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Costs associated with Barrett's esophagus screening in the community: an economic analysis of a prospective randomized controlled trial of sedated versus hospital unsedated versus mobile community unsedated endoscopy

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Abstract

Background and Aims—Data on the economic impact associated with screening for Barrett's esophagus (BE) are limited. As part of a comparative effectiveness randomized trial of unsedated transnasal endoscopy (uTNE) and sedated endoscopy (sEGD), we assessed costs associated with BE screening.

Methods—Patients were randomly allocated to 3 techniques: sEGD or uTNE in a hospital setting (huTNE) versus uTNE in a mobile research van (muTNE). Patients were called 1 and 30 days after screening to assess loss of work (due to the screening procedure) and medical care sought after

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JPM : Conducting economic analysis, statistical analysis, drafting manuscript, revision of manuscript.

NDS : Critical revision of manuscript.

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MJ: Data collection, creation and maintenance of research database

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KKW : Critical revision of manuscript.

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procedure. Direct medical costs were extracted from billing claims databases. Indirect costs (loss of work for subject and caregiver) were estimated using patient reported data. Statistical analyses including multivariable analysis accounting for comorbidities were conducted to compare costs.

Results—209 patients were screened (61 sEGD, 72 huTNE and 76 muTNE). 30 day direct medical costs and indirect costs were significantly higher in the sEGD than the huTNE and muTNE groups. Total costs (direct medical + indirect costs) were also significantly higher in the sEGD than in the uTNE group. The muTNE group had significantly lower costs than the huTNE group. Adjustment for age, sex, and comorbidities on multivariable analysis did not change this conclusion.

Conclusions—Short term direct medical, indirect and total costs of screening are significantly lower with uTNE compared with sEGD. Mobile uTNE costs were lower than huTNE costs, raising the possibility of mobile screening as a novel method of screening for BE and esophageal adenocarcinoma.

Keywords

Esophageal adenocarcinoma; reflux; obesity

INTRODUCTION

Screening for Barrett's esophagus (BE), the strongest risk factor and precursor of esophageal adenocarcinoma (EAC) has been suggested in individuals with multiple risk factors.¹ However, support for this recommendation remains weak due to the lack of conclusive evidence showing that BE screening reduces EAC mortality.^{2, 3} Although retrospective studies have shown that BE screening and surveillance may improve EAC outcomes, the potential for biases in these studies remains.⁴⁻⁶ Additional challenges to widespread BE screening include the lack of a validated BE risk prediction model, and an accurate EAC risk prediction model in BE subjects. This is most relevant given the low risk of progression to EAC in BE demonstrated in large population based studies.⁷

Despite these limitations, several economic modeling studies have shown that BE screening in subjects with gastroesophageal reflux (GER) symptoms and other risk factors (male gender, age > 50 years) followed by endoscopic surveillance in those with dysplasia may be cost-effective.⁸ This has been shown for techniques such as sedated endoscopy (sEGD),^{9, 10} unsedated transnasal endoscopy (uTNE)¹¹ and capsule endoscopy,^{12, 13} when compared with no screening. However, the results of these studies are variable and influenced by assumptions on BE prevalence in the population, participation rates (typically set at or near 100%), and costs associated with screening.

In addition to the cost of the procedure itself, indirect costs (costs of work lost for both the person being screened and the person accompanying the individual being screened) and additional direct medical costs resulting from any medical care sought in the short term as a result of adverse events from the screening test remain unknown. As modeling is often done from the perspective of third party payers, these sometimes-substantial patient-born costs have often been ignored. However, these hidden and uncovered patient costs may have a

significant impact on overall cost burdens for the patient and estimates of cost effectiveness of screening strategies.

In a randomized trial to compare the clinical effectiveness of 3 BE screening approaches in the community¹⁴: sedated endoscopy, uTNE in the hospital and uTNE in a mobile research van, we demonstrated that the 3 techniques had comparable clinical effectiveness (measured via participation rates, safety, tolerability, and yield). Using additional data collected prospectively during this study, we aimed to measure and compare short-term (30 day) direct and indirect medical costs associated with BE screening with these 3 approaches.

