Gastroesophageal reflux disease and Barrett’s oesophagus: an overview of evidence-based guidelines

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Title Page

Title: Gastroesophageal Reflux Disease and Barrett’s oesophagus: An overview of evidence-based guidelines

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Abstract

Gastroesophageal reflux disease (GERD) is an extremely common condition worldwide with prevalence varying from 2.5% in China to 51.2% in Greece. The economic and morbidity burden of it is vast and optimising care for this condition carries huge financial and patient related benefits. GERD can be complicated by progressing to Barretts Esophagus (BE) a precancerous condition which affects approximately 2% of the population and remains undiagnosed in many. The National Institute of Clinical Excellence (NICE) has produced guidelines to cost-effectively manage GERD in patients in the UK and the Benign Barrett’s and cancer task force (BoBCAT) consensus was the largest international review of evidence known into management of benign BE complications. This paper is a review of these guidelines with updates in new evidence. Areas for future development involve risk stratifying patients to surveillance, chemoprevention agents and genetic biomarkers to help decide who will be at highest risk of malignant progression. Evidence supports the safety of proton pump inhibitors for symptom control medium term (i.e. 9 years) and reducing the risk of progression of BE whilst surgical options are cost effective treatments for certain patients. BE surveillance should be directed towards high risk groups while those at lower risk may benefit for chemoprevention strategies

Key words: Barrett’s esophagus, Cancer, Chemoprevention, Mortality, Prevention.
Gastroesophageal reflux disease and Barrett’s esophagus: An overview of evidence-based guidelines

Gastroesophageal reflux disease (GERD) is a common phenomenon, affecting patients throughout their lives[1]. It covers a spectrum from infrequent irritating symptoms to a debilitating syndrome, and can lead to the formation of the premalignant condition Barrett’s Esophagus (BE). GERD carries both a huge burden of morbidity, and a financial burden through loss of functional days of work or to healthcare directly[2, 3, 4]. Add to that the potential mortality through development of esophageal adenocarcinoma (EAC) via BE[5] and this spectrum of disease requires significant investment from both primary and secondary healthcare[6, 7]. To address this the National Institute of Clinical Excellence (NICE)[8] has produced a comprehensive guideline for the management of GERD and there has been a thorough international consensus for the management of premalignant esophageal disease from the Benign Barrett’s and Cancer Taskforce (BoBCAT)[9] also endorsed by NICE. This paper serves to summarise the evidence of these guidelines and give an overview of current important updates in this field. The two guidelines reviewed in this article have been chosen as other guidelines did not reach a sufficient standard- according to criteria for assessing systematic reviews[10].

Gastroesophageal Reflux Disease

GERD is a common condition worldwide[11] which presents with a range of symptoms but typically characterised by upper abdominal pain, heartburn, acid reflux or vomiting. Though the NICE guideline attests there is no recognised universal diagnosis, they cite a broad consensus from the 1988 Working Party[12] classification supported by the British Society of Gastroenterology (BSG)[13] 1996 definition to class GERD as any symptom conferrable to the upper GI tract which has been present for at least 4 weeks.
Many conditions can give the sensation of what patients describe as “heartburn” or “reflux” but don’t actually involve true acid reflux. The differential diagnosis for this symptom includes true acid reflux, oesophageal motility problems such as achalasia or jack hammer esophagus, functional esophageal discomfort and even cardiac angina[14]. Moreover, actual gastroesophageal reflux can present insidiously with rhinitis, asthma, cough, hoarseness of voice and asymptotically[15]. The initial diagnosis of reflux can be complicated by atypical presentations hence a vigilance is key to suspect it, the diagnosis can then be supported by response to a trial of treatment and subsequently further investigations[8](Figure 1). This will include an upper GI endoscopic evaluation and less commonly esophageal pH and manometry studies. As these investigations are invasive the first step is clinical diagnosis then empirical treatment with proton pump inhibitor (PPI) alongside lifestyle modification by the patient.

