

## Cost-utility Analysis of the EOX Drug Regimen versus the DCF Drug Regimen for Patients with Advanced Gastric Cancer

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### Abstract

**Background:** Cancer is one of the major causes of mortality and as an effective factor in the burden of diseases for the future. Among all cancers, gastric cancer is the fourth most common and the second leading cause of cancer mortality worldwide. In this study, we aim to evaluate the cost-utility of two chemotherapy regimens – epirubicin, oxaliplatin, and capecitabine versus docetaxel, cisplatin, and fluorouracil in patients with advanced gastric cancer in a hospital in southern Iran.

**Method:** This cross-sectional study was an economic evaluation of cost-utility type that included all patients at Amir Hospital (Shiraz, Iran) who had advanced gastric cancer and received either the epirubicin, oxaliplatin, and capecitabine or docetaxel, cisplatin, and fluorouracil chemotherapy regimen. All costs and the quality-adjusted life years were calculated, followed by one-way sensitivity analysis to verify the results.

**Results:** A total of 54 patients participated in this study, amongst whom 20 received the epirubicin, oxaliplatin, and capecitabine regimen and 34 received the docetaxel, cisplatin, and fluorouracil regimen. The mean quality of life of patients that received docetaxel, cisplatin, and fluorouracil was 0.747, whereas it was 0.836 for patients that received epirubicin, oxaliplatin, and capecitabine. The docetaxel, cisplatin, and fluorouracil treatment group (\$5573) was more expensive than the epirubicin, oxaliplatin, and capecitabine group (\$3108). The results obtained from the cost-utility analysis showed that the epirubicin, oxaliplatin, and capecitabine drug regimen was cost-effective due to lower cost and higher utility than the docetaxel, cisplatin, and fluorouracil regimen. One-way sensitivity analysis confirmed the accuracy of these results.

**Conclusion:** Due to the cost-effectiveness of the epirubicin, oxaliplatin, and capecitabine drug regimen compared to docetaxel, cisplatin, and fluorouracil, we recommend that oncologists use this regimen to treat gastric cancer patients.

**Keywords:** Cost-utility, EOX, DCF, Gastric cancer

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## Introduction

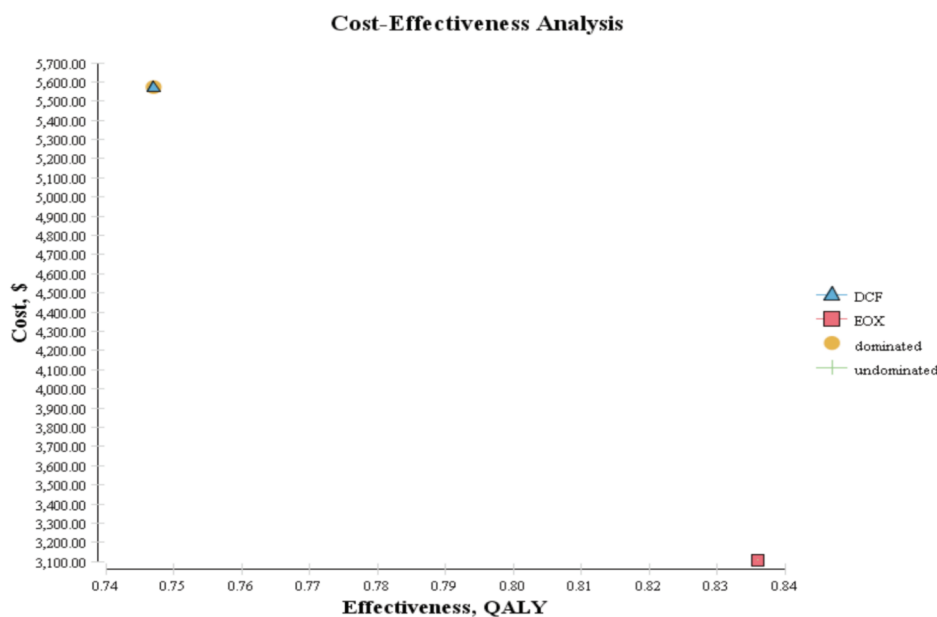
Cancer is one of the major causes of mortality and an effective factor in the burden of diseases for future decades.<sup>1</sup> Currently, 20 million people worldwide live with cancer. This number is expected to increase to 30 million by 2020.<sup>2</sup> In Iran, cancer is the third leading cause of death after heart diseases and traffic accidents.<sup>3</sup> Annually, approximately 70000 cases of cancer are diagnosed in Iran and about 30000 people die from this disease.<sup>4</sup>

