

Supplement: Quality of Life, Public Health Issues, and Health Economics

Statements:

BE is associated with a sizable decrement in quality of life.

BE is associated with substantial direct and indirect medical expenditures, which are increasingly borne by the patients.

Estimates of the cost-effectiveness of endoscopic screening and surveillance have been widely variable, and are sensitive to multiple poorly described variables.

Estimates of the cost-effectiveness of endoscopic therapy of BE with HGD suggest that it is both effective and cost-effective when compared to either endoscopic surveillance or surgical esophagectomy.

Summary of Evidence

The quality of life of patients with BE has been compared both to the general public, as well as those with other manifestations of GERD such as erosive esophagitis and non-erosive reflux disease. Most comparisons use generic quality of life measures, as there is no widely utilized disease-specific measure for BE; however GERD-specific and GI-specific measures have been used. Generally speaking, the quality of life of those with BE has been found to diminished compared to the general population.^{17, 199, 200} This finding likely reflects in part the diminished quality of life experienced by GERD patients generally, since most of the studied BE populations report substantial GERD symptoms. Interestingly, when compared to subjects with other manifestations of reflux, some work suggests that patients with BE may actually have a better QoL than subjects with non-erosive reflux disease.¹⁹⁹ Whether this represents a biological difference in the symptom complex of BE patients vs. NERD patients, or whether it reflects underlying differences in the psychological states of the patient populations, is not clear.

The impact on QoL of the cancer risk associated with BE has been more difficult to characterize and is currently poorly described. Patients with BE express worry about cancer risk, and feel that they have too little information to understand this risk.^{201, 202} When asked to estimate their risk of cancer incidence and cancer death, patients with BE may overestimate their risk of these outcomes.¹⁶ Patients ascribe significantly less utility to life lived with BE and dysplasia compared to heartburn alone.²⁰³ Further, patients successfully treated for their BE with ablative therapy have diminished worry about cancer risk and improved quality of life compared to either their pre-treatment condition or to controls who underwent sham treatment.²⁰² Taken collectively, these data suggest that there is a sizable decrement in quality of life associated with BE, which is at least partially attributable to the increased risk of EAC associated with this condition.

The direct and indirect costs associated with the care of subjects with BE are significant. Approximately 1% of the adult population undergoes upper endoscopy for a GERD-related diagnosis on an annual basis, and data suggest that patients with BE undergo endoscopy much more frequently than is recommended by professional associations.^{204, 205} These endoscopies are associated with substantial indirect costs, since they generally involve not only the absenteeism of the patient, but that of a driver as well. Medication costs associated with care of subjects with BE are substantial, given that 90% or more of BE patients in most series are on a PPI. Furthermore, because of the wide availability of over-the-counter PPI therapy, a cost shift among insured patients from the insurer to the patient has occurred with respect to these medication expenses. A diagnosis of BE is associated with a 2-3 fold increase in the cost of life insurance, and may make health insurance harder to obtain or unobtainable.²⁰⁶

A substantial literature exists with regard to the cost effectiveness of endoscopic screening, endoscopic surveillance, and endoscopic therapy of BE. In general, results of cost-effectiveness analyses of both endoscopic screening and endoscopic surveillance of BE are highly dependent on a number of poorly described variables, including the prevalence of BE in the general population, the effectiveness of endoscopic surveillance in averting death from EAC, and rates of progression of BE to EAC (Supplementary table 1).²⁰⁷⁻²¹⁰

In contrast, economic analyses of endoscopic therapy for BE with HGD demonstrate that this approach is effective and cost-effective when compared to either surgical esophagectomy or endoscopic surveillance, over a plausible ranges of input variables.^{150, 211} Endoscopic therapy of LGD may also be cost-effective, but, not surprisingly, cost-effectiveness varies based on the presumed rate of progression of this lesion.^{150, 211} Finally, estimates of cost-effectiveness of endoscopic treatment of non-dysplastic BE have been variable, but newer analyses incorporating more modest estimates of progression of non-dysplastic BE to EAC suggest that this approach is not cost-effective, being associated with a high cost per quality-adjusted life-year attained.¹⁵⁰

Supplementary Table 1: Summary of studies assessing cost effectiveness of endoscopic screening followed by surveillance for BE.

