

RESEARCH COMMUNICATION

Estimating the Costs of Esophageal Cancer Screening, Early Diagnosis and Treatment in Three High Risk Areas in China

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Abstract

Background: The incidence and mortality of esophageal cancer (EC) in some rural areas with poor health resources in China are the highest around the world. In these areas, screening programs for EC are conducted for prevention and control. However, costs associated with esophageal cancer screening have not been characterized in detail. This study is aimed to estimate the screening, early diagnosis and treatment costs of EC using micro-costing methods, which could provide basic cost inputs for further systematic health economic evaluation. **Materials and Methods:** Micro-costing methods were adopted to collect data on quantity and unit cost of used resources. Data was obtained from face-to-face interview with medical staff, local hospitals' database, and experts' input. We used 80% capacity utilization and 3% discount rate to annualize capital investments, and all costs were adjusted to year 2008 using the gross domestic production deflator, and then converted from Chinese currency unit to international dollars (I\$) using purchasing power parity. **Results:** Screening costs per case were around I\$60. For severe dysplasia, carcinoma in situ and intramucosal carcinoma, the costs per capita of endoscopic mucosal resection were I\$1292-I\$1620, and around I\$450 for argon plasma coagulation. For submucosal carcinoma (T₁N₀M₀), and invasive carcinoma treated by esophagectomy, the treatment costs ranged from I\$1485 to I\$2171. The costs of treatment of invasive carcinoma were: I\$497-I\$685.2 for radiotherapy; I\$4652-I\$7966.15 for chemotherapy; I\$1928-I\$2805 for combination of esophagectomy and radiotherapy; I\$6632-I\$8082 for esophagectomy, radiotherapy and chemotherapy in combination. **Conclusion:** The cost analysis found screening, early diagnosis and treatment for EC could provide great cost savings. The results provide important information for further health economic evaluation, and to help the local policy makers on updating such screening program in high risk areas in China.

Keywords: Esophageal cancer - screening and treatment cost - micro-costing

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Introduction

Incidence and mortality of esophageal cancer rank as eighth and sixth among all cancers, respectively, with 462,000 new cases and 389,000 deaths in 2002 worldwide (Parkin et al., 2005). The mortality rates for both genders from esophageal cancer in China are the highest in the world (Parkin et al., 2005). The Chinese National Death Causes Sampling Survey during 2004-2005 showed that most of the esophageal cancers occur in rural areas with limited health resources. Cancers of the esophagus are considered as a major disease burden, which accounts for over 50% of cancer deaths in these high-risk areas.

Esophageal cancer is often a fatal malignancy with 5-year survival rates of only 16% in the United States, and 10% in Europe (Sant et al., 2003; Jemal et al., 2006). Such poor survival rates are primarily due to the advanced stage of the

disease when diagnosed. Up to now, there are no specific primary prevention methods for esophageal cancer, while screening, early detection and treatment are considered as effective strategies of prevention and control, through which the 5-year survival rate of early esophageal cancer can be increased to 86.14% (Wang et al., 2004).

However, there are currently no worldwide screening guidelines for esophageal cancer. In high-risk areas of China, mass screening programs have been conducted for over 50 years, applying different techniques such as balloon cytology, liquid-based cytology, occult blood bead detector, and endoscopic examination, in order to explore the optimal screening methods for esophageal carcinoma in China. The studies show endoscopy to be suitable to an extent as an initial test due to its higher sensitivity (96%) (Shu, 1983; Guan and Song, 1987; Qin et al., 1988; Shen et al., 1993; Dawsey et al., 1997; Dawsey et al., 1998; Wang,

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2001; Wang et al., 2005; Wang et al., 2007; Pan et al., 2008; Guo et al., 2009). For smaller communities in China, endoscopy with or without iodine staining has already been recommended as the primary screening procedure (Wang, 1989). However, it is much more expensive than other techniques mentioned. Whether mass screening using endoscopy in high-risk areas of China with poor resources is cost-effective is unknown, due to shortages of systematic health economic evaluations.

In 2006, a multi-centre health economic evaluation on the "Early Detection and Early Treatment of Esophageal Cancer" Program (EDETTEC) using endoscopy with mucosal iodine staining and index biopsy technology was initiated in China. As the first step of the cost-effectiveness, cost-utility, and cost-benefit, this paper focused on costs estimation of screening, early diagnosis and treatment to provide basic cost inputs for further health economic evaluation.

