Screening for Barrett's Cancer: *Who, How and Why?*

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Professor of Medicine

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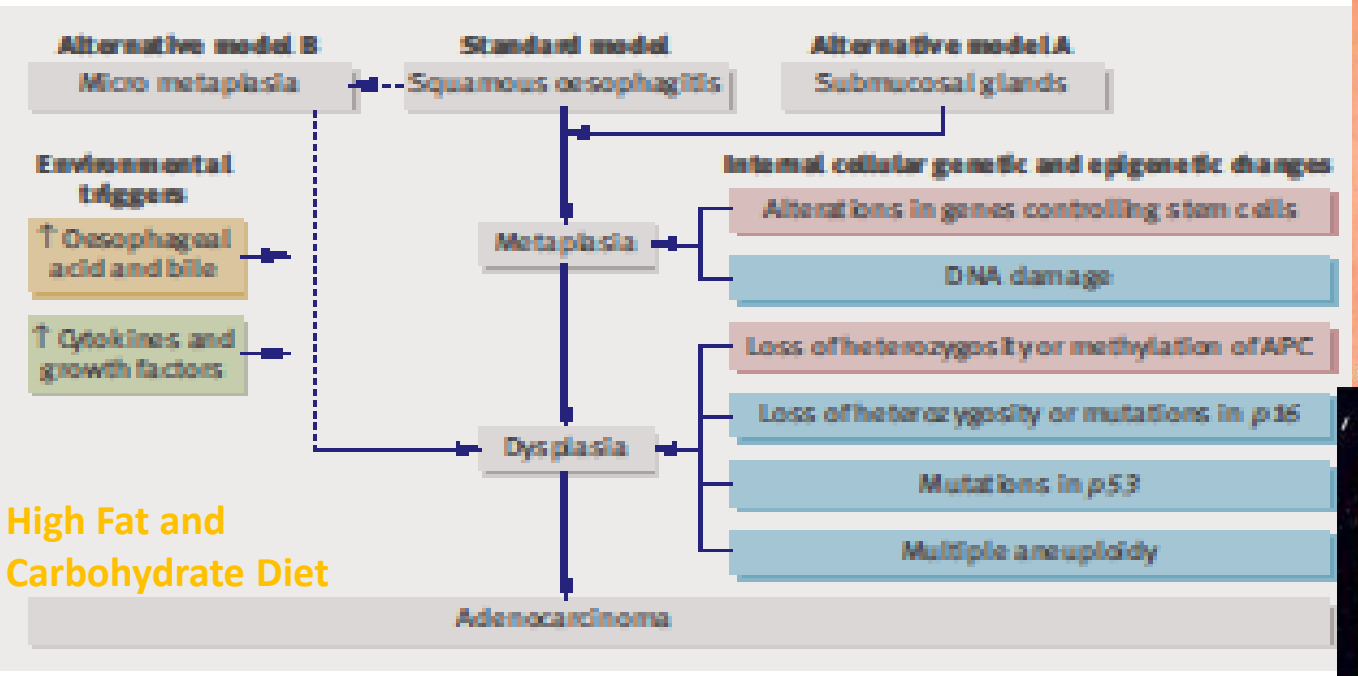
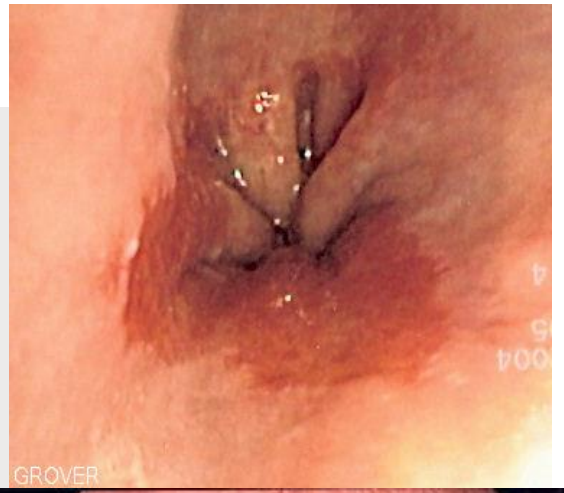
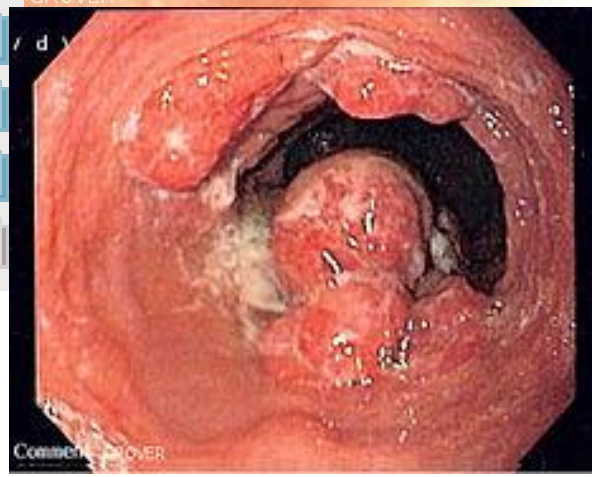
Complex Genetic interplay versus unclear Environment







