

Cost-effectiveness Analysis of Breast and Lung Cancer- A Review Study

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Abstract: According to estimation from the World Health Organization (WHO) in 2019, cancer is the first or second leading cause of death before the age of 70 years in 112 of 183 countries and ranks third or fourth in a further 23 countries. Cancer is a group of more than 100 different and distinctive diseases. Cancer is the second leading cause of death globally and is responsible for about 10 million deaths per year. Various studies have estimated that reduction in treatment costs through early screening detection may be 30% to 100% or more of the cost of screening. The basic cost-effectiveness calculation appears to be simple, choices about units of measurement, definitions of interventions, scope of costs, and prices to be included not only will alter the numerical results but also will affect the interpretation of the cost-effectiveness ratio. If the cost-effectiveness analysis uses number of deaths averted as its measure of health gain, then allocating resources to more cost-effective interventions will avert the most deaths. Cost-effectiveness analysis helps identify neglected opportunities by highlighting interventions that are relatively inexpensive, yet have the potential to reduce the disease burden substantially.

Keywords: CEA, Cost of Illness, Mammography, Breast & Lung Cancer Screening, Computed Tomography, Immunotherapy.

INTRODUCTION

Overall, the burden of cancer incidence and mortality is rapidly growing worldwide; this reflects both aging and growth of the population as well as changes in the prevalence and distribution of the main risk factors for cancer, several of which are associated with socioeconomic development [13-14]. Worldwide, an estimated 19.3 million new cancer cases (18.1 million excluding nonmelanoma skin cancer) and almost 10.0 million cancer deaths (9.9 million excluding nonmelanoma skin cancers) occurred in 2020. Breast cancer has now surpassed lung cancer as the leading cause of global cancer incidence in 2020, with an estimated 2.3 million new cases, representing 11.7% of all cancer cases. Because organized; population-based mammography screening programs may not be cost effective or feasible in low-resource settings [1]

Breast cancer

Breast cancer (BC) is a heterogeneous disease [18,19]. Breast cancer remains one of the most devastating diseases for women. Although women want to guard against breast cancer through early detection from screening, as the American health care system moves toward value-based medicine, it becomes increasingly important to understand the harm-benefit trade-off of various breast cancer screening strategies. The benefit of screening mammography in cancer control has been established in clinical trials and observational and modeling studies.

The risk factors of BC including age, obesity, family history, reproductive factors, estrogen, and lifestyle, etc. The Gail model was the first established BC risk prediction model, which includes six risk factors: age, age at first live birth, age at menarche, history of breast cancer in first-degree relatives, number of previous breast biopsies, and history of atypical hyperplasia, most of which are reproductive factors. Besides the aforementioned non-genetic factors, genetic factors related to breast cancer risk have also been studied for years. Family of breast cancer history associated with gene line mutations including variants in BRCA1 and BRCA2, as well as altered gene structure in other genes, such as TP53, PTEN, ATM, CHEK2, NBS1, RAD50, BRIP, and PALB2, were thought to be involved in cancer onset (Amir et al., 2010). BRCA1 and BRCA2 have long been linked to breast cancer.⁴ Some foods and nutrients (e.g., carbohydrates, saturated fat, red and processed meats) are considered potential risk factors for BC, as they increase circulating levels of endogenous estrogen, insulin-like growth factor (IGF)-1 and pro-inflammatory cytokines [18]

The management of BC include primarily loco regional treatments i.e. surgery. Adjuvant therapy includes chemotherapy, hormonal therapy and targeted therapy. Nutritional support like consuming green tea, vitamin c, e, d, poly unsaturated fatty acids all help in better prognosis. The new Neoadjuvant therapy also helps in management with less toxicity [20]

Lung cancer

Lung cancer or lung carcinoma is a malignant lung tumor characterized by uncontrolled cell growth in the lung tissues [17]. Lung cancer remains the most commonly diagnosed cancer type worldwide, with 2.1 million new cases annually. It accounts for an estimated 1.8 million deaths per year and is thus the most common cause of cancer-related deaths in men and the second most common cause in women [15]

RISK ASSESSMENT	RISK STATUS	SCREENING		
<ul style="list-style-type: none"> Smoking Radon exposure Occupational exposure Cancer history Family history of Lung cancer in first degree relatives. Disease history (COPD or Pulmonary fibrosis) Smoking exposure (Second-hand smoke) Absence of symptoms or signs of lung cancer (If symptoms, see appropriate NCCN guidelines) Lung cancer survivors see surveillance in the NCCN guidelines for non-small cell lung cancer 	High Risk <ul style="list-style-type: none"> Age 55-74 and ≥ 30 Pack-year history of smoking and Smoking cessation <15y (category 1) Or	In candidate for Screening shared Patients/Physician decision making is recommended including a discussion of benefits/risks	Low dose CT (LDCT) (Category 1)	See Screening findings (LCS-2)
	<ul style="list-style-type: none"> Age ≥ 50 year and ≥ 20 pack-year history of smoking Additional risk factors (other than second-hand smoke) that increase the risk of lung cancer to $\geq 1.3\%$ 	In candidate for Screening shared Patients/Physician decision making is recommended including a discussion of benefits/risks	Low dose CT (LDCT)	See Screening findings (LCS-2)
	Moderate Risk <ul style="list-style-type: none"> Age > 50 year >20 pack-year history of smoking or second-hand smoke exposure No additional risk factors 	Lung cancer screening not recommended		
	Low Risk <ul style="list-style-type: none"> Age <50 years and or <20 pack-year history of smoking 	Lung cancer screening not recommended		