Materials and Methods

Overview

As mentioned previously, a health economic evaluation study on EDETTEC was launched in 2006 to explore the adapted endoscopic screening strategy for esophageal cancer in high-risk areas, which could be extended and applied to different socio-economic areas of China (Tuncer, 2010). As a part of the systematic health economic evaluation, this paper presents the full screening and treatment costs of EDETTEC in Feicheng of Shandong province, Linzhou of Henan province, and Ci County of Hebei province.

Introduction of EDETTEC

The EDETTEC Program was a public health project for developing countries in high-risk areas of esophageal cancer with large shortages of health resources and poor economies. The ethics approval for the program was obtained at the Institutional Review Board of Cancer Foundation of China. The eligible subjects aged 40-69 years were screened using endoscopy with mucosal iodine staining and index biopsy, and then diagnosed by pathology detection. Each eligible participant without contraindications was examined from esophagus to duodenal bulb. The initial endoscopic inspection was performed without staining. Then, 1.2% Lugol's iodine solution was sprayed; normal squamous mucosa was stained brown, while squamous dysplasia and carcinoma unstained. One or more biopsies were taken from each unstained area. The biopsy slides were read by local pathologists. The detailed endoscopic examination procedures were the same as in other studies (Roth et al., 1997; Dawsey et al., 1998). By the end of 2008, over forty thousand subjects had been screened by endoscopy (Tuncer, 2010). The compliance rate was around 70%. There were two types of screening modalities. In sites like Linzhou, and Ci County, the participants were picked up by the local cancer hospital van for the examinations; in Feicheng, the screening group went to villages to perform the screening equipped with drugs and supplies.

For precancerous lesions and esophageal cancer

diagnosed by screening, the treatment principals were as follows: (1) for severe dysplasia, carcinoma in situ and intramucosal carcinoma, endoscopic mucosal resection (EMR) or argon plasma coagulation (APC) was recommended; in the first year after treatment, they should be follow up by endoscopy; (2) for submucosal carcinoma (T₁N₀M₀), esophagectomy was recommended; (3) for invasive carcinoma, common treatment modalities were chosen depending on disease severity and could include surgery, radiotherapy, or chemotherapy, or a combination (here, radiotherapy refers to conventional radiotherapy; the intermission of chemotherapy between neighboring cycles is 2~3 weeks, and according to the clinical practice guidelines, four- to six- cycle treatment is considered as a standard chemotherapy procedure). Local and general anesthesia was used for EMR/APC, and esophagectomy, respectively. The lengths of stay for severe dysplasia/carcinoma in situ/intramucosal carcinoma cases treated by EMR/APC were seven days; for submucosal carcinoma(T₁N₀M₀)/invasive carcinoma cases treated by esophagectomy alone, radiotherapy alone, chemotherapy alone, esophagectomy combined with radiotherapy, and esophagectomy, Radiotherapy and Chemotherapy in combination were 12-20 days, 42-49 days, 6-10 days per cycle, 54-69 days, and 78-109 days, respectively. These treatment plans used the most basic medicine and laboratory technologies possible to treat patients with esophageal cancer who do not have other serious complications (Cheng, 2008). These procedures for esophageal cancer treatment were defined based on literature (NCCN clinical practice guidelines in oncology TM esophageal cancer, 2009), clinical field experiences, and clinical protocols used at regional hospitals, as well as experts' opinions.

Screening and Treatment Costs of EDETTEC

For the process of cost estimation, the micro-costing (Barton et al., 2003; World Health Organization: WHO-CHOICE, 2003; Griffith et al., 2005; Barnett, 2009; Frick, 2009) approach was used to collect detailed data on the quantity of resources used in EDETTEC program and the unit value of these resources in each previous field station. It is well known that overall costs of projects are comprised of patient costs and program costs. The former includes all costs at the point of care delivery, such as drugs, supplies, and laboratory tests, while the latter refers to costs incurred at administrative levels, such as costs of management, training and media campaigns (Johns, Baltussen and Hutuvey, 2003; Philip and Julia, 2006). We omitted program costs and only included the patient costs here. The patient costs refer to medical costs, including drugs, staffs, supplies, equipment, etc. (Goldhaber-Fiebert and Goldie, 2006)

According to the treatment strategies described, the treatment costs can be called "basic treatment costs". Such costs for different treatment strategies of each stage of esophageal cancer are fully reported here.