Reductionism strongly reflects a certain perspective on causality

Transdisciplinary/**Holistic** system needed where causality unclear

Brit Med J Jankowski et al, 2010

Making sense of Barrett's oesophagus; doing more for the few

BOB CAT: a Large-Scale Review and Delphi Consensus for Management of Barrett's Esophagus With No Dysplasia, Indefinite for, or Low-Grade Dysplasia

Bennett C et al, Am J Gastroenterol. 2015;110:662-682

ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus

Nicholas J. Shaheen, MD, MPH, FACG[1], Gary W. Falk, MD, MS, FACG[2], Prasad G. Iyer, MD, MSc, FACG[3] and Lauren Gerson, MD, MSc, FACG[4]

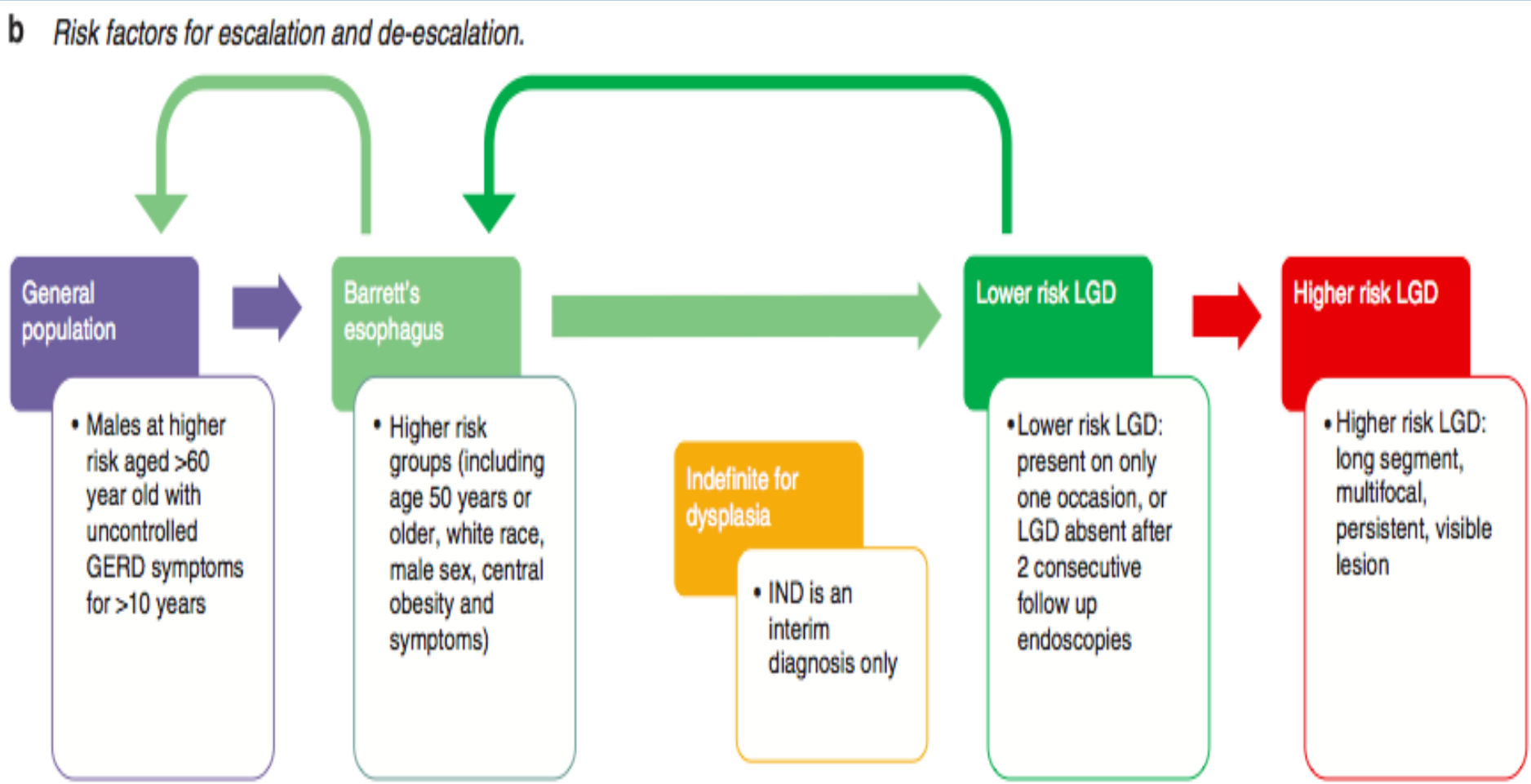
Am J Gastroenterol advance online publication, 3 November 2015; doi:10.1038/ajg.2015.322

What is screening?