**Lifestyle modification**

GERD has a number of specific triggers or risk factors which can be modifiable by the patient[16] and this can have improvements to patients’ perceived symptoms[17]. In the NICE guideline they reviewed evidence from studies- randomised controlled trials were lacking however retrospective cohort studies showed associations, a few of the significant are listed here. Most of the studies reported odds ratios of less than 2 hence no strong association: obesity (a study of 12,349 patients BMI>28.2Kg/m2 OR 1.93 (1.49-2.52)[18] and of 1524 patients BMI >30kg/m2 gave OR 2.8 (1.7-4.5)[19]), smoking (7015 patients, ever smoked OR 2.46 (1.89-3.19)[20], 1676 current smokers OR 1.69(1.27-2.26)[21], alcohol (1524 patients >6 drinks per week OR 1.9 (1.1-3.3)[19], oesophagitis 7015 any alcohol 1.87 (1.44-2.43)[20], coffee (no positive or protective association). For eating late at night, lying flat, chocolate and fatty foods there was a paucity of data. In summary individual changes
generally had low to modest effects on symptoms and there are few studies assessing these interventions on long term outcomes.

Weight reduction has shown some evidence of improving symptoms, with maximal benefit when reaching normal BMI[22], it also helps with many other medical comorbidities such as diabetes, hypertension and ischaemic heart disease. There has also been evidence to suggest increased visceral fat causes increased adipose tissue around the lower esophageal sphincter in obese patients weakening it’s action[23].

Educational materials can be extremely useful but vary with patient’s background, language and culture. Finding useful well researched information specific to a patient can be difficult and this can take a significant portion of time for each patient. Likewise, many patients will be distressed by the burden of their symptoms which may cause them to seek bad health behaviours thus compounding their condition. In a systematic review of studies looking at health related quality of life in relation to GERD symptoms, Becher et al found those with persistent symptoms had worse scores in both physical and mental health related quality of life scores[24], hence careful and sensitive exploration of this is important.

**Proton Pump Inhibitors (PPI)**

The main principle of PPI use for GERD is to use the lowest effective dose for a short period of time[25]. Rates of failure to respond to PPIs have been estimated between 17-32% in primary care settings and 26-44% in secondary care in systematic review and Cochrane review respectively[26, 27]. As with all refractory conditions initial confirmation of compliance with PPIs is important as rates of compliance of 44-56% have been reported in those with refractory symptoms verses 84% in those with adequate symptom control[28].

PPIs are overall extremely safe drugs with few side effects and interactions[29]. There have been multiple studies, many of them retrospective cohort studies which have shown links
between PPI use and several conditions. Their use has been implicated in increased risk of Clostridium difficile[30], pneumonia[31, 32], dementia through to myocardial infarction[33], chronic kidney disease[34] and fractures[35]. A common limitation of large retrospective cohort studies is that associations are often overstated as causation. Therefore, careful consideration of the literature is important in the case of PPIs which through multiple randomised controlled trials have been found safe. Recent data from the Esomeprazole and aspirin in Barrett’s esophagus (AsPECT) trial, a randomised controlled trial looking at long term high dose PPI to prevent BE progression to EAC, showed no increase in adverse events[36]. Within the trial, 2557 patients with BE were randomised to high dose PPI or low dose PPI with or without aspirin for a 10year period. Within the study only 13 serious (graded 3-5 on Common Terminology Criteria for Adverse Events) were deemed attributable to PPI and overall the amount of serious adverse treatment related events was <1%.

NICE acknowledges there is some association between PPI and fractures[37] and with clostridium difficile infection[38]. Therefore they should be used with caution in those at risk of osteoporosis and bone density scans considered if needing long term. Moreover, continuing to prescribe a drug in the absence of it helping contributes to polypharmacy and poor drug adherence[39]. The take home message is for GERD to give the lowest dose for shortest period but for conditions, such as BE, for which a PPI long term is necessary they are very safe.

