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Review Article

# Cost-effectiveness analyses in gynecologic oncology: methodological quality and trends☆

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**Abstract**

*Objective.* To evaluate methodological quality and trends of cost-effectiveness analyses (CEA) published in gynecologic oncology.

*Methods.* A medical literature search of articles from 1966 through 2002 was performed to identify original, English-language articles that included economic analyses in gynecologic oncology. We included articles that were cost-effectiveness or cost-benefit analyses or performed these analyses as part of their study. Ten methodological principles that should be incorporated in CEAs were assessed for each study. Each article was given a score of 0, 1, or 2 for each of the 10 methodological principles (max score = 20). Data were analyzed using the Student *t* test, ANOVA, and linear regression.

*Results.* We screened 693 articles to identify 68 that met our inclusion criteria. The articles focused on cervical cancer ($n$ = 53; 78%), ovarian cancer ($n$ = 11; 16%), uterine cancer ($n$ = 2; 3%), and general perioperative care ($n$ = 2; 3%). The mean (±SD) methodological principle score was 16.1 (±4.1) and we observed a significant improvement in the total score over time ($P$ = 0.01). Primary CEA's (CEA identified as the objective of the study) were of higher quality than secondary CEA's (primary objective of the study was not CEA but CEA was included in the study; total scores 18.2 vs. 11.6, respectively; $P$<0.0001). Studies with at least one investigator in public health or healthcare economies also had higher quality (mean total score 17.7 vs. 15.2; $P$=0.006). The most common limitations of published CEAs were in methodology or presentation of incremental analyses, sensitivity analyses, and discounting.

*Conclusion.* Cost-effectiveness analyses in gynecologic oncology showed significant improvement in quality over the last two decades. Despite this progress, methodological improvement is still needed in the areas of incremental comparisons and sensitivity analysis. Understanding the methodology of cost-effectiveness analysis is critical for researchers, editors, and readers to accurately interpret results of the growing body of CEA articles.


*Keywords:* Cost-benefit analysis; Economics; Gynecology–economics

## Introduction

Healthcare costs have risen dramatically in the past three decades and now exceed US$1.3 trillion dollars or 16% of the United States gross domestic product [1]. With this rise in costs and tightening budgetary constraints, closer attention is placed on the allocation of health care expenditures. The total cost of cancer care in the United States was than US$180 billion dollars in 2000 [2]. In California alone, the total cost for gynecologic cancer care was greater than US$600 million dollars in 1998 [3]. Technological advances in cancer screening, diagnosis, and treatment provide more options for patients but often at substantially increased cost. The challenge lies not only in showing clinical utility of new or existing diagnostic and treatment strategies, but also in finding an acceptable balance between improved health outcomes and increased costs. Economic evaluations are being utilized more frequently to provide information on the costs and cost-effectiveness of adopting new technology,

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changing clinical practice, and helping to guide healthcare policy regarding these developments.

Cost-effectiveness analysis (CEA) and cost-benefit analysis (CBA) are analytical techniques in healthcare that may assist with more rational, effective, and economically sound medical decision making [4–6]. These analyses assess both the costs and health outcomes of alternative healthcare programs or strategies, thus providing useful information about the relative benefits and trade-offs of different healthcare interventions. While the value of effectiveness in a CEA may be any unit (i.e. life years gained, lives saved), cost-benefit analysis values both costs and health outcomes in dollars by converting health outcomes into monetary values. Methods for CEAs and CBAs, which will be combined and called CEA for the remainder of this report, have been well described in the medical literature [4–11]. The U.S. Public Health Service and several peer-reviewed journals recently convened panels to establish strict criteria for the effective application of CEA and have begun to quantify the methodological quality of published CEAs [4,7–9]. However, cost-effectiveness continues to be a term used loosely in many peer-reviewed publications [9].

In gynecologic oncology, CEAs may help to evaluate new or existing tests, procedures, technologies, and interventions. In this study, we will review the use of CEA in gynecologic oncology specifically to evaluate methodological quality and trends in the performance of CEA. In addition, we will briefly review the accepted methods for performing and reporting CEA.

## Methods

### *Methodological review*

Ten basic principles that should be incorporated in CEA have been identified [12]. These principles were derived from guidelines established by the Panel on Cost-Effectiveness in Health and Medicine convened by the U.S. Public Health Service [4]. The 10 principles, summarized below, compose an appropriate minimum standard for performing and reporting CEAs. Each principle should be explicitly addressed in every CEA study.