Screening means testing people for early stages of a disease before they have any symptoms.
For screening to be useful the tests

- need to be reliable at picking up cancers
- need to be simple and quick
- shouldn't show that someone has cancer when they don't (false positive results)
- need to not cause any harm

Who?


b Risk factors for escalation and de-escalation.
General population
• Males at higher risk aged >60 year old with uncontrolled GERD symptoms for >10 years
Barrett's esophagus
• Higher risk groups (including age 50 years or older, white race, male sex, central obesity and symptoms)
Indefinite for dysplasia
• IND is an interim diagnosis only
Lower risk LGD
• Lower risk LGD: present on only one occasion, or LGD absent after 2 consecutive follow up endoscopies
Higher risk LGD
• Higher risk LGD: long segment, multifocal, persistent, visible lesion

EPIDEMIOLOGY AND NATURAL HISTORY OF BE

Top

Summary statements

What are the risk factors for BE?

1. The known risk factors for the presence of BE include the following:
    a. Chronic (>5 years) GERD symptoms
    b. Advancing age (>50 years)
    c. Male gender
    d. Tobacco usage
    e. Central obesity
    f. Caucasian race
2. Alcohol consumption does not increase risk of BE. Wine drinking may be a protective factor.
3. BE is more common in first-degree relatives of subjects with known BE.

What are the risk factors associated with dysplasia and development of EAC in patients with BE?

1. The known risk factors for the development of neoplasia in BE include:
    a. Advancing age
    b. Increasing length of BE
    c. Central obesity
    d. Tobacco usage
    e. Lack of nonsteroidal anti-inflammatory agent use
    f. Lack of PPI use
    g. Lack of statin use.

What is the cancer risk in BE, based on degree of dysplasia?

1. The risk of cancer progression for patients with nondysplastic is ~0.2–0.5% per year.
2. For patients with low-grade dysplasia (LGD) the annual risk of progression to cancer is ~0.7% per year.
3. For patients with high-grade dysplasia (HGD), the annual risk of neoplastic progression is ~7% per year.
4. The majority (>90%) of patients diagnosed with BE die of causes other than EAC.

Pre-Endoscopy - Screening

Recommendation

We suggest endoscopic screening to detect BE (and for the investigation of dyspepsia) in men >60 years old with prolonged GERD (≥10 years) symptoms.

Conditional recommendation, very low-quality evidence.

BOSS Trial (CI H Barr) awaited in 2021 for efficacy of surveillance

How?

SURVEILLANCE OF BE

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Recommendations

13. Patients should only undergo surveillance after adequate counseling regarding risks and benefits of surveillance (strong recommendation, very low level of evidence).
14. Surveillance should be performed with high-definition/high-resolution white light endoscopy (strong recommendation, low level of evidence).
15. Routine use of advanced imaging techniques other than electronic chromoendoscopy is not recommended for endoscopic surveillance at this time (conditional recommendation, very low level of evidence).
16. Endoscopic surveillance should employ four-quadrant biopsies at 2 cm intervals in patients without dysplasia and 1 cm intervals in patients with prior dysplasia (strong recommendation, low level of evidence).
17. Mucosal abnormalities should be sampled separately, preferably with endoscopic mucosal resection (EMR). Inability to perform EMR in the setting of BE with nodularity should lead to referral to a tertiary care center (strong recommendation, low level of evidence).
18. Biopsies should not be obtained in mucosal areas with endoscopic evidence of erosive esophagitis until after intensification of antireflux therapy to induce mucosal healing (strong recommendation, very low level of evidence).
19. For BE patients with dysplasia of any grade, review by two pathologists, at least one of whom has specialized expertise in gastrointestinal (GI) pathology, is warranted because of interobserver variability in the interpretation of dysplasia (strong recommendation, moderate level of evidence).
20. Use of additional biomarkers for risk stratification of patients with BE is currently not recommended (strong recommendation, low level of evidence).