Data source

In order to get information on staff time, quantities of drugs and disposable supplies, equipment and facilities

used in screening and each specific treatment for every pathological stage, face-to-face interviews with medical staff (clinicians, head nurses and laboratory personnel) of departments associated with screening and treatment of esophageal cancer were performed in each hospital. Then, from the hospitals' databases, we collected information on: (1) unit costs of drugs and supplies, as well as purchase costs of equipment and the year in which they were bought; (2) the yearly incomes of staff in 2008; and (3) other expenditures of related departments, such as expenses of water, electricity and medical oxygen.

Data processing and assumption

The principles for defining the useful life of equipment, used in the process of annualizing the capital investments (defined as inputs that last for more than one year, e.g. vehicles, computers, medical equipment and facilities) are described elsewhere (Yu, Liu and Tang, 2003). We also took the expert opinions into account when calculating this value. When annualizing, we used 80% capacity utilization and 3% discount rate and assumed that the resale value of capitals was equal to zero (Karlsson and Johannesson, 1998; World Health Organization: WHO-CHOICE, 2003). Moreover, if the purchase year of equipment or was unknown, we assumed that it was bought in the year 2002. When counting the unit costs of capital investment, we also considered the related maintenance costs.

Average hourly income for each category of medical staff was estimated by dividing the average yearly income by total working hours per year in 2008. 80% of capacity usage was also used in assessing the staff costs.

In this analysis, we made an assumption that no patients of esophageal cancer who undergo esophagectomy would have major side effects requiring hospital treatment, but we did take into consideration the minor adverse events of screening (e.g. minor bleeding) and radiotherapy as well as chemotherapy (e.g. leucopenia and gastrointestinal reaction) based on local clinical experience.

For severe dysplasia, carcinoma in situ and intramucosal carcinoma, both the treatment strategies and average hospital stays were very similar, so we assumed that there were no differences in their treatment costs. The same situation existed between the submucosal carcinoma (T₁N₀M₀) and some invasive carcinoma treated through esophagectomy.

Because the purchase costs of drugs, supplies and equipment were derived from more than one year, we used the Gross Domestic Product (GDP) deflator to adjust all costs to the common year 2008 (World Health Organization: WHO-CHOICE, 2003). The GDP deflator was computed according to the data available in the China Statistical Yearbook in 2008 (China Statistical Yearbook-2008, 2008). Costs expressed in Chinese currency were converted to international dollars (\$) using Purchasing Power Parity (PPP) exchange rates (World Health Organization: Purchasing Power Parity 2005, 2005).

The total cost per capita for screening and treatment was estimated by two steps: (1) multiplying the quantity of each resource by its associated unit cost; (2) summing

these results to assess the cost of each component, total cost per capita of screening and that of each specific-treatment for every pathological stage (Goldhaber-Fiebert and Goldie, 2006).

Sensitivity analysis

Because there was uncertainty in some parameters used to estimate total costs, we defined the plausible ranges for some parameters to analyze their impact on costs: (1) discount rate ranged from 0 to 6%; (2) Capacity utilization ranged from 33% to 200% (Goldhaber-Fiebert and Goldie, 2006).

Results

Screening costs

The screening costs incurred in two processes: (1) endoscopy with mucosal iodine staining and combined with index biopsy, and (2) laboratory sample processing— pathology detection. Total costs per eligible participant came to I\$58.5, I\$61.5 and I\$63.6 in Feicheng, Linzhou and Ci County, respectively. Full details of each component are given in Table 1. The costs of equipment and facilities together with staff accounted for more than 65% of the total screening costs.

Treatment costs

Since the treatment strategies were not the same among different stages of esophageal cancer, and even in the same stage, the treatment costs varied significantly.

For severe dysplasia, carcinoma in situ and intramucosal carcinoma, the costs per case of EMR were I\$1620 and I\$1292 in Feicheng and Linzhou respectively, and those of APC were around I\$450. Because of limited resources and technologies, EMR and APC were not performed in the Cancer Hospital of Ci County.