**Identification of the spectrum of functional and organic reflux disease**

Before considering endoscopy there are other etiologies of discomfort to rule out. If a patient presents with any suggestion of gastrointestinal bleeding, endoscopy transcends the importance of all other investigations in that situation. Aside from that scenario other things
are important to consider prior to escalating to endoscopic investigation. Commonly the patient group presenting with symptoms will be middle-aged or elderly and often have multiple medical comorbidities[28]. Cardiac disease is important to rule out in these patients as indigestion can be a common interpretation of the heavy retrosternal discomfort patients experience and those who present with atypical chest pain have been shown to have worse outcomes with acute coronary syndromes[40, 41]. Women particularly can have atypical chest pain, radiation to the neck or jaw, which may easily mimic the tract of the esophagus/pharynx for both patients and clinicians[42, 43]. If there is an exertional relationship with the onset of discomfort this may suggest a cardiac cause but a careful consideration of the demographic, risk factors and age of the patient may offer some stratification. If it is suspected ruling out inconspicuous cardiac disease first may be the safest option prior to further GI investigation.

Many medications used in the treatment of other conditions can compound reflux symptoms. NSAIDS and steroids are particularly irritant to the upper GI tract and may need to be considered as culprits, either reduced or stopped where possible. A recent meta-analysis of global trends in GERD showed an odds ratio of 1.44 (95% CI 1.10 to 1.88) in patients using NSAIDs or aspirin[44]. Another important consideration is that of biliary disease which if a patient reports an association with fatty foods or more right sided pain an ultrasound abdomen should be requested.

If the symptom burden is high for reflux and alternative diagnoses have been considered, then endoscopy is the next step. Findings at endoscopy can vary and don’t always correlate to the severity of the symptoms. The Los Angeles (LA) Grade Classification of Erosive Esophagitis is a tried and tested system, appreciated for its diagnostic accuracy and reproducibility[45]. It is a graded description of stages of esophageal mucosal damage from small areas of erosion to full circumference ulceration in grade D. As well as quantifying the
amount of reflux damage, endoscopy allows for screening for associated complications, namely BE, but also esophageal cancer. Initially assessment for BE may be difficult in the presence of inflammation hence if it is suspected, the reflux is treated with high dose PPI and the patient is brought back for reassessment. The management of suspected BE will be discussed later.

There is an important distinction to make with GERD patients regarding the relationship between symptoms and level of inflammation at the endoscopy and there are three phenotypes[17]. In the first, there is good correlation between the severity of symptoms with the visualised mucosal abnormality or grade at endoscopic assessment. In the second, which could be termed hypersensitive esophagus, is where the patient reports very significant symptoms however the actual evidence of mucosal damage is low at endoscopy. These patients will often have a poor response to PPI management as there is likely to be underlying upper GI visceral hypersensitivity which is contributing to their experience[39]. To help mediate this element of their symptoms, alternative modes of therapy can be selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants. Beyond the scope of this paper is the group of patients who have no reflux but functional esophageal pain and esophageal motility problems all of which may mimic reflux symptoms, the key here is they are unlikely to respond to PPI therapy and therefore need alternative treatments. Diagnosis with oesophageal pH and high resolution manometry can distinguish these from true GERD [46, 47, 48]. The third phenotype, insensitive esophagus, are those who have very minimal symptom burden but very significant mucosal damage at endoscopy, and asymptomatic individuals have been shown to have established BE[49]. Unfortunately, due to lack of symptoms compliance with medications is poor and therefore their risk of progression to dysplasia may go unchecked. Hence, these patients require quality counselling to optimise engagement with medication, and if they do progress to BE, with surveillance.
Surgical management

There is clear advice from NICE regarding patients who should be referred for laparoscopic fundoplication. The three main groups are: individuals who are responding to PPIs but do not want to stay on long-term treatment because of fear of complications; people who respond to PPIs who already have complications or side effects; those who have definitive evidence on pH studies that they have severe disease that is only partially managed by the PPIs. PH and manometry studies are vital prior to referral. This is to confirm the symptoms and inflammation are related to true acid reflux but also to confirm the patient has working esophageal motility as once the fundoplication is in situ the patient will require the functioning peristalsis of the esophagus to avoid dysphagia.