DIAGNOSIS OF BE

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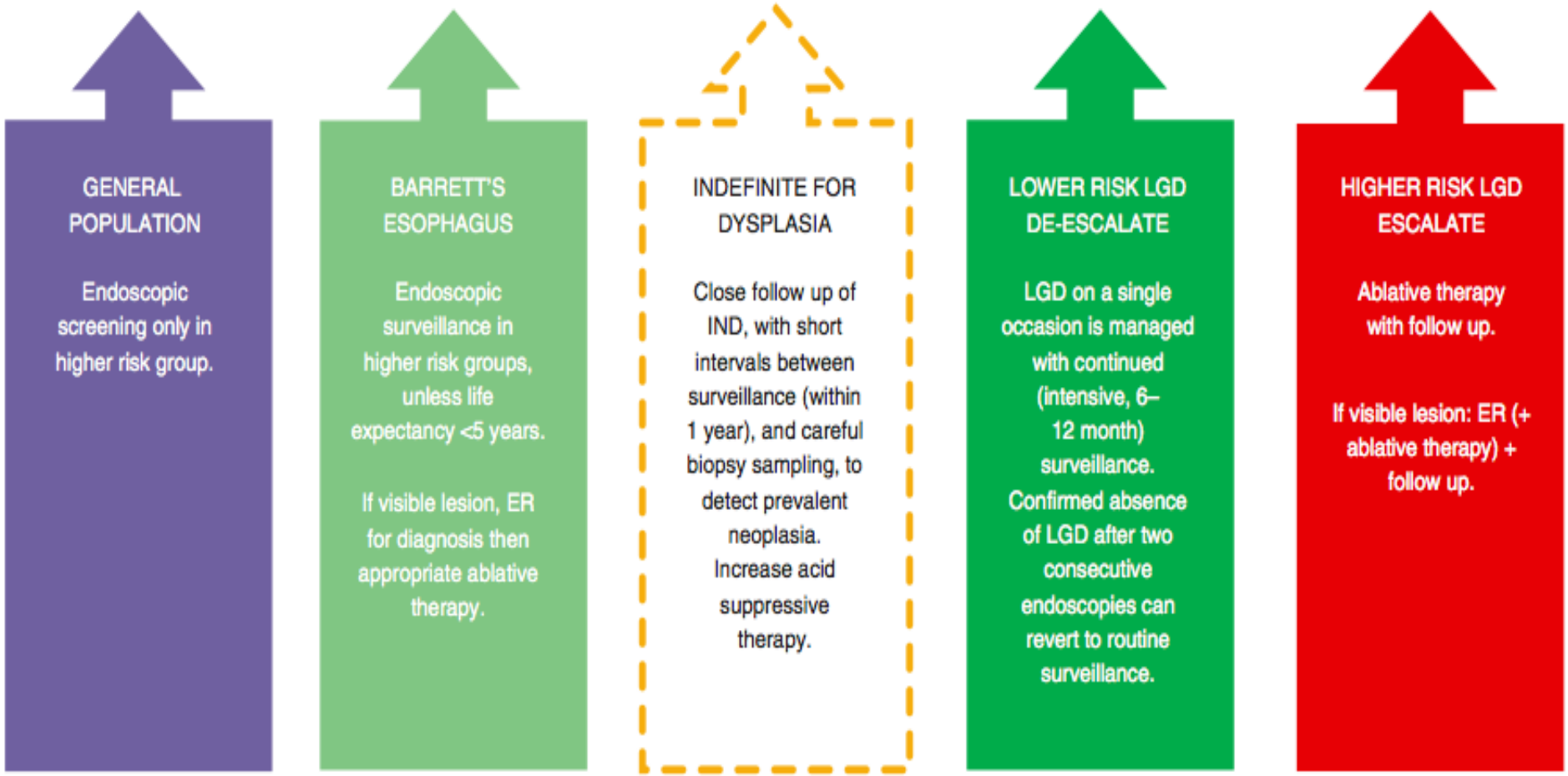
Recommendations

1. BE should be diagnosed when there is extension of salmon-colored mucosa into the tubular esophagus extending ≥1 cm proximal to the gastroesophageal junction (GEJ) with biopsy confirmation of IM (strong recommendation, low level of evidence).
2. Endoscopic biopsy should not be performed in the presence of a normal Z line or a Z line with <1 cm of variability (strong recommendation, low level of evidence).
3. In the presence of BE, the endoscopist should describe the extent of metaplastic change including circumferential and maximal segment length using the Prague classification (conditional recommendation, low level of evidence).
4. The location of the diaphragmatic hiatus, GEJ, and squamocolumnar junction should be reported in the endoscopy report (conditional recommendation, low level of evidence).
5. In patients with suspected BE, at least 8 random biopsies should be obtained to maximize the yield of IM on histology. In patients with short (1–2 cm) segments of suspected BE in whom 8 biopsies may be unobtainable, at least 4 biopsies per cm of circumferential BE, and one biopsy per cm in tongues of BE, should be obtained (conditional recommendation, low level of evidence).
6. In patients with suspected BE and lack of IM on histology, a repeat endoscopy should be considered in 1–2 years of time to rule out BE (conditional recommendation, very low level of evidence).