Study	Screening and surveillance technique studied	Design	Results	Assumptions
Inadomi et al ⁷¹	Sedated endoscopy	Markov model 50 year old Caucasian men with reflux symptoms Screening and surveillance (only for dysplasia or for all) compared to no screening. Esophagectomy for HGD or EAC	Screening followed by surveillance only for dysplasia : ICER 10.4K per QALY Screening followed by surveillance in all BE every 5 years : ICER 596K per QALY (compared to surveillance only for dysplastic BE)	BE prevalence 10% Progression rates : BE to cancer 0.5% No data on participation rates or performance characteristics of endoscopy for screening
Gerson et al ⁷⁰	Sedated endoscopy	Markov model 50 year old men with chronic reflux symptoms Screening and surveillance strategies (for NDBE, LGD, HGD) compared to no screening Esophagectomy (HGD, EAC), surveillance or endoscopic therapy for HGD	Screening followed by surveillance : ICER 12,140 per QALY Screening followed by surveillance in women (one third prevalence of BE) : ICER 44.5K per QALY	BE prevalence 10% Progression rates : NDBE to cancer 0.5% Prevalence of cancer at initial endoscopy with BE : 0.8% No data on participation rates or performance characteristics of endoscopy for screening incorporated.

Rubenstein et al ⁷²	Sedated endoscopy and esophageal video capsule endoscopy. Cost utility analysis.	Markov model 50 year old Caucasian men with chronic reflux. Screening with endoscopy or ECE followed by endoscopy, compared to no screening.	Screening with endoscopy compared with no screening: ICER 11.3K per QALY. Screening with ECE compared to no screening: ICER 13.2K per QALY.	BE prevalence 10% Progression rates : NDBE to cancer 0.5% Accuracy of endoscopy for BE diagnosis : 100%, error rates incorporated Sensitivity of ECE : 85% ECE cost : \$740 No risk associated with ECE Loss of work from endoscopy incorporated. No data on participation rates incorporated.
Gerson et al ⁷³	Sedated endoscopy and esophageal video capsule endoscopy	Markov model 50 year old males with chronic reflux. Screening with endoscopy or ECE followed by endoscopy, compared to no screening.	Screening and surveillance with endoscopy compared to no screening : ICER 4.5K per QALY Screening and surveillance with ECE compared to no screening: ICER 24.8K per QALY	BE prevalence 10% Progression rates : NDBE to cancer 0.5% Sensitivity of endoscopy : 85% Sensitivity of ECE : 70% ECE cost : \$785 (estimated) Loss of work from endoscopy incorporated. No data on participation rates incorporated.
Nietert et al ⁷⁴	Sedated endoscopy and unsedated transnasal endoscopy	Markov model 50 year old males with chronic reflux. Screening with uTNE and endoscopy compared with no screening.	Screening with uTNE compared to no screening: ICER 55.7 per QALY Screening with endoscopy compared to uTNE : ICER 86.8K per QALY	BE prevalence : 3% Progression rates : BE to EAC : 0.5% Sensitivity and specificity of uTNE : 95% Participation rate with uTNE : 95% uTNE cost : \$97

			Screening with endoscopy compared to no screening : ICER 709K per QALY.	
Benaglia et al ⁹⁴	Sedated endoscopy, Cytosponge and unsedated transnasal endoscopy	Microsimulation model, 50 year old males with chronic GERD symptoms Screening with Cytosponge and EGD compared to no screening RFA and esophagectomy modelled as options of treatment	Screening with Cytosponge compared to no screening : ICER 15.7K per QALY Screening with endoscopy compared to no screening: ICER \$22.2K per QALY Screening with uTNE compared to no screening: ICER 19.1-28.4K per QALY	BE prevalence 8% Progression rates : NDBE to EAC : 0.15% LGD to EAC : 0.54% EGD participation 23% Cytosponge participation 45%, endoscopy participation after Cytosponge positive 80% Cytosponge cost : \$152 Endoscopy sensitivity and specificity 100% Cytosponge sensitivity 73%, specificity 94%

ICER : Incremental cost effectiveness ratio, QALY : Quality adjusted life year, NDBE: non dysplastic BE,

LGD: low grade dysplasia, HGD: high grade dysplasia, EAC: esophageal adenocarcinoma, RFA: radiofrequency ablation

ECE: esophageal capsule endoscopy, uTNE : unsedated transnasal endoscopy