METHODS

Study Population and Setting

Eligible patients (Olmsted County, Minnesota residents 50 years of age or older, without a known diagnosis of BE or EAC, who had previously completed a GI symptom questionnaire) were recruited and randomized to screening by conventional sEGD, uTNE in the hospital (huTNE) or in a mobile research van (muTNE). sEGD and huTNE were performed at the research endoscopy unit in the Clinical Research Unit (CRU) of the Center for Clinical and Translational Sciences at Mayo Clinic Rochester, whereas those in the muTNE group took place in a mobile research van that went to various pre-designated locations throughout the county.¹⁴

The study protocol and results are outlined in detail in a prior publication.¹⁴ All patients were called by a research coordinator at 1 day and 30 days after the screening procedure to assess hours or days of work lost by the participant and his caregiver (if one accompanied him to the screening test) and any medical care sought in the 30 days after the screening procedure due to adverse effects from the screening procedure. Additional details obtained during these telephone calls included tolerability and patient preference for these procedures.

Data Sources

Financial data were retrieved from the Rochester Epidemiology Project Cost Data Warehouse (REPCDW), formerly known as the Olmsted County Healthcare Expenditure and Utilization Database (OCHEUD). This claims-based data repository contains details on healthcare resource utilization, associated charges, and estimated economic costs for patients cared for at the 2 medical groups (Mayo Clinic and Olmsted Medical Center) that provide most medical services in Olmsted County, MN.^{15, 16} The REPCDW provides a standardized inflation-adjusted estimate of costs in constant dollars for each service or procedure provided by the two local providers. Specifically, a “bottom-up” approach is conducted to group services into the Medicare Part A and Part B classification system. This approach adjusts Part A hospital-billed charges with Medicare Cost Report department-level cost-to-charge ratios. Part B physician services are estimated with Medicare reimbursement rates. Although the types of services provided are driven by the clinical practice patterns of the local providers, the value of each unit of service has been adjusted to reflect national norms

with the use of widely accepted valuation techniques.¹⁷ All costs were inflated to 2013 U.S. Dollars using the Gross Domestic Product Implicit Price Deflator.^{18, 19}

No clinical charges were generated from the research procedure due to the study being funded by the National Institutes of Health and conducted in the CRU. Thus, the costs of these services were not available in the REPCDW. As an approach to valuing costs of the initial study procedure, we identified patients in the administrative billing databases that would appropriately represent each study group. Potential billing data were identified using CPT-4 procedure codes. Patient data used to estimate costs of the sEGD population were identified using CPT-4 procedure code 43239 (Esophagogastroduodenoscopy, flexible, transoral; with biopsy, single or multiple), whereas data used to estimate the 2 TNE groups were identified using CPT-4 procedure code 43200 (Esophagoscopy, rigid or flexible; diagnostic, including collection of specimen(s)). Costs of the muTNE patients were based on professional services only, identified from the proxy TNE patients. All proxy patients were seen on an outpatient basis, had the appropriate CPT-4 procedure code used as the principal CPT-4 procedure code of the visit, satisfied the age criteria (>50) used for the study patient selection, and were seen in 2011.

As there are currently no standard approaches for costing the use of a mobile van for patient outreach, costs of the mobile van were estimated with the use of a multiplier. This multiplier was determined by the ratio of 2013 Medicare non-facility reimbursement rates of home visit evaluation and management CPT codes (99341–99350) to the corresponding office evaluation and management CPT codes (99201–99215). The mean value of these ratios was used as the multiplier in base-case analysis. Additionally, sensitivity analyses were conducted varying the multiplier of muTNE between high and low values of these reimbursement ratios.

Outcome Measures

Three cost outcome measures were calculated: direct medical costs, indirect costs, and total costs (direct medical costs plus indirect costs). Direct medical costs consisted of costs related to the initial diagnostic visit and 30-day follow-up. Indirect costs consisted of time missed from work during the visit and follow-up period for the patient and the person accompanying the patient to the procedure. This information was collected from post procedure phone interviews. The cost of lost wages was based on the average Olmsted County weekly wage rate for the third quarter in 2013.²⁰ A 40-hour work-week was assumed to determine hourly wage. Patients stating they were retired had indirect costs valued at 64% of an employed individual as has been done previously in the literature.²¹ Time of missed work reported by the accompanying person was assumed to be for an employed individual. In the event that no work hours were reported as being missed (for the patient or accompanying person) it was assumed that the person was retired. Missed work hours were then imputed from the reported data.