1. Research question: The research question must be clearly stated, interesting for either clinical care or health policy, and appropriate for CEA (i.e., comparison of at least two different healthcare strategies with different costs and health outcomes). Sufficient data should be available on probabilities of events, outcomes, and costs.
2. Time frame: The period of time over which costs and benefits are measured should be long enough to capture future health outcomes and the economic impact of an intervention.
3. Perspective: The viewpoint from which the analysis is conducted is called the perspective. The choice of perspective is determined by the research question and the goals of analysis (i.e., societal, managed care organization, insurer, and patient perspective).
4. Analytic model: Each treatment intervention or program being assessed must be described and possible courses of events identified, including the disease process, expected course, treatments, complications, and outcomes. This may be performed using a spreadsheet or decision tree and may include a Markov state transition model that cycles over fixed intervals of time.
5. Probabilities: Probabilities are estimated for each event described in the analytic model. The most accurate estimates of probabilities for each event in the model should be included with documentation of sources.
6. Costs: Costs are identified and estimated for the economic component of the CEA. Different types of costs can be used; however, the source of the cost data, quality of the data, and appropriateness for the analysis and perspective should be evaluated. Costs may include direct, indirect (productivity loss), and/or intangible (pain and suffering) costs and they may be measured or estimated using many methods (i.e., resource use, adjusted charges, reimbursements, lost wages).
7. Outcome measure: Measures of effectiveness depend on the type and objectives of analysis and should be expressed in the most appropriate natural units, such as days of hospitalization averted, lives saved, or life-years gained. Quality of life may also be incorporated into the outcome by assigning a weight (or utility) to each time period that reflects an individual's quality of life in a specific health state (range from a health state equivalent to death or 0 to perfect health or 1). This is summarized by quality-adjusted life years (QALY).
8. Incremental analysis: Since the purpose of a CEA is to describe the relative value of one healthcare strategy compared to another, incremental analysis identifies the additional cost and effectiveness when one healthcare option is compared with another. In all models, a baseline analysis should be presented. Each strategy should be compared to the alternative with the next lower cost. The incremental costs and effectiveness are used to create an incremental cost–effectiveness ratio between alternative strategies.
9. Sensitivity analysis: Evaluation of the effects of uncertainty inherent in CEA requires the performance of sensitivity analyses, which demonstrate whether a conclusion is robust to changes in assumptions made in the analysis (i.e., probabilities, costs, utilities). Data in the model are varied over plausible ranges and the cost–effectiveness ratio is recalculated.
10. Discounting: Since the value of both costs and utilities may decrease over time, discounting is used to calculate the present value of money that will be spent and health states that will occur in the future. Future costs and utilities should be discounted to present value, usually 3–5% per year.

*Article selection and scoring*

We performed a comprehensive computerized medical literature search using the MEDLINE database of all articles published from January 1966 through December 2002 and manually searched bibliographies of relevant articles. Medline search terms included gynecologic oncology, female genital neoplasm, and economic analysis. English language articles containing original research that were primarily cost-effectiveness or cost-benefit analyses were included in this review. Articles that included CEA as an objective of the study were identified as a "primary CEA." In addition, articles that were not a primary CEA (i.e., the primary objectives or analyses were to evaluate non-CEA outcomes) that also included a CEA were identified as a "secondary CEA" and included in this review. Review articles, letters, cost analyses, and cost-minimization analyses were excluded from this review.

Articles were examined by four independent, unblinded reviewers (MRM, LMC, ABC, and LLS) and scored for each of the 10 basic principles that should be incorporated in a CEA (see Methodological review). Each study was graded for adhering (score of 2), partially adhering (score of 1), or not adhering (score of 0) to each methodological principle for performing cost-effectiveness analysis. Any discrepancy in scoring was resolved through a consensus meeting attended by all reviewers. Each study also received a total score for the number of all methodological principles to which it adhered (sum of all principles, range from 0 to 20). Data are presented as number of and percent of total and compared using Student *t* test and ANOVA. Total scores were evaluated with ordinal logistic regression analysis and checked with a linear regression model, which had similar results. Trends over time were evaluated with logistic regression analyses.