Among various cancer types, gastric cancer is the fourth most common and second leading cause of cancer deaths worldwide.<sup>5</sup> There are an estimated 930000 new gastric cancer cases recorded each year, of which 700,000 lead to death.<sup>6</sup> The highest prevalence of gastric cancer in Iran has been recorded in the northern and northwest provinces. Ardebil reported the highest prevalence of cancer in Iran, with 49.1 cases per 100,000 population.<sup>6</sup>

In 2009, the cost of cancer in EU member states was 126 billion euros – 51 billion was related to medical expenses, 42.6 billion attributed to lost production cost, 9.43 billion was caused by absenteeism from work, and 23.3 billion

comprised other incurred costs.<sup>7</sup> Cancer costs include direct, indirect, and mental health costs. Direct medical costs include hospital costs as well as medical care, physiotherapy and laboratory charges, and re-visiting costs. Direct non-medical costs include the costs of transferring to hospitals, child nursing at home, and special clothing or nutrition due to cancer.<sup>8</sup> A study conducted in Shiraz has shown that households with cancer patients face catastrophic health care costs.<sup>9</sup>

Gastric cancer has no symptoms at first; therefore, the patients usually refer for clinical diagnosis at an advanced phase or metastatic disease stage.<sup>10</sup> Approximately 84% of the patients develop advanced gastric cancer and, if they do not receive chemotherapy, they will survive for 3 to 4 months.<sup>11</sup> Chemotherapy, radiotherapy, and surgery are current gastric cancer treatments.<sup>10</sup> Chemotherapy regimens use one drug or combinations of several drugs. The most advanced new drug combinations are docetaxel, cisplatin, and fluorouracil (DCF), and epirubicin, oxaliplatin, and capecitabine (EOX).<sup>11</sup> The EOX regimens include epirubicin (50 mg/m<sup>2</sup>), oxaliplatin (130 mg/m<sup>2</sup>), and capecitabine (1000 mg/m<sup>2</sup>), which are used for 1 to 21 days.<sup>12</sup> The DCF combined



**Figure 1.** Comparison of the cost-utility of the EOX\* versus DCF\*\* regimens in patients with gastric cancer admitted to Amir Hospital based on QALY. EOX: Epirubicin, oxaliplatin, and capecitabine; DCF: Docetaxel, cisplatin, and fluorouracil; QALY: Quality-adjusted life years.

regimen consists of the same dosages of docetaxel (75 mg/m<sup>2</sup>) and cisplatin (75 mg/m<sup>2</sup>) on the first day and fluorouracil (1000 mg/m<sup>2</sup>) for 1-5 days.<sup>13</sup>

These two treatment regimens need to be evaluated economically to determine an appropriate treatment strategy for gastric cancers, prevent the imposition of additional costs on patients and the treatment system, and prevent numerous adverse effects.<sup>14</sup>

Cost-utility analysis, an economic evaluation method, is the result of two or more options based on utility. This type of economic evaluation is used if the consequence quantity is expressed as a quality. This feature distinguishes cost-utility from other methods of economic evaluation.<sup>15</sup>

In this study, we examined the cost-utility of EOX versus DCF drug regimens from the community viewpoint in order to determine the most appropriate treatment method for patients with advanced gastric cancer.

## Materials and Methods

This cross-sectional study was an economic evaluation and cost-utility analysis conducted at Amir Hospital, Shiraz, southern Iran. Patient participants were hospitalized in Amir Hospital for their chemotherapy treatments. The subjects included all patients with advanced gastric cancer who received either EOX or DCF chemotherapy regimens. The EOX regimen was administered in the Medical Oncology Clinic. Patients in DCF group were admitted in the hospital for 5-fluorouracil (5FU) infusion due to two problems: first, handling of pump infusion in home was difficult for our patients, second, accommodation in the hotel for patients who are from other cities was not possible. However, these problems have additional costs for our patients. This study included 54 patients who used one of these two regimens from April 2015 to April 2016. A total of 34 patients used the DCF regimen and 20 received the EOX regimen. The treatment period was 6 cycles at 21 day intervals.

