COST-EFFECTIVENESS OF SPONGE-BASED SURVEILLANCE WITH GENETIC TESTING FOR EARLY DIAGNOSIS OF ESOPHAGEAL ADENOCARCINOMA

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Introduction

Esophageal adenocarcinoma (EAC) is a deadly cancer with increasing incidence rates over the past three decades [1] and a 5-year relative survival of individuals diagnosed with EAC of only 14% [2]. Barrett's Esophagus (BE) is a major risk factor for developing EAC. BE is often preceded by a diagnosis of gastroesophageal reflux disease (GERD) [3]. Epidemiological studies have identified important individual-level risk factors for development of BE, including gender, race/ethnicity, age, duration of GERD symptoms, smoking, and obesity [4-5]. Numerous cost-effectiveness analyses have established that endoscopic screening and surveillance in high-risk patients for BE and BE with dysplasia is not cost-effective [6-7]. Non-endoscopic methods have been proposed [8] yet few studies have evaluated their cost-effectiveness against endoscopic methods [9]. Complementing non-endoscopic sponge-based methods with a genetic test for early detection of BE with dysplasia may lead to early diagnosis and reduce risk of developing EAC.

Aims

To compare health benefits and costs-effectiveness of current (endoscopy+biopsy) and alternative (sponge-based cytological sampling with genetic testing) surveillance strategies for early detection of Barrett's esophagus, which is a risk factor for esophageal adenocarcinoma.

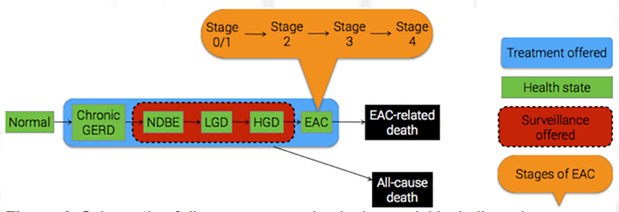

Figure 1. Schematic of disease progression in the model including when treatment and surveillance was offered to individuals. Abbreviations: GERD, gastroesophageal reflux disease; NDBE, non-dysplastic Barrett's esophagus; LGD, low-grade dysplasia; HGD, high-grade dysplasia; EAC, esophageal adenocarcinoma

Methods

A microsimulation model was developed to track individual-level health trajectories accounting for:

i. demographic and lifestyle risk factors for developing Barrett's esophagus (BE);

ii. medication use, screening/ surveillance for BE;

iii. treatment algorithms for each health state using established guidelines and expert opinion (Figure 1).

Two surveillance strategies were tested:

i. endoscopy+biopsy (baseline);

ii. sponge-based cytological sampling followed by genetic test precursors to EAC (alternative).

Clinical outcomes were compared under each surveillance strategy and cost-utility analysis was used to estimate average lifetime costs (2014 Canadian dollars) and health benefits (quality-adjusted life years, QALYs) per person. Sensitivity analysis (deterministic and probabilistic) and value-of-information analysis were also performed.

Results

Calibrated model matched well with the observed data and had low absolute percent error values with a 7% and 13% error for the male and overall EAC incidence rate, respectively. Model validation results also showed good comparisons with observed data on EAC incidence rates (Figure 2). Under the alterative surveillance strategy, EAC incidence rates were reduced by up to 40% under increased sensitivity of the genetic test for dysplasia in NDBE patients.

Cost-effectiveness of the alternative strategy was dependent on the percent uptake of the alternative strategy and percent increase in sensitivity of the genetic test. Under 100% uptake of sponge-based genetic testing and 50% improvement in sensitivity relative to the baseline strategy, the additional per person cost was $404 with gains in QALYs of 0.0154 resulting in an incremental cost-effectiveness ratio of $26,286/QALY gained (Table 1). The ICER was most sensitive to the false negative rate of the genetic test among NDBE patients and the cost of sponge-based genetic testing.

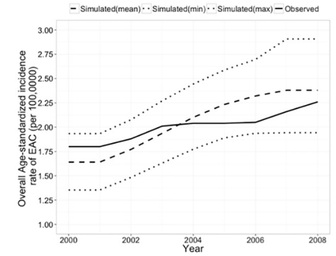

Figure 2. Model validation using simulated (long-dashed) and observed (solid) age-standardized overall EAC incidence rate over time. The observed data was reported as a moving average and so the simulated values have also been smoothed in the same manner. Short-dashed lines represent minimum and maximum values from all simulations (n=3000) assuming endoscopy+biopsy surveillance. Observed EAC incidence rate values were from Ontario cancer data collected from 2000-2008.

Table 1. Cost-effectiveness analysis comparing Endoscopy+biopsy vs. sponge-based genetic testing at various levels of uptake and sensitivity of sponge-based genetic testing. Costs and effects are discounted at 5% annually. 95% confidence intervals (CI) were obtained through non-parametric bootstrapping method.

Strategy	Uptake (%)	Sensitivity of genetic test (% better than Endoscopy+ biopsy)	Percent reduction in EAC incidence relative to baseline	Costs ($)	Effects (QALYs)	Incr. Cost ($)	Incr. Effect (QALYs)	ICER ($/QALY gained, 95%CI)
Endoscopy+ biopsy	-	-	-	$210,913,571	626,843,686	-	-	-
Sponge-based genetic testing	50	0.869 (5%)	12%	$307,555,629	626,985,154	$96,642,058	141,468	$683($562-$873)
		0.913 (11%)	24%	$303,989,145	627,128,041	$93,075,574	284,355	$327($291-$372)
		0.956 (16%)	36%	$300,256,224	627,273,096	$89,342,653	429,410	$208($189-$230)
	100	0.869 (5%)	25%	$404,222,719	627,123,828	$193,309,148	280,142	$690($616-$789)
		0.913 (11%)	48%	$397,065,695	627,400,197	$186,152,124	556,511	$334($307-$366)
		0.956 (16%)	71%	$389,689,908	627,692,744	$178,776,337	849,058	$211($194-$228)

Conclusion

Sponge-based surveillance+genetic testing was cost-effective when compared to the current practice of endoscopy+biopsy surveillance. Sensitivity analyses demonstrated that the magnitude of cost-effectiveness was dependent on critical parameters, such as sensitivity of the genetic test, uptake of the novel non-endoscopic surveillance method and cost of the genetic test. In order for the sponge-based genetic test strategy to be cost effective it will need to have a sensitivity of 50% or better relative to that of the current surveillance strategy (Endoscopy+biopsy).

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Bibliography available upon request from Ayaz Hyder, hyder.22@osu.edu.

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