## Results

Of the 152 articles identified, 68 included CEA as a primary or secondary focus of the study and were included in this review (Fig. 1) [13–80]. Most of the excluded

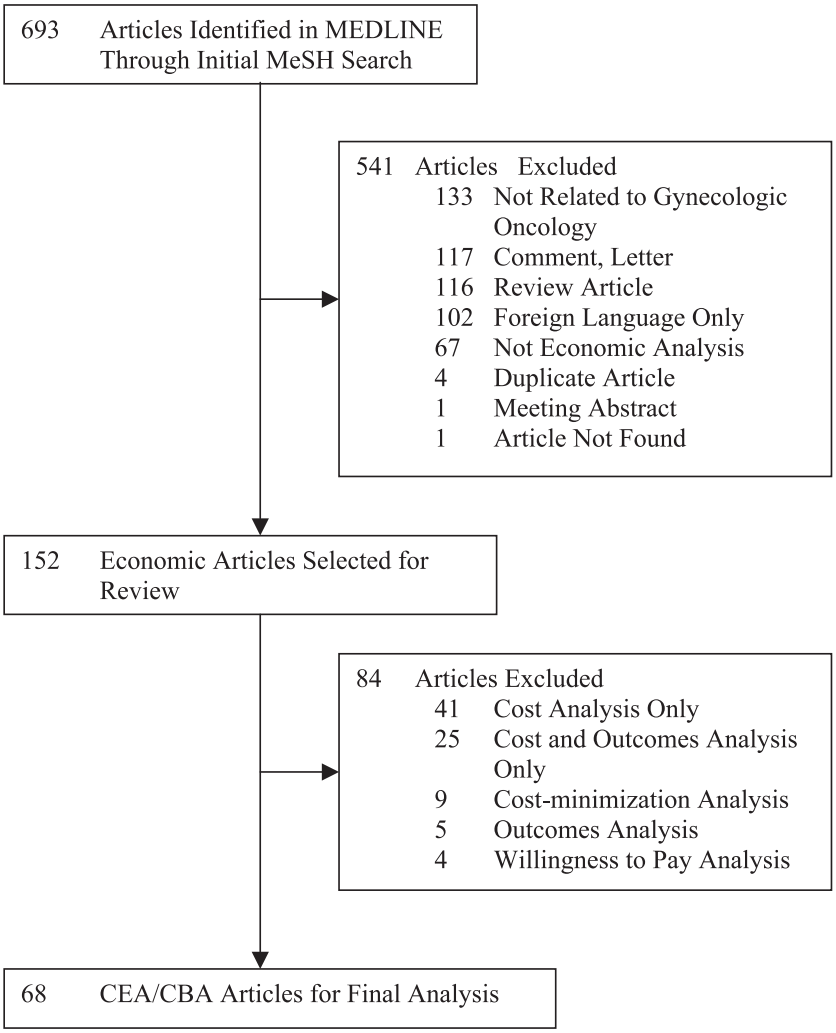


Fig. 1. Article screening process.

articles performed only cost, outcomes, or cost-minimization analyses.

The mean total score (±SD) for adherence to methodological principles for all of the articles reviewed was 16.1 (±4.1) (Table 1). Mean scores for each of the 10 individual principles ranged from a low of 1.1 (±0.9) for perspective to a high of 2.0 (±0.1) for probabilities.

Primary CEAs were performed in 47 of 68 (69%) articles, and mean total scores for adherence to methodological principles for primary CEA analyses were greater than for secondary CEA analyses (18.2 vs. 11.6, respectively; *t* test $P < 0.0001$). Secondary CEAs had lower individual scores in 9 of 10 methodological principles compared to primary CEAs (Table 2).

Articles included in the final review were published between 1972 and 2002. The number of CEAs published increased from 5 in the 1970s to 41 in the 1990s. In addition, we observed significant improvement over time in mean total score for adherence to methodological principles (logistic regression $P = 0.01$; Table 3).

Of the 68 articles reviewed, cervical cancer was the gynecological cancer most frequently evaluated by CEA ($n = 53$ articles; 78%), followed by ovarian cancer ($n = 11$ articles; 16%), uterine cancer, and general gynecologic oncology topics ($n = 4$; 6%). Cervical cancer articles were published from 1972 to 2002 and focused on screening ($n = 46$ articles; 87%), treatment ($n = 6$ articles; 11%), and diagnosis ($n = 1$ article; 2%). Ovarian cancer articles were published more recently (1996–1999) and primarily focused on treatment ($n = 9$; 82%). Analyses of ovarian and cervical cancer had similar mean total scores (17.6 and 15.8, respectively; *t* test $P = 0.14$).

Articles were performed by investigators in both academic and industry settings. The largest contributions of CEA in gynecologic oncology came from departments of public health, economics, and epidemiology ($n = 22$; mean score: 16.5). First author affiliations also included departments of obstetrics and gynecology ($n = 13$; mean score: 16.2), pathology ($n = 10$; mean score: 14.7), oncology ($n = 10$; mean score: 14.9), community or family medicine ($n = 8$; mean score: 16.4), and pharmacy ($n = 2$; mean score: 20). There were no differences in mean total scores for adherence to methodological principles by the first author's affiliation. However, articles with at least one author from a public health or healthcare economics department had significantly higher scores than those without this contribution (mean score 17.7 vs. 15.2; *t* test $P = 0.006$).

