55 years, non-responsive to PPI and/or *H. pylori* therapy or *H. pylori*-negative **Dyspepsia** *and:* • age < 55 years, with • any **additional symptom** or • **abnormal blood test** or imaging	**Dyspepsia** *and:* • age < 55 years, non-responsive to PPI and/or *H. pylori* therapy or *H. pylori*-negative

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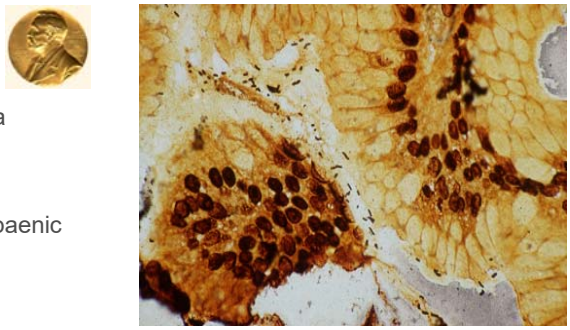
Helicobacter pylori

GI Disease association
- Peptic Ulcer Disease
- Gastric Cancer
- Gastric MALT lymphoma

Extragastric associations
- Iron deficiency anaemia
- Idiopathic Thrombocytopaenic Purpura (ITP)



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Who to eradicate H. pylori?

H. pylori infected persons with
- Peptic ulcer disease
- Early Gastric Cancer treated curatively
- Gastric Intestinal Metaplasia
  - Although only ~50% regress (atrophic gastritis)
- Unexplained iron deficiency anaemia
- ITP
- Vitamin B12 deficiency
- MALToma
- Dyspepsia (with no alarm symptoms)
  - test and treat strategy
- chronic NSAID or aspirin use
  - Particularly if previous peptic ulceration

(Malfertheiner et al, *Gut*, 2017)

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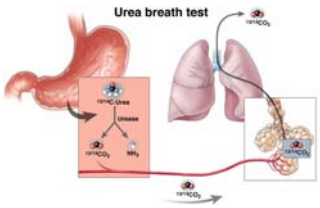
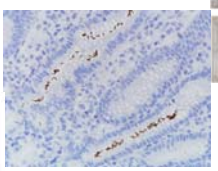
What test to use?



Non-invasive testing
- Urea Breath Test – C^{13}
  - Sensitivity 88-85%; Specificity 95-100%
    (Howden and Hunt, *Am J Gastro*, 1998)(Gisbert et al, *Am J Gastro*, 2006)
- Stool antigen test
  - Sensitivity 94%; Specificity 97%
    (Braden et al, *BMJ*, 2000; Vaira et al, *Lancet*, 1999; Veijola et al, *WJG*, 2005; Calvet et al, *Clin Inf Dis*, 2009)
- Serology
  - Sensitivity ~85%; Specificity ~79%
    (Loy et al, *Am J Gastro*, 1996)



Invasive testing
- Rapid Urease Test
- Histology
- Culture

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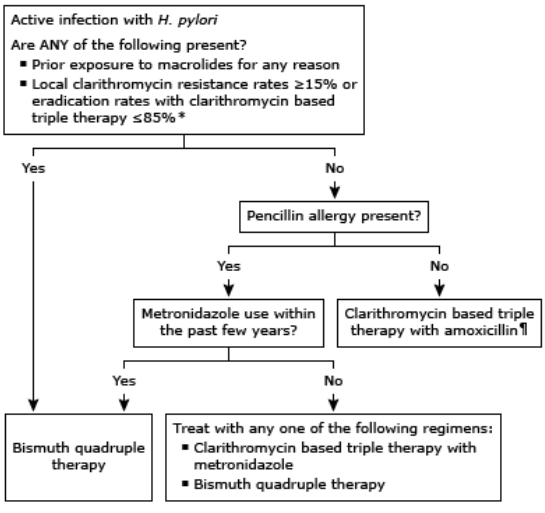
Initial therapy for H. pylori infection



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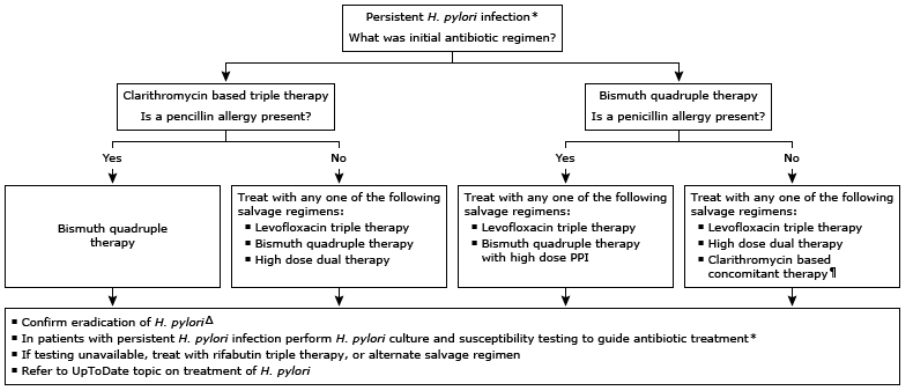
Second line therapy for H. Pylori