The information in this study consisted of two parts: cost information and information that pertained to patient quality of life. The cost

information was collected from the community viewpoint and through the use of a data collection form by the researcher. The costs that related to the one-year study period included all direct medical and non-medical costs, and indirect costs. The direct non-medical costs and indirect costs were collected through face-to-face interviews with the patients. We used a human capital approach, which included the costs of days absent from work, to determine the indirect costs. The wage rate was calculated according to the Ministry of Labor Act, which set the basic salary of \$203.50. This wage was calculated for all people over the age of 18, including housewives. Since the study was conducted over one year, there was no need to determine a discount rate. In addition to the above mentioned items, we recorded the patient's demographic information, type of insurance, and job on the form. The EQ-5D questionnaire was used to collect the information on quality of life (utility). This questionnaire is a general tool for assessing quality of life, and includes 5 questions that examine mobility, self-care, daily activities, pain and anxiety or depression.<sup>16</sup> We interviewed the patients one month after their last chemotherapy session. According to oncology specialists, patients experience the onset of adverse effects from the drugs one month after the last chemotherapy treatment. We used patients' telephone numbers to be informed about their subsequent referrals to plan the future interviews. The purpose of the interviews was explained to the patients as they were interviewed. The patients entered the study when the informed consent form was obtained.

After completion of the interviews and questionnaires, we calculated the costs and quality-adjusted life years (QALY). After we determined the costs and QALY for the two treatment groups, we calculated the incremental cost-effectiveness ratio (ICER).

In order to perform the cost-utility analyses in this study, both Tree Age 2011 and SPSS 19.0 software were used.

The Ethics Committee of Shiraz University of Medical Sciences approved this study and all

**Table 1.** Mean quality of life in patients with DCF and EOX drug regimens

Patient group	Number	Mean	Standard deviation	P-value
DCF	34	0.747	0.173	0.304
EOX	20	0.836	0.181	

DCF: Docetaxel, cisplatin, and fluorouracil; EOX: Epirubicin, oxaliplatin, and capecitabine

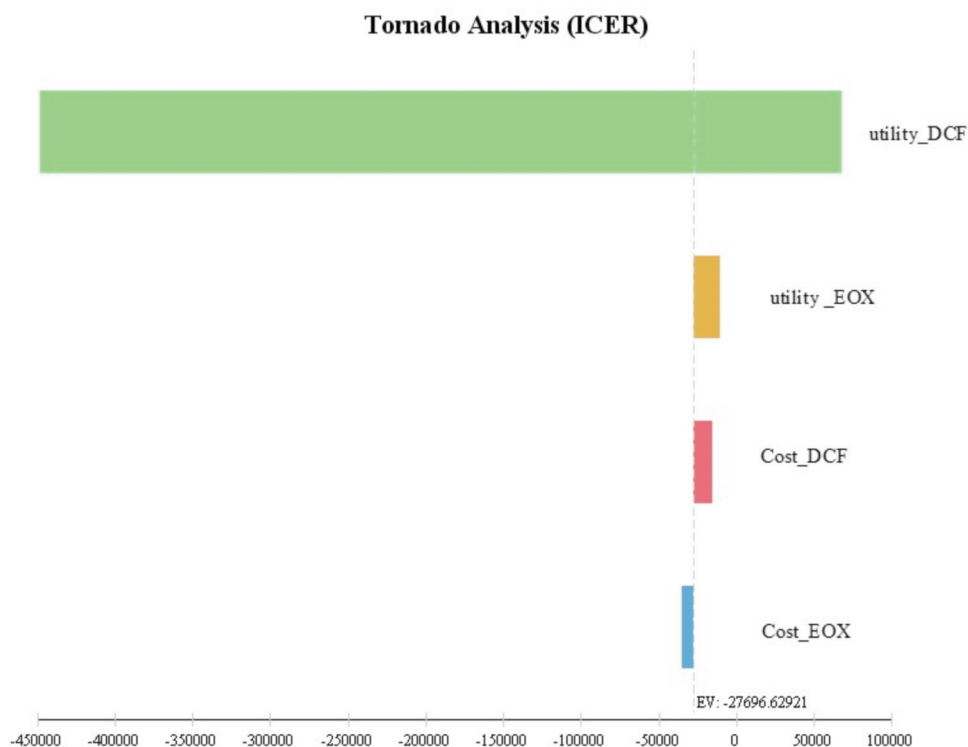
participants signed or marked (if illiterate) the informed consent forms.