Treatment for lung cancer depends on the cancer's specific type, how far it has spread, and the person's performance status. The common treatments include palliative care, surgery, chemotherapy, and radiation therapy. Targeted therapy of lung cancer is growing in importance for advanced lung cancer [17]

Surgery : In most cases of early-stage NSCLC, removal of a lobe of lung (lobectomy) is the surgical treatment of choice. In people who are unfit for a full lobectomy, a smaller sub lobarexcision (wedge resection) may be performed. Radioactive iodine brachytherapy at the margins of wedge excision may reduce the risk of recurrence. Rarely, removal of a whole lung (pneumonectomy) is performed. Video-assisted thoracoscopysurgery (VATS) and VATS lobectomy us a minimal invasive approach to lung cancer surgery. [17]

Radiotherapy and Chemotherapy: Radiotherapy is often given together with chemotherapy and may be used with curative intent in people with NSCLC who are not eligible for surgery. This form of high-intensity radiotherapy is called radical radiotherapy. A refinement of this technique is continuous hyper- fractionated accelerated radiotherapy (CHART), in which a high dose of radiotherapy is given in a short time period. Prophylactic cranial irradiation (PCI) is a type of radiotherapy to the brain, used to reduce the risk of metastasis. For both NSCLC and SCLC patients, smaller doses of radiation to the chest may be used for symptom control (palliative radiotherapy). [17]

Chemotherapy: Chemotherapy regimen depends on the tumor, even relatively early stage disease, is treated primarily with chemotherapy and radiation. In SCLC, cisplatin and etoposide are most commonly used. In advanced non-small-cell lung cancer (NSCLC), chemotherapy improves survival and is used as first-line treatment, provided the person is well for the treatment. Chemotherapy may be combined with palliative care in the treatment of the NSCLC. In advanced cases, appropriate chemotherapy improves average survival over supportive care alone, as well as improving quality of life. In targeted therapy, several drugs that target molecular pathways in lung cancer are available, especially for the treatment of advanced disease. Some of the drugs used in targeted therapy may be useful in the treatment of bone metastases. [17]

Cost of Illness (COI) studies indicate the importance of a particular disease and provide a baseline for assessing new interventions [2]. In future, the cost of cancer care will increase as new sophisticated, expensive treatment modalities are adopted to raise the standard of care [3] Drug therapy was found to be the major driver behind the high overall cost [4] Since health care resources are scarce, the clinical decision regarding the use of cancer treatment should be based on the value of the monetary costs of these treatments, which is known as ‘cost-effectiveness [9]

There are four main types of studies involving economic evaluation: *cost analysis*, *cost-utility analysis* (CUA), *cost-benefit analysis* (CBA), and *cost-effectiveness analysis* (CEA) [21], CEA differs from these other types of analysis in that it looks at only one consequence of an intervention. Cost-Effectiveness Analysis (CEA) estimates the costs and health gains of alternative interventions.

Components of CEA

The most commonly used measure of benefit in CEA is the QALY. The QALY is a metric that captures gains from reduced morbidity (quality gains) and reduced mortality (quantity gains) and combines them into a single measure. A key rationale for using QALYs in the development of health policies is to assist in comparing interventions and finding the alternative—for example, intervention A versus its alternative intervention B—that provides the greatest value for the money. This is accomplished through comparison of incremental cost-effectiveness ratios (ICERs), defined as the difference in cost between two possible interventions, divided by the difference in their effect.