Table 1
Mean (±SD) score[a] for adherence to methodological principles for performing and reporting cost-effectiveness analyses[a]

| Methodological principle | Mean score (SD) |
|---|---|
| Research question | 1.8 (±0.5) |
| Time period | 1.8 (±0.5) |
| Perspective | 1.1 (±0.9) |
| Model | 1.5 (±0.7) |
| Probabilities | 2.0 (±0.1) |
| Cost | 1.8 (±0.5) |
| Outcome measure | 1.9 (±0.2) |
| Incremental analysis | 1.5 (±0.8) |
| Sensitivity analysis | 1.4 (±0.9) |
| Discounting | 1.5 (±0.8) |
| Total[b] | 16.1 (±4.1) |

SD = standard deviation.
[a] Score for each methodological principle is based on adhering (score of 2), partially adhering (score of 1), or not adhering (score of 0) to each methodological principle.
[b] Total score is the sum of all methodological principles and may range from 0 to 20.

Table 2
Mean (±SD) score[a] for adherence to methodological principles for performing and reporting cost-effectiveness analyses for primary vs. secondary cost-effectiveness analyses[a]

| Criteria | Primary CEA[b] mean score (SD) | Secondary CEA[c] mean score (SD) | *P* value[d] |
|---|---|---|---|
| Research question | 2.0 (±0) | 1.4 (±0.7) | 0.0009 |
| Time period | 1.9 (±0.3) | 1.5 (±0.7) | 0.02 |
| Perspective | 1.3 (±0.9) | 0.7 (±0.8) | 0.01 |
| Model | 1.9 (±0.4) | 0.6 (±0.5) | 0.0001 |
| Probabilities | 2.0 (±0.1) | 2.0 (±0) | 0.3 |
| Costs | 1.8 (±0.4) | 0.6 (±0.5) | 0.3 |
| Outcome measure | 2.0 (±0) | 1.8 (±0.4) | 0.04 |
| Incremental analysis | 1.7 (±0.5) | 1.0 (±1.0) | 0.001 |
| Sensitivity analysis | 1.8 (±0.6) | 0.5 (±0.7) | 0.0001 |
| Discounting | 1.8 (±0.6) | 0.5 (±0.9) | 0.0002 |
| Total[e] | 18.2 (±2.2) | 11.6 (±3.6) | 0.0001 |

CEA = cost-effectiveness analysis; SD = standard deviation.
[a] Score for each methodological principle is based on adhering (score of 2), partially adhering (score of 1), or not adhering (score of 0) to each methodological principle.
[b] Primary CEA is defined as a study that includes CEA as an objective of the study.
[c] Secondary CEA is defined as a study that is not a primary CEA but includes a CEA.
[d] Students *t* test.
[e] Total score is the sum of all methodological principles and may range from 0 to 20.

Table 3
Mean (±SD) and median total scores for adherence to methodological principles by time period

| Time period (years) | Number of articles published | Mean total score[a] (SD) | Median total score |
|---|---|---|---|
| 1970–1974 | 2 | 17.0 (±2.8) | 17.0 |
| 1975–1979 | 3 | 12.7 (±2.3) | 14.0 |
| 1980–1984 | 2 | 9.0 (±4.2) | 9.0 |
| 1985–1989 | 4 | 13.3 (±3.4) | 12.5 |
| 1990–1994 | 6 | 14.8 (±4.6) | 17.5 |
| 1995–1999 | 35 | 16.9 (±3.7) | 18.0 |
| 2000–2002 | 16 | 17.1 (±4.2) | 19.0 |

$P = 0.01$ for trend over time using logistic regression analysis; SD = standard deviation.
[a] Total score is the sum of all 10 methodological principles and may range from 0 to 20.

## Discussion

Overall, CEAs in gynecologic oncology follow the 10 established methodological principles for performing and presenting cost-effectiveness analyses. The number of CEAs has increased and methodological quality of CEAs improved over the last 30 years. This increased interest in economic analyses likely reflects growing pressures for cost containment and more efficient resource allocation. In addition, CEA has been a valuable method to evaluate new healthcare technology, which is often expensive.

Our review suggests that many of the published cost-effectiveness analyses in gynecologic oncology follow basic recommended analytical guidelines. Strengths of these CEAs include the definition of the research question and outcome measure and quality of probabilities used for the analyses. However, further improvement is needed in describing the perspective of and model used for the analysis in addition to explicit presentation of incremental and sensitivity analyses. It is possible that many studies incorporated the basic principles of CEA in their methods but failed to explicitly report them in their manuscripts. Specific areas that may not be explicitly reported but are essential to developing an analysis include model development, time frame, and perspective.