c *Intervention steps for escalation and de-escalation.*



J Gastroenterol 2008; 43:38–44
DOI 10.1007/s00535-007-2124-y

Journal of Gastroenterology

Autonomic nervous function in upper gastrointestinal endoscopy: a prospective randomized comparison between transnasal and oral procedures

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Unsedated transnasal EGD

1. Feasibility
2. Safety
3. Accuracy & quality of biopsies
4. Tolerance
5. 2 way or 4 way angulations
6. Self-training
7. Cost savings

Health Benefits and Cost Effectiveness of Endoscopic and Nonendoscopic Cytosponge Screening for Barrett's Esophagus

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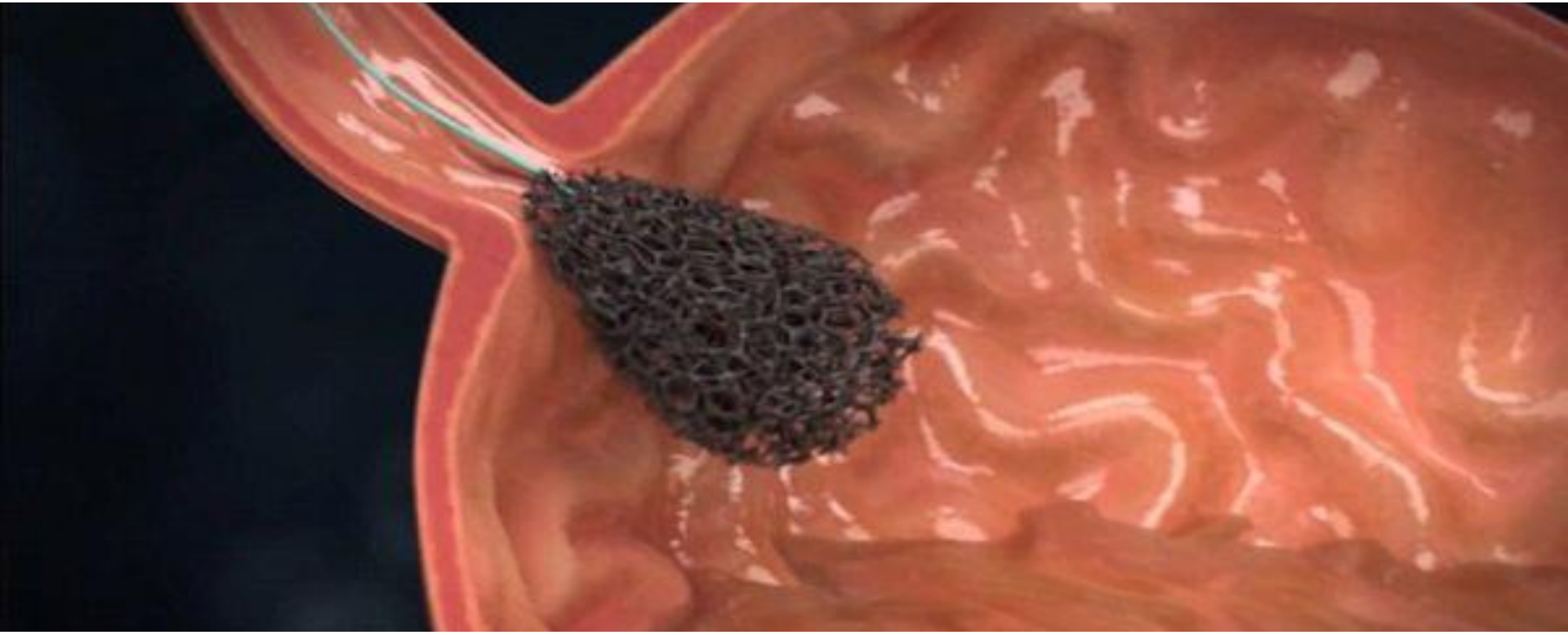


Accuracy of screening tests		
Endoscopy sensitivity and specificity	100%	
Cytosponge sensitivity	73.3%	60%–90%[a]
Cytosponge specificity	93.8%	60%–100%[a]
Endoscopy uptake rate	23%	20%–60%
Cytosponge uptake rate	45%	20%–60%
Endoscopy uptake after positive Cytosponge testing	80%	
Cycle length	30 days	

Screening to detect BE

7. Endoscopic screening for BE is not justified in the general population. STATEMENT ENDORSED, overall agreement 94.2%. A+, 58.7%; A, 35.5%; U, 2.5%; D, 1.7%; D+, 1.7%.