In the 2014 guideline NICE reviewed evidence for laparoscopic fundoplication over continued PPI use. In 6 studies, all randomised controlled studies of patients with confirmed GERD by endoscopic or pH studies, outcomes for health related quality of life favoured laparoscopic fundoplication over continued PPI[50, 51, 52, 53, 54, 55]. They looked at 1 year and 5-year outcomes and there was significant improvement for all the studies in symptoms, GERD-related and general wellbeing. Only one group looked at mortality which found no cases[53, 54], but in 5 studies’ pooled data showed 15/337 serious adverse events in the laparoscopic fundoplication arm verses none with PPI[50, 51, 53, 54, 55]. Cost analysis was performed based around data which had been reviewed from the REFLUX trial, a large UK-based 21 centre trial looking at surgical verses medical management of GERD[56, 57]. Overall laparoscopic fundoplication had a greater cost at outset but had lower costs over time compared with medical management, however patients need to be properly counselled regarding the risks associated with Nissen’s Fundoplication which is essentially being performed for a non-life-threatening condition. Fundoplication carries a mortality risk of approximately 0.45% within the first month[58, 59], the risk of perioperative complications
such as esophageal perforation, post operative dysphagia (1.8-10.8%) and only a 67% cure rate (in longer studies >7years)[60].

Summary

In summary there is a clear algorithm set out by NICE for the diagnosis, investigation and management of GERD. Take home messages include

- Lifestyle advice takes time, multiple interactions and requires sensitivity particularly when discussing weight reduction
- GERD symptoms can be atypical and other conditions may mimic “heartburn”
- A clinician must be vigilant to complications of GERD particularly BE.
- Endoscopic findings may not correlate well with symptom burden which can cause marked impacts on quality of life
- PH and manometry studies must be performed prior to consideration of surgery
- Laparoscopic Nissen’s fundoplication and PPI are superior to other endoscopic/surgical techniques but surgery carries risks.

Barretts Esophagus and the Benign Barrett’s and Cancer Taskforce(BoBCAT)

In this section of the paper the focus will be on Barrett’s esophagus(BE). Though the NICE guideline offers some advice regarding decisions on surveillance and management, a structured international consensus for the management of benign BE conditions was created in 2015. This was: BOB CAT: A Large-Scale Review and Delphi Consensus for Management of Barrett’s Esophagus With No Dysplasia, Indefinite for, or Low-Grade Dysplasia[61]. This was a process of international multicentre systematic review of the evidence around the management of these conditions and was the largest gathering of expert opinion for BE. Using a Delphi process, which is a validated tool to decide on group
consensus where questionnaires are completed by individuals separately and the group decisions are fed back to individuals to avoid unbalanced group dynamics and individual dominance[62]. During the process consensus statements were created regarding the management of BE, these were discussed and judged for their importance and evidence using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system. The GRADE system is a process of reviewing, condensing the evidence around a specific question where all important outcomes have been made explicit, then tables of evidence are produced with a rating for the strength of evidence around that question[63]. It remains to this day one of the largest systematic evidence-based reviews in medicine.

During this process an international consensus regarding the definition of BE was created:

“BE is defined by the presence of columnar mucosa in the esophagus and it should be stated whether intestinal metaplasia (IM) is present above the gastro esophageal junction.”[61]