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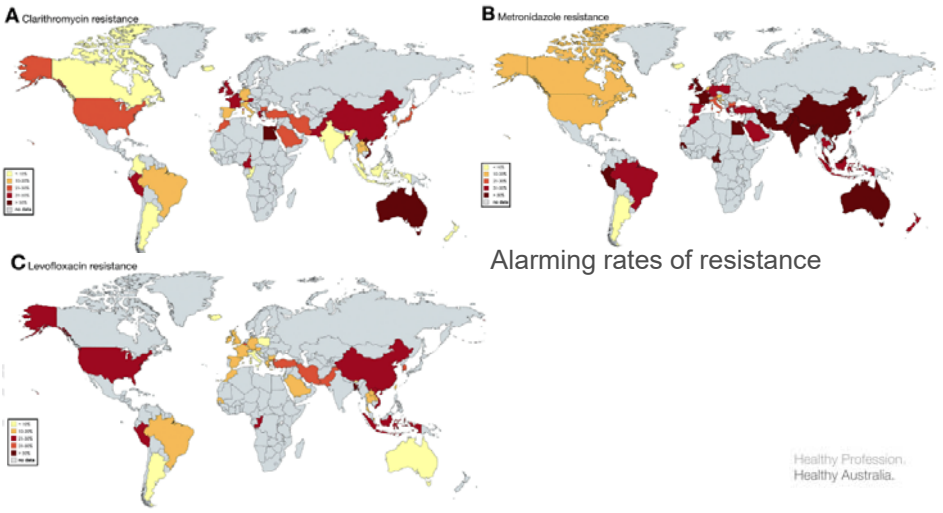
Prevalence of Antibiotic Resistance in *Helicobacter pylori*: A Systematic Review and Meta-Analysis in World Health Organization Regions

Alessia Savoldi,[1] Elena Carrara,[2] David Y. Graham,[3] Michela Conti,[2] and Evelina Tacconelli[1,2]

[1]*Division of Infectious Diseases, Department of Internal Medicine I, German Center for Infection Research, University of Tübingen, Tübingen, Germany;* [2]*Division of Infectious Diseases, Department of Diagnostic and Public Health, G.B. Rossi University Hospital, University of Verona, Verona, Italy; and* [3]*Department of Medicine, Michael E. DeBakey Veterans Affairs Medical Center and Baylor College of Medicine, Houston, Texas*



Alarming rates of resistance

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How to eradicate H. pylori?

1st line therapy
- PPI + amoxicillin + clarithromycin for 7 days
- Beware global resistance to clarithromycin and metronidazole

2nd line therapy
- Dependent on region and rates of clarithromycin and metronidazole resistance
- Bismuth containing Quadruple therapy
  - (Bismuth + PPI + metronidazole + tetracycline (14 days)
- Or
- Levofloxacin triple therapy
  - Levofloxacin + PPI + amoxicillin (10-14 days)

3rd line therapy
- Endoscopy and culture for sensitivities

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Thank you

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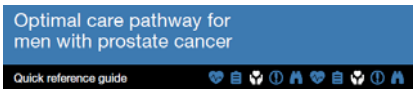
Supportive care resources

- Cancer Council
  - Phone 13 11 20
- OCP - quick reference guide & full version
- What to expect: only if a positive diagnosis
- LiveLighter program
  - www.livelighter.com.au
  - Resources for HPs and Patients
- Quitline
  - www.quit.org.au for HP referral
  - GP software link
  - 13 78 48



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Quit

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Learning Outcomes

By the end of this online QI & CPD activity you should be able to:

1. Describe the current evidence related to prevention, early detection, presentation, initial investigations and referral for oesophagogastric (O-G) cancer
2. Describe the current evidence about surveillance for Barrett's oesophagus
3. Use evidence-based tools and resources to determine patients risk of O-G cancer and to help the assessment of common symptoms associated with O-G cancer
4. Identify how to access local referral pathways for diagnostic imaging and specialist appointment for patients presenting with signs and symptoms of oesophagogastric cancers

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