An ICER is a ratio of incremental cost (cost of A minus cost of B) and incremental effect (effectiveness of A minus effectiveness of B). Incremental cost, in the numerator, represents additional resources needed due to using intervention A instead of B. The incremental effect, in the denominator, represents additional health outcomes, such as additional QALYs gained through use of A instead of B. Assuming intervention A is more costly and more effective than B, the resulting low ICER value indicates that A provides improvement in health at a small extra cost per unit of health, and therefore dominates B as better value for the money.

also be considered. As examples, one could reference a threshold value of \$50,000 to \$150,000 per QALY gained, or even an individual willingness-to-pay value of twice one's annual salary [22]

There are three things that affect the use of these data in CEAs: quality, relevance, and comprehensiveness [21]. Effectiveness data is not always derived from systematic reviews, and comparisons made against current practice do not necessarily permit effective CEA analysis of other alternatives, or no intervention at all. The following is a summary of CEA methods as they have been refined and developed by the WHO CHOICE (Choosing Interventions that are Cost- Effective) project:

- ✓ Calculation of the number of healthy life years, measured in DALYs, in a population with no specific intervention, based on input parameters such as disease incidence, remission, cause-specific and background mortality as well as health status evaluations.
- ✓ Calculation of the same estimate (DALYs) using parameters reflecting the impact of the intervention or a combination of interventions.
- ✓ Effectiveness data for specific interventions are derived from a systematic review of previous interventions, where available.
- ✓ Calculation of the difference in DALYs gained by the population with the intervention (denominator of the cost-effectiveness ratio).
- ✓ Calculation of the cost of the intervention, including labour, materials, transport, education, administrative, training, etc. This constitutes the numerator of the cost effectiveness ratio. (Averted health care treatment costs such as hospitalization, pharmaceutical costs, etc. as a result of less illness or disease are regarded as "cost offsets." These may be deducted from the gross intervention cost to obtain the net intervention cost.)
- ✓ Sensitivity analyses are carried out on parameters whose values are not precisely known.
- ✓ Results provide guidance on prioritizing selected interventions.
- ✓ Estimates of health gain are often calculated with different levels of coverage for an intervention (80%, 95%, 98%, etc.)
- ✓ Sets of interventions that interact in terms of effectiveness or cost are considered together.[23]

The cost-effectiveness of screening can be described using several different parameters: the cost per breast cancer detected is calculated by dividing the total cost of a screening program by the number of cancers detected. Screening program costs depend on screening protocols. Annual screening finds most cancers earlier than biennial screening but doubles the cost [3]

Despite documented effectiveness of mammography screening in the early detection and mortality reduction of breast cancer [6-10], not all women receive or have access to breast cancer screening. The US Preventive Services Task Force (USPSTF) recommends lung cancer screening (LCS) with low-dose computed tomography (LDCT) for asymptomatic individuals at high risk for lung cancer [11], based on the results of the National Lung Screening Trial (NLST) [12]

Depending on patients' overall health and their lung cancer stage, treatment patterns can be very complex and overwhelming for patients. Chemotherapy, immunotherapy, radiotherapy, surgery, or therapy combinations are possible treatment options in curative or palliative settings. Furthermore, targeted therapy can be applied. These care options are provided by numerous different health care professionals within and across health care sectors [16]

Outcomes

The main outcomes of CEA include:

- ✓ CEA results can help decision-makers who want to achieve a specific health objective.
- ✓ estimates of screening history,
- ✓ breast cancer incidence
- ✓ screening or clinical detection, stage at detection
- ✓ costs, life-years, quality-adjusted life-years (QALYs)
- ✓ incremental cost-effectiveness ratios (ICERs)

Abbreviations:

Breast Cancer (BC)
Lung Cancer (LC)
Chemotherapy (CT)
Radiation Therapy (RT)
World Health Organization (WHO)
Tumor protein (TP53)
Phosphatase and tensin homolog (PTEN)
Ataxia telangiectasia mutated (ATM)
Checkpoint kinase 2 (CHEK2)
Breast CAncer gene (BRCA)
Nijmegen breakage syndrome (NBS1)
Double Strand Break Repair Protein (RAD)
Partner and localizer of BRCA2 (PALB2)
Cost-effectiveness analyses (CEAs)
Cost of Illness (COI)
Lung cancer screening (LCS)
National Comprehensive Cancer Network (NCCN)
Low-dose computed tomography (LDCT)
US Preventive Services Task Force (USPSTF)
National Lung Screening Trial (NLST)
Non-small-cell lung cancer (NSCLC)
Video-assisted thoracoscopysurgery (VATS)

Conclusion:

Pharmacoeconomic evaluations, like cost-effectiveness analyses (CEAs), are needed for cancer medications to inform decision-making, designing, and promoting efficient cancer control strategies among responsible authorities and practitioners. Further studies are needed to determine whether MRI is cost-effective for those at moderately high (15%–20%) lifetime risk. Future technical advances could make MRI more cost-effective than it is today. An attempt is made to represent the systematic review of CEA which would save time and use as a powerful tool for decision making.

There is a need for a high-quality systematic review regarding the cost-effectiveness of cancer medication. The net effect on quality of life incurred by patients with indeterminate findings and the impact of lung and breast cancer on the cost-effectiveness are not known. An attempt is made to review the cost effectiveness for the same which will assist decision makers in planning, at an average risk of developing cancer. A promising approach is made to improve patient-oriented outcomes (e.g., health-related quality of life) and to reduce health care costs for patients with cancer and chronic diseases.

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