Statistical Analysis

Costs were analyzed descriptively and using multivariate regression. Descriptive comparisons among groups included mean, median, standard deviation, and interquartile

range. Multivariate regression consisted of one-part generalized linear models to account for the skewed nature of cost data. Three two-way comparisons were performed, resulting in 3 separate generalized linear models. Covariates in the model included age, sex and comorbidities. Comorbidities were measured using the Hwang method.²² Due to limited degrees of freedom, comorbidities were modeled as a categorical count variable rather than controlling for all individual comorbid conditions.

Predicted mean costs and mean incremental costs were calculated using recycled predictions.²³ Confidence intervals of predicted mean costs and predicted differences were performed using nonparametric bootstrapping.²⁴ Significance was determined by 95% confidence intervals of incremental means that did not contain zero. Statistical analyses were performed in SAS (version 9.3; SAS Institute) and Stata (version 12.1; StataCorp).

RESULTS

A total of 4,973 patients met the criteria to be used as proxies for the sEGD group, whereas 18 patients met the criteria to be used as proxies for the TNE study groups. Direct estimated costs for these visits are depicted in Table 1. As can be seen, costs were higher for sEGD compared with uTNE. Mean costs were used as proxies for the visit costs in the 3 groups studied: sEGD - \$1,821; huTNE - \$406; muTNE - \$188.

The mean value of the home visit ratio applied to muTNE costs was 1.14. This multiplier was applied to the assumed muTNE costs of \$188. The low and high values of the home visit ratio used in sensitivity analyses were 1.05 and 1.24, respectively.

Descriptive data for the indirect costs of missed days of work for trial patients and the accompanying individual are depicted in Table 2. As can be seen, mean costs were highest for the sEGD group at \$113.35, with muTNE being the lowest at \$64.55. Notably, variation in costs was highest for sEGD and lowest for muTNE.

Understanding that our approach to valuing indirect costs could potentially introduce an unintended bias based on the variability in rates of retirement across the 3 groups (see supplementary data tables), we performed a sensitivity analysis using the following alternative approaches: (1) using indirect costs of zero for those reporting they were retired and those reporting no missed hours of work, (2) assuming a wage rate for retired individuals that was 100% of the assumed wage rate of employed individuals, (3) standardizing the wage rate of all individuals using the weighted average valuing retired individuals at 64% of the employed wage rate based on the proportion of retired individuals of the entire study population (based on our data this worked out to be 83%), and (4) imputing hours of missed work based on modality specific data rather than the entire study population and then incorporating the standardized wage rate of 83% of a fully employed person as described in no. 3 above. Results from these sensitivity analyses (outlined in the supplementary data tables) consistently showed sEGD with the highest mean indirect costs (ranged from \$89.36 to \$140.35), followed by huTNE (ranged from \$40.83 to \$111.04) followed by muTNE (ranged from \$23.34 to \$89.53).

Descriptive data of the one-month direct medical costs (cost of screening visit plus any additional direct medical costs within 30 day follow-up) are shown in Table 3. One huTNE patient had a hospitalization (unrelated to screening visit), which resulted in a high SD for the huTNE group. 30 day direct medical costs were also substantially higher in the sEGD group compared with both uTNE groups. This primarily stemmed from the high costs of the initial sEGD procedure.

Descriptive data of total costs (one-month direct medical costs plus indirect costs) are shown in Table 4. Again, the sEGD group had the highest mean costs whereas the muTNE group had the lowest costs. This difference also was driven primarily by the cost of the sEGD procedure.

The predicted means, predicted incremental mean differences, and 95% confidence intervals of the 3 two-way comparisons are shown in Table 5. As shown by the 95% CI of the difference in means not including zero, the sEGD group had significantly higher costs compared with both the huTNE and muTNE groups. The muTNE had significantly lower costs than the huTNE group.