### Results

A total of 93% of the participants were male and 51% were married. All patient participants had health insurance. The mean age of the patients in the DCF group was 49.9 years, whereas patients in the EOX group had a mean age of 56.3 years.

According to table 1, the mean quality of life of patients that received the DCF regimen was 0.747 and for the EOX group, it was 0.836. Patients who used the EOX regimen had a higher quality of life score and more satisfaction with their treatment process. However, there was no significant difference between the quality of life scores in the two groups.

Table 2 shows that the average direct medical costs (\$4200) and average indirect costs (\$1166) in the DCF treatment group were higher than the average direct medical costs (\$2132) and the average indirect costs (\$658) in the EOX group. However, direct non-medical costs had the opposite findings. The average direct non-medical costs in the EOX treatment group (\$318.1) were higher than those in the DCF treatment group (\$206.6). The standard deviation for direct medical costs, direct non-medical costs, and indirect costs in the DCF treatment group was higher compared to the EOX treatment group. The total mean cost of the patients in the DCF group (\$5573) was higher than the EOX group (\$3108). In both treatment groups, direct medical costs accounted for the largest portion of costs, whereas direct non-



**Figure 2.** Tornado diagram of cost-utility for advanced gastric cancer patients treated with the EOX and DCF regimens. EOX: Epirubicin, oxaliplatin, and capecitabine; DCF: Docetaxel, cisplatin, and fluorouracil; ICER: Incremental cost-effectiveness ratio

**Table 2.** Costs of patients with gastric cancer in both DCF and EOX treatment groups during a one-year treatment period.

Types of cost	DCF			EOX		
	Mean	Standard deviation	Percentage	Mean	Standard deviation	Percentage
Direct medical costs	4200	1027.14	75.3%	2132	415.52	68.6%
Direct non-medical costs	207	354.92	3.7%	318	114.64	10.2%
Indirect costs	1166	1043.17	21%	658	987.94	21.2%
Total costs	5573	-	100%	3108	-	100%

DCF: Docetaxel, cisplatin, and fluorouracil; EOX: Epirubicin, oxaliplatin, and capecitabine

medical costs comprised the least.

Table 3 and figure 1 show the cost-effectiveness results of the QALY index in the EOX treatment group compared to the DCF group. In this table, the highest utility unit is the best. As can be seen, EOX compared with DCF reduced the costs by \$2465 and increased the utility by 0.089; therefore, the EOX treatment was superior. There was no need to calculate ICER. As a result, the EOX treatment method was considered quite cost-effective in this study.

*Sensitivity analysis*

We performed a one-way sensitivity analysis to validate the results. To do so, each variable was changed up to 20% and drew the respective tornado diagrams.<sup>17</sup> In tornado diagram 2, U1 and C1 represent utility and cost for the EOX regimen, whereas U2 and C2 represent utility and cost for the DCF regimen.

As seen in figure 2, the results of the one-way sensitivity analysis show that the study results (ICER) had the highest sensitivity to the utility value U1 (EOX) and no sensitivity to the cost C2 (DCF). Therefore, if the utility value in the EOX method increased, the ICER value would become negative and, according to the results of table 3 and figure 1, a definite decision could be made in terms of cost-utility of the EOX method in comparison to DCF. Thus, it could be stated that

the EOX method was the preferred regimen.

**Discussion**

This study is one of the first economic evaluation models conducted in Iran. The intent was to determine the best drug regimen according to the community perspective to treat patients with advanced gastric cancer.