For submucosal carcinoma (T₁N₀M₀), and invasive carcinoma treated by esophagectomy, the costs ranged from I\$1485 to I\$ 2171 at the three sites. For invasive carcinoma, the costs of radiotherapy were between I\$497 and I\$685.2; the costs of chemotherapy for 4 cycles were I\$5328, I\$4652, I\$4758, and for 6 cycles were

Table 1. Estimates of the Screening Cost (I\$) per Capita and the Percentage of Total Costs Attributable to each Cost Category

	Feicheng	Linzhou	Ci county
Endoscopy + Mucosal Iodine Staining + Index Biopsy			
drugs	9.7 23.5%	9.6 20.7%	9.7 21.0%
supplies	5.0 12.2%	5.4 11.6%	5.3 11.4%
equipment	17.1 41.6%	25.6 55.0%	22.3 48.4%
staff	9.0 21.9%	5.1 10.9%	8.3 18.0%
others	0.3 0.8%	0.8 1.8%	0.6 1.3%
total	41.2 100%	46.5 100%	46.1 100%
Pathology Detection			
supplies	5.2 30.2%	4.5 30.2%	6.1 34.8%
equipment	4.4 25.5%	5.2 34.7%	3.4 19.6%
staff	7.6 43.6%	4.6 30.9%	7.7 44.0%
others	0.1 0.7%	0.6 4.2%	0.3 1.7%
total	17.3 100%	15.0 100%	17.5 100%
Total costs per capita	58.5	61.5	63.6

Table 2. Estimates of the Treatment Cost (\$) per Capita for each Stage of Esophageal Carcinoma and the Percentage of Total Costs Attributable to each Category

Disease	Feicheng		Linzhou		Ci county	
Severe Dysplasia, CIS and Intramucosal Carcinoma						
A. Endoscopic Mucosal Resection						
drugs	105.6	6.5%	72.0	5.6%	—	—
supplies	1158	71.5%	897.0	69.4%	—	—
equipment	186.4	11.5%	171.3	13.3%	—	—
staff	154.1	9.5%	124.0	9.6%	—	—
others	16.0	1.0%	27.6	2.1%	—	—
total	1620	100%	1292	100%	—	—
B. Argon Plasma Coagulation						
drugs	90.1	20.2%	71.3	14.7%	—	—
supplies	104.6	23.4%	128.7	26.5%	—	—
equipment	114.9	25.7%	155.7	32.0%	—	—
staff	121.8	27.3%	105.0	21.6%	—	—
others	15.7	3.5%	25.7	5.3%	—	—
total	447.0	100%	486.3	100.0%	—	—
Submucosal Carcinoma (T ₁ N ₀ M ₀)-Esophagectomy						
drugs	856.7	39.5%	851.3	48.2%	556.4	37.5%
supplies	415.6	19.2%	342.3	19.4%	376.9	25.4%
equipment	400.9	18.5%	180.3	10.2%	205.4	13.8%
staff	462.4	21.3%	346.4	19.6%	308.1	20.7%
others	35.0	1.6%	47.7	2.7%	38.7	2.6%
total	2171	100%	1768	100%	1485	100%
Invasive Carcinoma						
A. Esophagectomy-the same as Submucosal Carcinoma						
B. Radiotherapy						
drugs	57.2	8.4%	42.8	7.8%	61.9	12.5%
supplies	98.5	14.4%	85.7	15.6%	53.4	10.7%
equipment	269.6	39.4%	213.3	38.8%	178.7	36.0%
staff	215.4	31.4%	179.8	32.7%	137.6	27.7%
others	44.5	6.5%	28.0	5.1%	65.4	13.2%
total	685.2	100%	549.6	100%	497.0	100%
C. Chemotherapy*						
4 cycles						
drugs	4598	86.3%	3935	84.6%	3958	83.2%
supplies	299.3	5.6%	224.6	4.8%	338.8	7.1%
equipment	180.8	3.4%	174.0	3.7%	202.5	4.3%
staff	204.6	3.8%	261.9	5.6%	208.0	4.4%
others	45.6	0.9%	56.9	1.2%	50.3	1.1%
total	5328	100%	4652	100%	4758	100%
6 cycles						
drugs	6896	86.6%	5902	84.9%	5937	83.5%
supplies	442.9	5.6%	332.0	4.8%	502.6	7.1%
equipment	259.8	3.3%	245.6	3.5%	290.9	4.1%
staff	299.1	3.8%	388.0	5.6%	304.0	4.3%
others	68.2	0.9%	84.7	1.2%	75.0	1.1%
total	7966	100%	6953	100%	7110	100%
D. Esophagectomy combined with Radiotherapy						
drugs	913.7	32.6%	894.0	39.5%	618.1	32.1%
supplies	502.0	17.9%	418.0	18.5%	419.0	21.7%
equipment	647.9	23.1%	362.8	16.0%	358.4	18.6%
staff	662.3	23.6%	516.4	22.8%	429.7	22.3%
others	79.1	2.8%	74.3	3.3%	103.2	5.4%
total	2805	100%	2266	100%	1928	100%
E. Esophagectomy, Radiotherapy and 4 cycles Chemotherapy						
drugs	5511	68.2%	4829	70.3%	4576	69.0%
supplies	789.2	9.8%	632.7	9.2%	746.5	11.3%
equipment	805.9	10.0%	506.0	7.4%	535.1	8.1%
staff	851.4	10.5%	768.7	11.2%	621.7	9.4%
others	124.2	1.5%	129.8	1.9%	152.6	2.3%
total	8082	100%	6866	70.3%	6632	100%