Sensitivity analyses of the cost of the mobile van showed no overall change in results comparing to either sEGD or huTNE. Costs of muTNE were statistically lower than sEGD and huTNE costs for both the high and low sensitivity analyses (results not shown). Because the sensitivity analyses only had an effect on costs of the muTNE group, results for the sEGD versus huTNE group did not change.

DISCUSSION

This study found that 30-day total costs (direct medical plus indirect) for patients undergoing BE screening in the community, were highest for the sEGD group and lowest for the muTNE group. The sEGD group remained statistically more costly than the muTNE group across a range of assumed mobile van costs. These findings remained significant after costs were adjusted for comorbidity scores. These findings are an important addition to the literature, which has lacked real world data for short-term direct and indirect costs after BE screening by different modalities.

Current estimates of the cost-effectiveness of endoscopic screening and surveillance have been widely variable, and are sensitive to multiple poorly described variables. One study which assessed the cost-effectiveness of screening with uTNE presumed a BE prevalence of 3% in the population (recent estimates in U.S. studies have found higher prevalence rates^{14, 25}). 95% of those offered screening were assumed to accept the procedure. uTNE and sedated endoscopy cost was estimated to be \$97 and \$346–506 (cost estimates were obtained from the author institution, with sensitivity analyses performed varying costs from \$50–300). Short-term direct or indirect costs were not included in the analysis. This was stated to be a limitation by the authors.¹¹ The authors also acknowledged uncertainty in the assumptions used in the model and attempted to mitigate this partially by performing additional sensitivity analyses. Furthermore, the authors reported that if the cost of uTNE exceeded \$330, screening with sedated endoscopy would become more cost-effective.

Rubenstein et al estimated that patients undergoing sEGD missed 1 day of work and their driver missed 1/2 day of work, each earning the national median income whereas patients undergoing esophageal capsule endoscopy (ECE) missed 1/3 day of work¹³. In this study we have calculated actual indirect costs by obtaining data on work missed by participants and their caregivers while undergoing BE screening in the trial.

This new data can be used to reduce the uncertainty of the highly varied results from prior modeling studies comparing cost-effectiveness of screening modalities of BE versus no screening.^{9–11, 26–28} Conclusions from these studies have ranged from screening being cost-effective^{10, 29} to being more costly and associated with reduced quality of life³⁰, and thus dominated by no screening. Data from more recent modeling studies^{12, 31, 32} still assume several of the costs involved in and after BE screening. With the advent of minimally invasive techniques, which have led to renewed interest in BE screening, accurate direct and indirect cost estimates of this strategy are imperative.⁸ Our results challenge some of the assumptions such as participation rates of 100% for uTNE reported in prior studies¹⁰ and also provide data on the indirect costs associated with screening such as the economic costs of work lost both for the participant and the caregiver, which are currently unavailable. This is particularly true for sEGD, which continues to be the predominant method recommended in guidelines and followed by practitioners.¹³ However, as demonstrated by several recent studies, uTNE is also an equally effective BE screening modality^{33, 34} and is recommended as an alternate method of BE screening. Similar cost data will need to be gathered for newer tools such as the capsule sponge, which was found to be a cost effective strategy compared with no screening or screening with sedated endoscopy using participation rates of 45% as a minimum threshold.³¹

The strengths of this study include cost data obtained from participants in a prospective randomized study of community participants. Data on direct medical costs were obtained from the REPCDW, which provides a comprehensive and accurate estimate of medical costs, in addition to data on indirect medical costs (which have not been available before) obtained from interviews with participants conducted in temporal proximity to the procedures. Estimates of direct medical costs were further strengthened by access to the REP database, which provides a comprehensive account of medical care provided or obtained by all Olmsted County residents. Given that the procedures (sEGD and uTNE) conducted in the study were funded by the research study, they did not lead to clinical charges. However these costs were extrapolated from procedures performed clinically in similar group of patients from the same time frame and population. There are currently no standard approaches to reimbursement for use of a mobile van for patient outreach with diagnostic screening methods. Our results were robust to assumed costs of the mobile van comparing muTNE with both sEGD and huTNE. As reported in an earlier study, newer non-invasive sponge based tests may be cost effective screening tests compared with sedated endoscopy, in individuals with chronic reflux symptoms.