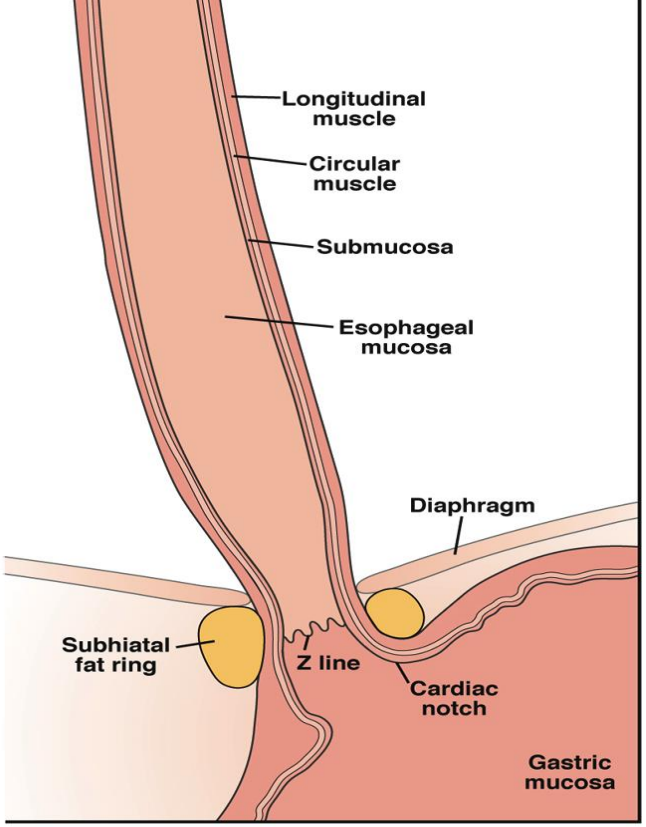
Table 1. GI disorders for which clinical genetic testing is currently available