Costs are critical assumptions of any CEA. The sources of cost estimates should be identified and costs should be explicitly itemized. Estimates such as local charges are unlikely to be either generalizable or truly reflect resources used or money spent. In healthcare systems without a single payer, costs may best be estimated by accounting of actual resources used, charges adjusted by a cost-to-charge ratio, reimbursements, or actual direct medical payments. Many of the articles included in this review did not provide explicit information to evaluate the accuracy of cost data.

Incremental and sensitivity analyses are also essential components of cost-effectiveness analysis. The purpose of performing a CEA is to compare the benefits and trade-offs of different healthcare strategies [11]. Incremental analysis is imperative to compare a series of possible intervention strategies and provides evaluation of the cost-effectiveness of each successive strategy. For analyses with more than two alternative strategies, a common methodological error is to compare each strategy to the base case rather than performing an incremental analysis where each strategy is compared to the next less costly strategy. The simple comparison to the base case tends to minimize the cost-effectiveness ratio (i.e., makes a strategy appear more ‘‘cost-effective’’) and neglects intermediate and clinically possible strategies evaluated by the study. While a strategy may appear acceptable or ‘‘cost-effective’’ compared to the base case, it may not be ‘‘cost-effective’’ when compared to an intermediate strategy.

Sensitivity analyses allow investigators to vary the inputs within clinically reasonable ranges. Methods of performing sensitivity analysis must be clearly described to understand the context in which the analysis is relevant. Results may then be interpreted by readers for variations that may occur in their individual practice or healthcare system.

Secondary CEAs had consistently lower mean total scores for adherence to methodological principles. In these papers, lower scores on CEA principles of perspective, model, and costs, in addition to inadequate incremental and sensitivity analyses, were common. Most studies defined a cost-effectiveness ratio by dividing an estimate of cost by an outcome without describing additional assumptions using a model.

The cost-effectiveness of cervical cancer screening has been well described by several excellent CEAs [13–15,18–23,26,29,31,35,37,38,42,43,47–49,52,57,63,64,67,70,79]. The conclusions of these studies were based on clearly presented methodologic criteria. Incremental and sensitivity analyses were performed based on the model presented and specifically addressed the research question. Through these careful analyses, conclusions regarding the cost-effectiveness of several different cervical cancer screening strategies could be made in a quantitative manner. Policy recommendations for cervical cancer screening have been based on effectiveness. While costs per se and cost-effectiveness have not been considered in policy recommendations, cost-effectiveness analyses results have informed the expert panel discussions and had a limited role in the final recommendations [81].

This study has several limitations. We did not include non-English language articles in our final analyses due to translation limitations. Approximately 15% of articles identified in the initial search were excluded because of language. Abstract review of these non-English language articles showed that 15% may have used CEA methodology. Inclusion of these articles may have changed the results of this study. Our search method used Medical Subject Heading (MeSH) terms and specific keywords that may not have been comprehensive. In addition, reviewers were not blinded to authors, author’s affiliations, year of publication, or journal. However, methodological criteria used to evaluate each study were designed to be objective and applied consistently to all articles evaluated. All discrepancies in scoring were resolved with a consensus process in which all reviewers participated.

Reviews of CEAs in the fields of critical care medicine, radiology, and obstetrics and gynecology have been published [82–85]. The reviews emphasize that CEA is an important tool to inform decision making for healthcare policy. They found that published CEAs adhered to approximately half of the methodological criteria for performing and reporting cost-effectiveness analyses. We found that cost-effectiveness analysis in gynecologic oncology had much better adherence to accepted methodological criteria.

Healthcare decision makers are being forced to make difficult choices between alternative uses of limited healthcare resources. Economic considerations, in addition to clinical outcomes and quality of life, will continue to

influence healthcare policy. Cost-effectiveness analysis is one of many research methods that provides evidence that may contribute to the decision-making process. However, CEA results are only as accurate and generalizable as the assumptions and models that produced them. Investigators who conduct cost-effectiveness analyses are strongly encouraged to follow the recommended basic methodological principles for performing and reporting CEAs [4–12]. In addition, journal reviewers should be familiar with accepted methodological principles for performing cost-effectiveness analyses that have been formalized as published guidelines [7,10]. Understanding the methodology of cost-effectiveness analyses is also critical for readers of the literature to accurately interpret results of CEA. In gynecologic oncology, formal CEAs should continue to be an important resource in evaluating the many different diagnostic and treatment options and new technologies available to care for our patients.

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