It was deemed appropriate to not make IM conditional of the definition given the differences between British and American guidelines[64, 65], also the evidence that suggests sampling error in missing IM and that not all EAC is preceded by the presence of IM[66]. The NICE guideline has advised at least 8 biopsies at random be taken to increase the yield of IM but in short segments 4 biopsies per 1cm of abnormal mucosa over the first cm should be taken. For surveillance this has been expanded into the Seattle protocol where quadrantic biopsies are taken at every 2cm of BE in non-dysplastic patients and every 1cm in those with prior dysplasia in order to maximise the yield[67, 68]. Visual evidence of BE correlates with pick up rate of IM but not finding it should not prevent ongoing surveillance. For NICE if there is the presence of mosaic of metaplasia then it is BE and this is supported by consensus statements.
The prevalence of BE has been difficult to formally calculate given it is often asymptomatic but in BoBCAT using an epidemiological paper from 2005 it was deemed to be approximately 2%[69]. Studies have looked at prevalence at endoscopy which could have selection bias due to the presence of this being a saturated population of symptomatic GERD patients, to overcome this a study in the US where patients undergoing surveillance colonoscopy had an upper GI endoscopy, showed a prevalence of 6.8% for BE in asymptomatic patients[70]. In a review of 51 studies mostly from East Asia showed endoscopically diagnosed BE rate of 7.8% with histological diagnoses confirmed in 1.3%[71]. The variation in BE prevalence is unsurprising as there is large variation in prevalence of the precursor of GERD – a recent metaanalysis of GERD around the world showed a range of prevalence from 2.5% in China to 51.2% in Greece[44].

Barrett’s esophagus is a consequence of genetic predisposition and reflux injury causing changes to the columnar epithelium of the esophagus[5, 23]. Predominantly a disease of middle aged men, it has an increasing frequency in populations particularly with the spread of the so called westernised diet[5]. Risk factors associated with BE include chronic GERD, advancing age (over 50), smoking, male gender[72], Caucasian race and particularly central obesity[73]. The overall risk of progression of nondysplastic BE to EAC is approximately 0.2-0.5% per year[74], this is a low but has been deemed comparable to the risk of progression to breast cancer for carriers of BRCA 1 or BRCA2 genes[75, 76]. The risk once low grade dysplasia(LGD) occurs increases and further with high grade dysplasia(HGD)[75]. However overall the risk is low, these patients are often middle to older ages with obesity and metabolic syndrome and 90% will die of another condition[77]. This message is often not clearly translated to patients and many live in fear of developing cancer disproportionate to their actual risk[78]. Surveillance programmes have been widely adopted in spite of little
research evidence to support this – the first randomised controlled trial investigating surveillance verses patient-reported symptom-based approach is ongoing and known as the Barrett’s esophagus surveillance verses endoscopy at need study (BOSS)[79]. Surveillance is costly both to the health service but also physically and psychologically to patients, putting them through regular invasive procedures alongside the worry of cancer. Therefore BoBCAT did not support population screening for BE, or standard surveillance for non-dysplastic BE to reduce mortality[61]. Further research is ongoing into minimally invasive cell sampling techniques for population screening such as Cytosponge including a large cluster randomisation study is currently underway within primary care units in the UK[80].

Until better patient stratification can be achieved the most important key to a successful programme is patient education and involvement. BoBCAT did support that when surveillance is undertaken it should be targeted at higher risk groups (84% agreement). Also that it should be undertaken with high resolution endoscopy by experienced hands (89% agreement), this is supported in a recent research priority setting exercise which showed for clinicians and patients surveillance is a high priority and assessing whether a dedicated BE service is better was 4th out of 10 key priorities[81]. Allowing patients to have a clear understanding of the actual risk and the benefits and risks of BE surveillance empowers patients to engage or disengage. Some of the risk factors described above can help a clinician explain an individual’s risk of progression with more accuracy but the reality of a regular endoscopy should be clearly explained, and a clinician needs to be wary of their ability to bias a patient’s decision to engage or not. A key part of the education must be to encourage patients to contact if they are concerned about symptoms between surveillance endoscopies.

At the time of BoBCAT there was limited research evidence for surveillance intervals for low grade dysplasia (LGD) (89% agreement). Since this the BSG guideline has had to introduce an update after the 2013 guideline following a randomised controlled trial published in the
Journal of American Medical Association which looked at surveillance verses radiofrequency ablation for LGD[82]. The study showed reduced risk of progression to high grade dysplasia of 25% in the RFA group, and a reduction of 7.4% for EAC, given the significance of the findings the study was terminated early and the BSG guideline has been changed to advise RFA for patients with confirmed LGD[83]. The BSG guideline group have emphasised the importance of two experienced pathologists confirming the diagnosis of LGD which was also a recommendation in BoBCAT as part of a statement around surveillance intervals for LGD (88% agreement), and that they should be considered for ablative therapy if high risk and LGD is present twice (89% agreement).