*Chemotherapy: according to the clinical practice guidelines,

four to six cycles treatment is considered as a standard chemotherapy procedure, so the 4-cycle and 6-cycle treatment costs are shown, respectively.

—Ci County has never developed EMR and APC.

US\$7966, US\$6953, and US\$7110.71 in Feicheng, Linzhou, and Ci county, respectively; the costs of combination of esophagectomy and radiotherapy were US\$1928~US\$2805; and the costs of esophagectomy, radiotherapy and chemotherapy in combination ranged from US\$6632 to US\$8082.

For EMR, the supplies costs accounted for around 70% of the totals; for radiotherapy, the equipment together with staff costs accounted for over 60% of the totals, while the drugs costs accounted for over 80% of chemotherapy costs (Table 2).

Sensitivity analysis

The sensitivity analysis showed that the discount rate had a slight impact on both screening and treatment costs. When the discount rate was transformed from 0% to 6%, most costs were increased by less than 10%. Nevertheless, the capacity utilization affected the costs considerably, especially for those in which the equipment costs and staff costs accounted for large percentages. This namely affected those which relied more on equipment, and personnel such as the radiotherapy and screening costs, where the costs of equipment, and staff accounted for over 60% of the total. These costs increased by more than 200% when the capacity utilization changed from 200% to 33% (data not shown).

Discussion

As far as we know, our study is the first to systematically assess the screening and treatment costs of esophageal cancer from the perspective of hospital resource expenditure as opposed to hospital charges. Researchers widely agree that charges are not a good proxy for costs of medical service, since the mark-up of items differs and thus masks the actual resource expenditure (Finkler, 1982; Shwartz, Young and Siegrist, 1995). In EDETEC program, screening costs per case were around US\$60. For severe dysplasia, carcinoma in situ and intramucosal carcinoma, the costs per capita of EMR were US\$1292~US\$1620, and around US\$450 for APC. For submucosal carcinoma (T₁N₀M₀), and invasive carcinoma treated by esophagectomy, the treatment costs per capita ranged from US\$1485 to US\$2171. The costs of other treatment of invasive carcinoma varied significantly: the costs for radiotherapy were lowest (around US\$ 600), and highest for esophagectomy, radiotherapy and chemotherapy in combination (US\$6632~US\$8082). The treatment costs of precancerous lesions and early esophageal cancer, including severe dysplasia, carcinoma in situ, intramucosal carcinoma and submucosal carcinoma (T₁N₀M₀), were greatly lower than that of late esophageal cancer (invasive carcinoma). Early detection and early treatment for esophageal cancer can provide great cost savings.

There are only two previously published papers on economic evaluation of screening and treatment of

esophageal cancer in China, but they both report the hospital charges from a perspective of payers instead of actual costs to the hospital. In addition, Liu et al did not report the treatment costs of specific stages of esophageal cancer (Liu et al., 2006). Although Lv et al distinguished stages of esophageal cancer when showing costs, they did not consider treatment methods for each specific stage (LV et al., 2010). Accordingly, their treatment costs are not comparable with ours. Moreover, these prior studies were conducted at only one site (Linzhou County), limiting the external validity.