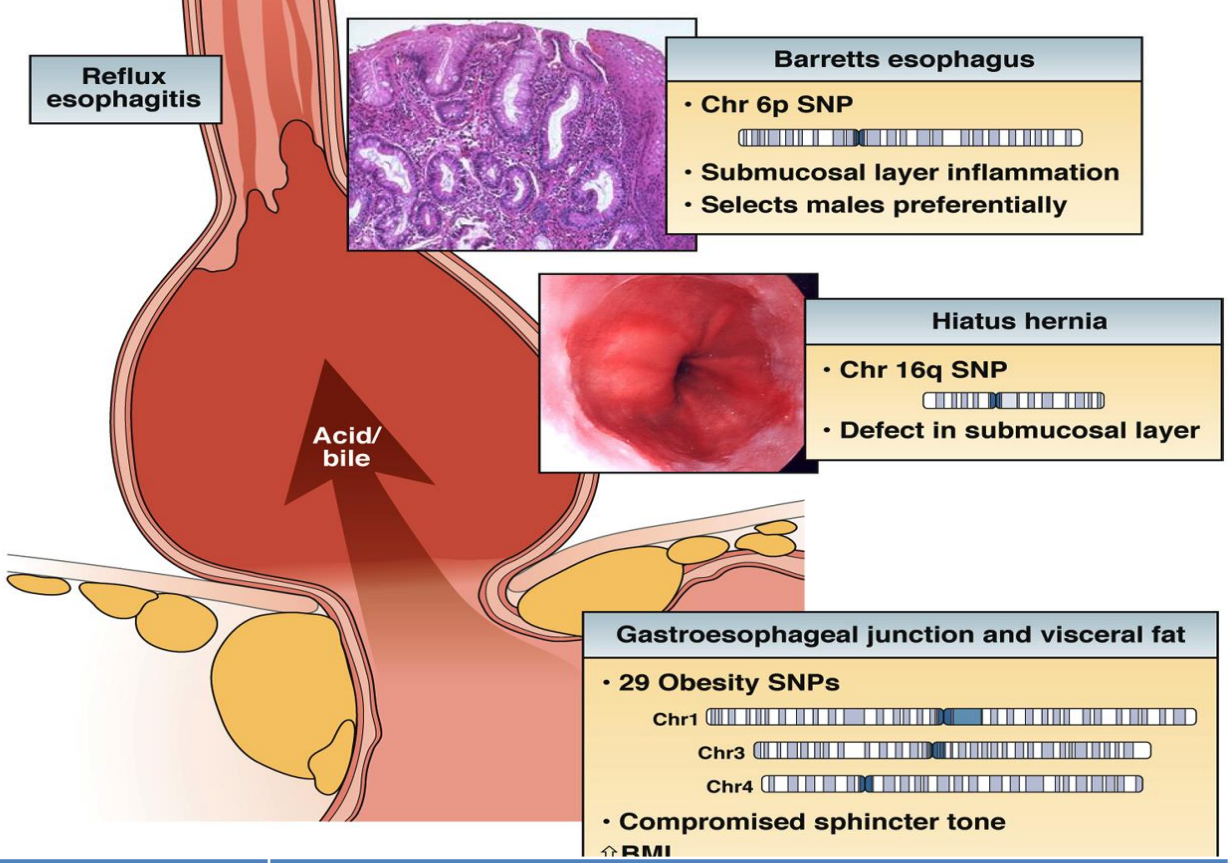
- Figures and tables index

Class	Condition	Gene(s)	Inheritance
Colon cancer (polyposis syndromes)	Familial adenomatous polyposis (FAP)	*APC*	AD
	Gardner syndrome	*APC*	AD
	Attenuated FAP (AFAP)	*APC*	AD
	MYH-associated polyposis (MAP)	*MUTYH*	AR
	Polymerase proofreading-associated polyposis (PPAP)	*POLD1, POLE*	AD
	Peutz–Jeghers syndrome	*STK11*	AD
	Cowden syndrome	*PTEN*	AD
	Bannayan–Riley–Ruvalcaba	*PTEN*	AD
	Juvenile polyposis	*BMPR1A, SMAD4*	AD
Colon cancer (nonpolyposis)	Lynch syndrome	*MLH1, MSH2, MSH6, PMS2, EPCAM*	AD
Gastric cancer	Hereditary diffuse gastric cancer	*CDH1*	AD
Pancreatic cancer	Familial pancreatic cancer	*BRCA1&2, ATM, CDKN2A, PALB2, STK11,* Lynch syndrome genes	*AD*
Pancreatic endocrine tumors	MEN-1 syndrome	*MEN1*	AD
Inflammatory bowel disease	Crohn's disease	*Multiple, including ATG16L1, NKX2.3, STAT3, IL-10, NOD2*	Complex
	Ulcerative colitis	*Multiple, including NKX2.3, STAT3, ECM1, IL-10*	Complex
Pancreatitis	Hereditary pancreatitis	*PRSS1, CFTR, SPINK1*	AR (SPINK1, CFTR) AD (PRSS1) Complex (CFTR)
Celiac disease	Celiac disease	Haplotypes *HLA-DQ2, HLA-DQ8*	Complex
Metabolic liver disease	Wilson disease	*ATP7B*	AR
	Alpha-1-antitrypsin deficiency	*A1AT*	Autosomal codominant
	Hereditary hemochromatosis	*HFE, TFR2, SLC40A1*	AR (HFE, TFR2) AD (SLC40A1)
Hyperbilirubinemias	Crigler–Najjar syndrome, type II	*UGT1A1*	AR
	Gilbert's syndrome	*UGT1A1*	AR
	Dubin–Johnson syndrome	*ABCC2*	AR
	Rotor syndrome	*SLCO1B1, SLCO1B3*	AR
Auto-inflammatory disorders	Familial Mediterranean fever	*MEFV*	AR
	Hibernian fever (TRAPS)	*TNFRSF1A*	AD
GIST	Hereditary GIST	*CKIT*	AD
Other	Autosomal dominant polycystic liver disease	*LRP5, PRKCSH,SEC63*	AD
	Hirschsprung disease	*Multiple*	
	Acute porphyrias	*PBGD, ALAD, CPOX, PPOX*	AD (*PBGD, CPOX, PPOX*)