For visible lesions in LGD patients there was consensus that these should be removed by endoscopic resection to aid histological diagnosis (94.7%) and that there was strong recommendation to RFA if HGD or cancer was found. This is based on little evidence directly that visible lesions in LGD should be removed but based on reviewing patients with dysplasia as lesions have been found to contain HGD or EAC in situ. Lesions should be defined with the Paris classification[84] of lesions as the most common for having dysplasia or EAC within are polypoidal or depressed lesions 2c/2b and in a retrospective study histology from endoscopic resection samples changed the diagnosis in 49% of cases[85].

BE and Genetics

To further risk stratify patients, research into genetic biomarkers for BE has been gaining ground in the last few decades since the human genome project. Reflecting this two statements in BoBCAT highlighted growing emphasis on aberrant p16, p16 methylation, or p16 loss being associated with progression from non-dysplastic BE to LGD (80% agreement), and over expression of p53 as a risk factor for progression to dysplasia (87%) agreement. Wang et al compared findings from biopsies taken of BE, LGD, HGD, EAC
specimens and normal controls, looking at the presence of hypermethylation of p16 and APC genes. They found none of the normal control samples showed the presence of promoter hypermethylation of these genes, whereas there was significant presence in non-dysplastic BE(31%), LGD BE (50%), HGD (54%) and EAC (68%)[86]. The same group found higher prevalence of DNA methylation in those who had undergone RFA and showed evidence of residual BE with or without LGD suggesting a need to monitor this group more closely post intervention to predict progression to HGD[87]. Other areas of study include HPP1, RUNX3, AKAP12, CDH13, SST, TAC1, and NELL1 and their aberrant methylation[88, 89].

For p53 though the following statement was endorsed at 87.7% agreement “Aberrant p53, p53 mutation, or p53 loss in nondysplastic BE is associated with an increased risk of developing dysplasia”[61] consensus could not be reached regarding the use of p53 abnormalities in clinical practise. Likewise, with other biomarkers the research is not consistent enough to use these as predictive markers in routine clinical practice awaiting further evidence.

The first genome wide association study was published in 2013 which was performed by the Esophageal Adenocarcinoma Genetics Consortium as part of the Wellcome Trust Case Control Consortium into 15 common diseases located two genetic foci of significance in EAC[90]. On the HLA 6p21 region there was a highly significant association, which showed predominance in males (OR 1.38 95% confidence interval [CI], 1.25–1.53) compared to women ( OR 1.11 [95% CI, 0.95–1.30]). This foci also showed changes geographically though without strong significance but seemed associated with areas of higher EAC prevalence eg. Scotland. The second locus was found at 16q24 significant for its locality near the transcription factor FOXF1 which in mice deletion studies has been associated with multiple esophageal abnormalities[23]. Further to this a strong proportion of shared genes were found in BE sufferers, obesity and cardiac disease. There is evidence of increased
visceral fat in those with BE and obesity, BE patients have a strong predisposition to visceral fat and an overall higher mortality in these patients may be related to this link with the metabolic syndrome[91].

BE is a multifactorial condition but future research into genetic biomarkers may help shape the way future surveillance and screening is achieved. However, at this stage clinical practice lags behind evidence and in the recent BE research priority setting exercise finding ways to accurately identify high risk groups for BE screening and how can we achieve individual risk stratification of patients with BE to target surveillance were deemed priority 1 and 2 respectively[81].