CONCLUSIONS

Economic analyses from our randomized trial showed that short-term direct medical, indirect and total costs of BE screening are significantly lower with uTNE compared with

sEGD. Given the comparable effectiveness of sEGD and TNE techniques, and lower costs, mobile uTNE, may be a cost-effective method of screening for BE and esophageal adenocarcinoma in the community.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

BE	Barrett's esophagus
EAC	esophageal adenocarcinoma
GER	gastroesophageal reflux
huTNE	unsedated transnasal endoscopy in a hospital setting
muTNE	unsedated transnasal endoscopy in a mobile research van
OCHEUD	Olmsted County Healthcare Expenditure and Utilization Database
REPCDW	Rochester Epidemiology Project Cost Data Warehouse
sEGD	sedated endoscopy
uTNE	unsedated transnasal endoscopy

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Table 1

Direct procedure costs of proxy patient populations

	Mean	Median	SD	IQR
sEGD	1,821	1,559	860	1,238 – \$2,176
uTNE				
With hospital and professional fee (proxy for uTNE)	406	110	884	110 – \$240
Professional fee only (proxy for muTNE) ^{\$}	188	110	243	110 – \$110

SD: standard deviation, IQR: interquartile range

Cost of screening procedure in U.S.\$ in proxy patients (obtained from Olmsted county patients undergoing clinical sEGD with biopsy or uTNE with biopsy at Mayo Clinic in 2011).

^{\$} Costs obtained accounting for multiplier determined from ratio of 2013 Medicare reimbursement of home visit CPT codes to corresponding office evaluation and management CPT codes

Table 2
Indirect costs of missed work (in U.S.\$) due to screening procedures by study group.

	Mean	Median	SD	IQR
sEGD (n=61)	\$113.35	\$77.76	96.75	\$62.21 – \$128.30
htTNE (n=72)	\$84.55	\$62.21	77.19	\$62.21 – \$79.70
muTNE (n=76)	\$64.55	\$62.21	19.95	\$60.63 – \$67.55

SD : Standard deviation, IQR: interquartile range

Table 3

One month direct medical costs (U.S.\$) by study group.

	Mean	Median	SD	IQR
sEGD (n=61)	\$2,036.02	\$1,897.61	528.86	\$1,850.68 – \$1,958.31
htTNE (n=72)	\$891.83	\$420.22	2,088.69	\$420.22 – \$541.20
muTNE (n=76)	\$433.38	\$221.83	633.70	\$217.81 – \$340.14

SD : Standard deviation, IQR: interquartile range

Table 4
One month total sum of direct medical and indirect costs (in U.S.\$) by study group

	Mean	Median	SD	IQR
sEGD (n=61)	\$2,149.37	\$2,022.03	536.49	\$1,940.56 – \$2,107.29
htTNE (n=72)	\$976.38	\$511.04	2,090.40	\$482.43 – \$649.63
muTNE (n=76)	\$497.92	\$286.67	636.91	\$280.02 – \$395.54

SD : standard deviation, IQR: interquartile range

Table 5

Two-way comparisons of total costs between sEGD, huTNE and muTNE groups.

Pairwise comparison (first modality vs second modality)	Mean costs in U.S.\$ (95% CI) of first modality	Mean costs in U.S.\$ (95% CI) of second modality	Difference in mean costs in U.S.\$ (95% CI)
sEGD vs muTNE	\$2,187.67 (\$2,110.40 to \$2,217.72)	\$490.70 (\$481.89 to \$506.44)	\$1,617.02 (\$1,615.83 to \$1,727.14)
sEGD vs huTNE	\$2,273.23 (\$2,215.19 to \$2,393.15)	\$928.93 (\$883.69 to \$954.98)	\$1,386.72 (\$1,291.79 to \$1,486.07)
muTNE vs huTNE	\$512.31 (\$488.61 to \$533.72)	\$944.34 (\$905.64 to \$983.51)	−\$432.66 (−\$479.47 to −\$390.26)

Predicted mean total costs, incremental mean differences and 95% confidence intervals of two-way analyses.