AD, autosomal dominant; AR, autosomal recessiv

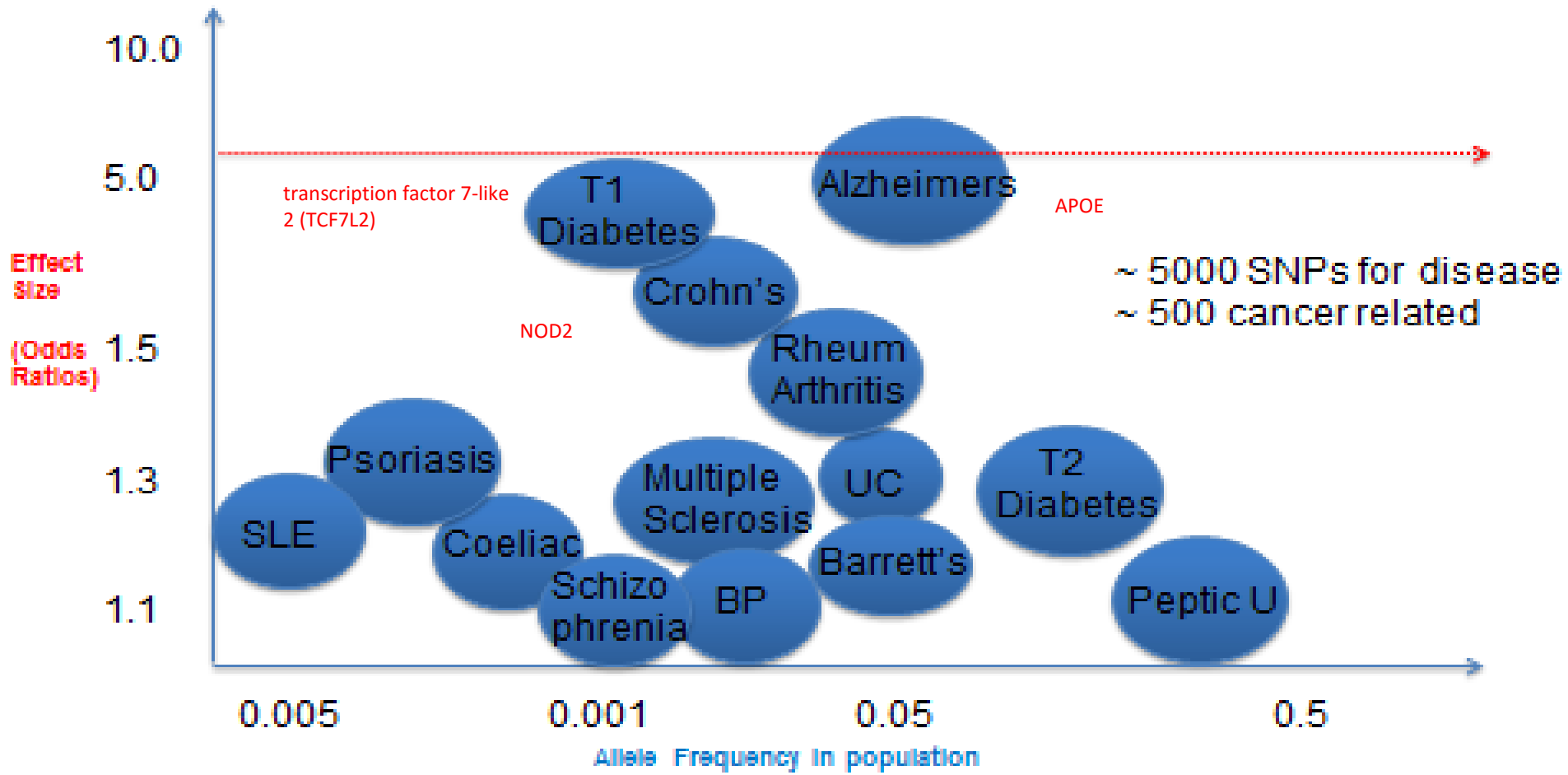
Citation: Clinical and Translational Gastroenterology (2016) 7, e167; doi:10.1038/ctg.2016.23





GI Disease	No. SNPs currently identified
IBD	~ 165
Colorectal Cancer	~ 30
Coeliac Disease	~ 20
Barrett's Oesophagus	16
Oesophageal Adenocarcinoma	16 + 1 (independent of BE)

Complex Diseases and Genetic component



Environmental Component: High Sugar, Salt, Fat, Alcohol and Cigarettes

So how do we fix the clinical problems now?

Prevention of progression

Chemoprevention with aspirin (acetylsalicylic acid; ASA), statins, or diet was not agreed upon in this consensus (see **Appendix 2** online, Results).

34. The use of PPIs (compared with no therapy or histamine receptor type 2 antagonists) is associated with a decrease in progression from benign BE metaplasia to BE neoplasia (dysplasia and EA). STATEMENT *NOT* ENDORSED, overall agreement 53.3%. A+, 10.8%; A, 42.5%; U, 20.8%; D, 23.3%; D+, 2.5%.

Recommendation

Strong research recommendation for more data from the aspirin esomeprazole chemoprevention trial (AspECT) and chemopreventive trials of PPIs in patients with BE.

AspECT Trial (CI J Jankowski) will report 2017

Why?

- Patients with Barrett's esophagus, approximately 2 percent will die of esophageal cancer.
- Patients with Barrett's esophagus died more frequently of other causes, such as ischemic heart disease and pneumonia.
- Therefore need for adequate weight, diet, smoking and alcohol modification strategies.
- Need for better quality endoscopy and perhaps FNE in select centers in the community.

Summary

- Who
  - 60 years (men)
  - Obese
  - Smokers/alcohol
  - Long standing heartburn
- How
  - Quality endoscopy
  - Unsedated TNE
- Why
  - Increase global health benefits CVS and cancer deaths
  - Decrease burden and cost of BE surveillance

Cumbria recruiting now; contact jjankowski@uclan.ac.uk