Chemoprevention and BE

Chemoprevention is the regular use of common, safe drugs or dietary supplements to prevent cancer. Aspirin and PPIs have shown promise as chemopreventative agents, fitting with the hypothesis that EAC is an inflammatory-mediated malignant response to prolonged acid exposure. Laboratory data to show a cellular mechanism for PPI chemoprevention is lacking however some have shown absolute acid suppression reduced cell proliferation[92][93] and increased expression of cyclin dependent kinase inhibitors p21 and p16[94]. Aspirin has numerous anti-cancer actions which have been hypothesised, namely it’s anti-inflammatory actions on prostaglandin E2 via the COX pathway- prostaglandin E2 has been linked to preventing apoptosis, increasing cell proliferation and migration and also stimulation of angiogenesis[95]. It has been shown to reduce cellular β-catenin[96], reducing cell proliferation via platelet-mediated thromboxane effects[97] and reducing circulating inflammatory cytokines[98].
A statement regarding chemoprevention in BoBCat stated “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 EAC)” [61]

At the time of BOBCAT this could not be endorsed and reached only 53.3% agreement due to at that stage evidence being mostly cohort or retrospective data. Since this the results of the AspECT trial have been released and published in the Lancet[36]. The AspECT trial was an international multicentre phase 3 randomised controlled trial looking at 10 years of patients with BE given high dose esomeprazole (40mg twice daily) or low dose (20mg once daily) with or without aspirin. The main outcomes reviewed were rates of all-cause mortality, EAC and HGD.

High dose PPI was superior to low dose PPI in decreasing all-cause mortality, it also increased length of time to events developing (8 verses 10.2 years). Use of aspirin and high dose PPI together was superior to no aspirin and low dose PPI and appeared to have an additive effect (TR 1·59, 95% CI 1·14–2·23, p=0·0068)[36]. The team calculated numbers needed to treat for each intervention which were on average 43 patients needing aspirin verses no aspirin to prevent one event and for high dose PPI this was 34 verses low dose. Less than 1% of participants had a treatment related serious adverse event.

The study was limited in the sense of it studying only a fraction of the population of BE patients, a predominantly Caucasian population and the drug treatments not being blinded. However, as a randomised controlled trial the data supports previous observational data which suggested a chemopreventative link between EAC aspirin and PPI, and metanalysis data from cardiovascular studies with aspirin which showed lower EAC rates (though these were not primary end points). How the AspECT data is interpreted may be similar to the
other recommendations discussed in this paper – targeting of high-risk groups to streamline interventions is likely to be the future.

Summary

This paper has outlined two high quality guidelines for the management of two common conditions, GERD and BE. Vigilance to new evidence and research is key to ongoing good clinical practice and contradictory evidence should not always be avoided if it is robust and post-dates a guideline. For GERD, PPIs are a safe medical treatment to augment lifestyle changes and research supports an emphasis on weight reduction and smoking cessation. Surgery has shown good outcomes for quality of life in certain patient groups but carries a risk of complications for which excellent counselling is paramount. A vigilance to alternative aetiology should remain strong and if doubt occurs endoscopy and pH manometry studies can confirm the diagnosis.

BE remains a significant target for intervention as a precursor to a malignancy that carries a dismal 5-year survival rate relative to other luminal malignancies[99]. Currently surveillance is based on spreading a wide net to intervene in certain cases but it is not always achieved to a sufficient standard. There are specific groups for whom to emphasise the need for surveillance – male, obese, smokers with family history and those with long segment BE- whilst randomised controlled study data for surveillance is awaited. Approaches to BE will be shaped significantly in the coming years with advances in chemoprevention, as well as early detection through minimally invasive techniques and endotherapy for dysplasia. Until then good quality education of patients will help improve the appropriate use of surveillance, medication and engagement in studies to address ongoing research needs.
JJ provided an initial outline for the paper. ER wrote the initial detailed draft, JJ reviewed and advised on the draft which ER then revised. Both authors edited and approved the final version of the manuscript.

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Figure 1: Taken with permission from NICE guideline CG184: Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management 2014[8]. This flow diagram shows the progress through interventions for GERD in adults and when to refer to specialist care.