The screening costs presented in this paper were slightly more than those from the research of Liu et al (I\$58.5~I\$63.6>I\$44.7) (Liu et al., 2006). This difference may be due to the different lifetime of screening equipment and facilities used in the prior study, which was twice that of our paper.

As described previously, the screening modality of Feicheng was different from that of Linzhou and Ci County, although no significant differences were found in terms of the total costs of endoscopy with collection of samples and laboratory sample processing. Nevertheless, the cost for each treatment in Feicheng seemed higher than at the other two sites, mainly due to higher staff incomes and purchase costs of equipment, drugs, and supplies in Feicheng. What needs to be emphasized was that the program was conducted at high-risk sites where the economy is underdeveloped and the labor costs were relatively low. If such an analysis were performed in other more-developed areas, the costs would be higher.

The treatment costs reported in this paper were around half that of the associated local hospital charges. It needs to be stressed that the EDETEC Program was a public health project of developing countries in areas where the incidence of esophageal cancer were viewed as the highest of the world combined with high shortages of health resources and poor economies. The whole procedure of screening and treatment was based on using the most basic but effective medicine and laboratory technologies to screen and treat patients, and did not consider serious complications. Accordingly, in this case, the screening and treatment costs of our study can be defined as minimum costs.

The sensitivity analysis revealed that the costs, relying more on equipment as well as staff, changed a lot when capacity utilization ranged from 33% to 200%, suggesting that interventions undertaken efficiently could cost significantly less than those done in a technically inefficient manner. The base-case costs in this analysis were estimated based on 80% capacity utilization, but in the real world, the productivity of equipment for some departments cannot reach this high percentage because of low patient numbers in local hospitals. Accordingly, the 'real costs' may be higher than those estimated in this paper.

Limitations of the equipment and facilities costs estimate include a reliance on experts' opinion and literature to define product lifetime instead of using directly observed data, and the assumption of 2002 for the

purchase year for many of the facilities and equipment. Furthermore, we only received maintenance expenses for a small number of the equipment units due to imperfect information registration in primary hospitals. All of these may lead to underestimation or overrating of the equipment costs. The assumption that no serious side effects would occur during the treatment may also have resulted in an underestimation of the treatment costs.

The program costs were not included in our paper for the following reasons: firstly, our three sites are the Early Detection and Treatment Demonstration Sites for esophageal cancer, so screening programs have been conducted there for several decades. There was already a high screening participation rate among the population and a high quality of training among staff, so we presumed the costs of training and media campaigns would be low enough to be omitted. Secondly, the EDETEC programs in each place depend on local hospitals, which make small changes of costs at the administrative levels within the existing administrative set-up. Therefore, it would be difficult to extrapolate to other situations; it is recommended that when using the costs of our paper in other areas, it is better to add local program costs. Moreover, our study just considered the direct medical costs and omitted costs such as patient time lost, which may occupy a certain part of the costs (Goldhaber-Fiebert and Goldie, 2006; LV et al., 2010). Therefore, further cost analysis studies of these need to be conducted in the near future.

Micro-costing studies mainly focus on quantity and value of resources used. There are several methods for quantity data collection: 1) administrative databases at single facilities, 2) insurer administrative data, 3) expert panels, 4) surveys or interviews of one or more types of providers, etc. (Frick, 2009). Unlike developed countries, developing countries have a shortage of mature administrative data, so we used face-to-face interviews together with expert's opinions to collect quantity data, confirming this method is feasible in rural areas of China. Moreover, we also tried to collect data by interviewing patients, but the quality and reliability of data was poor because the patients were highly sensitive to economic data and were reluctant to answer truthfully.

In conclusion, for a few decades, extensive mass endoscopic screening programs for esophageal cancer have been conducted in high-risk areas of China, mostly in rural areas with poor health resources. However, there were few prior economic evaluations on these programs. In this paper, we presented detailed screening and treatment costs of esophageal cancer, which can provide important cost inputs for health economic assessments of esophageal cancer screening projects, and provide useful information to policy makers making decisions about ongoing screenings in these areas. The costs here were considered as minimum costs in a public health project of a developing country. The methods used in this study also provide a practical method of cost estimation in rural areas that can be extrapolated to other developing countries.

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