The findings showed that the mean quality of life in the DCF group was 0.747, whereas it was 0.836 in the EOX group. The patients who used the EOX treatment had a higher quality of life score and more satisfaction with their treatment process. Studies conducted in other countries reported various results. Chen et al.<sup>14</sup> showed that the EOX drug regimen was more effective than the other regimens in their study. Another study by Sendur et al.<sup>18</sup> indicated that the EOX drug regimen had fewer complications such as anemia and blood poisoning. In contrast, a multi-national study by Ajani et al. indicated that the DCF treatment, compared to CF medication, significantly improved the quality of life score. They reported better results for DCF compared to the present study.<sup>19</sup>

According to the cost-related findings of this study, the mean direct medical costs (\$4200) and the mean indirect costs (\$1166) of the DCF treatment group were higher than the mean direct medical costs (\$2132) and mean indirect costs

**Table 3.** Results of cost-utility analyses in patients with advanced gastric cancer who were treated with EOX and DCF.

Compared groups	Mean total costs of patients in the treatment group	Mean utility of patients in the treatment group	Incremental cost	Incremental utility	Result (ICER)
EOX	3108	0.836	2465	- 0.089	No need to calculate ICER
DCF	5573	0.747			

ICER: Incremental cost-effectiveness ratio; EOX: Epirubicin, oxaliplatin, and capecitabine; DCF: Docetaxel, cisplatin, and fluorouracil

(\$658) of the EOX group. However, direct non-medical costs of the EOX group (\$318.1) were higher than those of the DCF group (\$206.6). The standard deviation of direct medical costs, direct non-medical costs, and indirect costs in the DCF group was higher compared to the EOX group.

The DCF group was hospitalized longer or they needed an infusion pump for continuous infusion of 5-FU whereas the EOX group received part of their treatment as outpatients in the clinic. Thus, there was a significant difference between the direct medical costs and indirect costs of the two treatment groups. The EOX group received part of their treatment at an outpatient clinic and needed more visits and more travel with possibly more stay in hotels or inns. Therefore, their direct non-medical costs were higher than those of the DCF group. The total mean cost of the patients in the DCF group (\$5573) was higher than the EOX group (\$3108). The standard deviation was also higher because of the difference in the indirect costs of the patients in the DCF group.

Findings of the study by Chen et al. in China also showed that direct medical costs of the DCF drug regimen in the patients with advanced gastric cancer were 9979 Yuan. The results were consistent with those of the present study as the DCF drug regimen brought about the highest costs among all drug regimens.<sup>20</sup> A cost minimization study by Zhou et al. in China found that the direct medical costs for each treatment period of the EOX drug regimen for the patients with advanced gastric cancer were \$1068 and the direct medical costs per patient were \$5549.6. Their study showed that the EOX drug regimen reduced patient costs compared to the FOLFOX4 drug regimen.<sup>21</sup>

According to the sensitivity analysis, the results of this study had the highest sensitivity to the EOX group and no sensitivity to the costs of the DCF group. Therefore, if the utility in the EOX group increased, the ICER value would become negative and the EOX drug regimen could be considered the dominant option. Chen et al. reported that the combined DCF drug was not

cost-effective because it was higher than the threshold. This finding was consistent with the findings of our study.<sup>20</sup>

Chongqing et al. evaluated the cost-utility of gastric surgery versus the use of capecitabine and oxaliplatin (drugs in the EOX regimen). They showed that the use of gastric surgery along with the use of capecitabine and oxaliplatin had lower ICER than gastric surgery alone.<sup>15</sup>

Given that the EOX treatment regimen reduced the costs and increased the quality of life scores of the patients, which was confirmed by one-way sensitivity analysis, oncology specialists have recommended that gastric cancer patients receive the EOX drug regimen instead of the DCF regimen.

The results of this study can be generalized to other hospitals in Iran, but they cannot be generalized to other countries because of the differences in disease prevalence, the patients' ability to pay the costs, and the insurance coverage. Limitations of this study include cost recall bias by the patients.

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### Conflict of Interest

None declared.

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