

## Cervical cancer: a review of economic evidence for different prevention and treatment strategies

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Cervical cancer remains a significant global health concern, affecting thousands of women annually. It is the fourth most common cancer in women. Almost all cases of cervical cancer are caused by human papillomavirus (HPV). Prophylactic strategies such as HPV vaccination and screening are proven effective approaches to prevent cervical cancer and are also cost-effective. This article presents a scoping review of current economic evidence for cervical cancer prevention and treatment.

**Keywords:** cervical cancer; treatment; HPV vaccination; costs; cost-effectiveness; cost-utility; pharmacoeconomic evaluation.

### INTRODUCTION

Cervical cancer remains a significant global health concern, affecting thousands of women annually [1]. The prevalence of cervical cancer varies worldwide, with higher rates reported in specific regions [2]. It is important to note that prevalence figures can change over time due to factors such as alterations in risk factors, screening practices, and healthcare access. Prevalence is often expressed as the number of cases per 100,000 women. In 2020, the World Health Organization (WHO) estimated 604,000 new cases of cervical cancer worldwide, resulting in approximately 342,000 deaths [3]. Cervical cancer is more common in less developed regions, where access to screening and preventive measures may be limited. Sub-Saharan Africa, South-Central Asia, and parts of Latin America have been identified as regions with higher cervical cancer incidence and mortality rates [4].

As advances in medical science continue to enhance treatment options for this malignancy, the economic implications of these interventions come under increased scrutiny [5]. Pharmacoeconomic

evaluation, a critical component of health economics, provides a systematic framework to assess the financial impact of healthcare interventions [6]. In the context of cervical cancer treatment, understanding the cost-effectiveness, cost-benefit, and cost-utility of various therapeutic approaches becomes essential for healthcare decision-makers, clinicians, and patients [7].

The importance of pharmacoeconomic evaluations in cervical cancer treatment lies in their potential to inform healthcare policies, resource allocation, and treatment decisions. As healthcare systems strive for optimal allocation of limited resources, understanding the economic outcomes associated with cervical cancer interventions becomes imperative [8].

Through this review, we aim to contribute to the body of knowledge that guides evidence-based decision-making, ultimately fostering improved patient outcomes and resource utilization in the realm of cervical cancer care.

### METHODS

The following electronic databases were searched for relevant publications: PubMed, Google Scholar, and Scopus. Key terms used in the search

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were *cervical cancer, treatment, HPV vaccination, costs, cost-effectiveness, cost-utility, and pharmacoeconomic evaluation*. Only publications in English were considered. Full-text articles using different economic methodologies were included in the analysis. Review articles and those not written in English were excluded.

## RESULTS AND DISCUSSION

### Cervical cancer treatment

The treatment options for cervical cancer depend on several factors, including the stage of the cancer, the patient's overall health, and individual preferences. Treatment may involve a combination of surgery, radiation therapy, and chemotherapy [9] (Fig. 1). Removal of the uterus is a common surgical procedure for cervical cancer. Depending on the extent of the cancer, the surgeon may also remove surrounding tissues, such as the ovaries and fallopian tubes [10]. If cancer has spread, the surgeon may remove nearby lymph nodes to assess the extent of the disease [11].

During external beam radiation, high-energy rays are directed at the cancer from outside the body [12]. This is often used after surgery to eliminate any remaining cancer cells. In brachytherapy, radioactive sources are placed directly into or near the tumor. This type of radiation therapy is often

used to treat small tumors or as part of the overall treatment [13].

Medicines are administered intravenously or orally to destroy cancer cells throughout the body. Chemotherapy is often used in conjunction with radiation therapy [14]. Neoadjuvant chemotherapy is given before surgery or radiation therapy to shrink the tumor and make other treatments more effective. Adjuvant chemotherapy is administered after surgery or radiation to eliminate any remaining cancer cells [15]. Bevacizumab, an available targeted therapy that targets blood vessel formation in tumors, may be used in combination with chemotherapy for advanced or recurrent cervical cancer [16]. Pembrolizumab is an immune checkpoint inhibitor that may be used for advanced cervical cancer that has not responded to other treatments.

### HPV vaccination

There are several HPV (human papillomavirus) vaccines that have been developed and are used globally. *Gardasil 9* is a vaccine that protects against nine types of HPV. It is approved for use in both males and females. In addition to preventing cervical cancer, it also provides protection against other HPV-related cancers and genital warts [17]. There is also 4-valent *Gardasil*. *Cervarix* is a bivalent vaccine that protects against two types of HPV: HPV types 16 and 18. It is primarily designed to prevent cervical cancer and is approved for use in females [18].

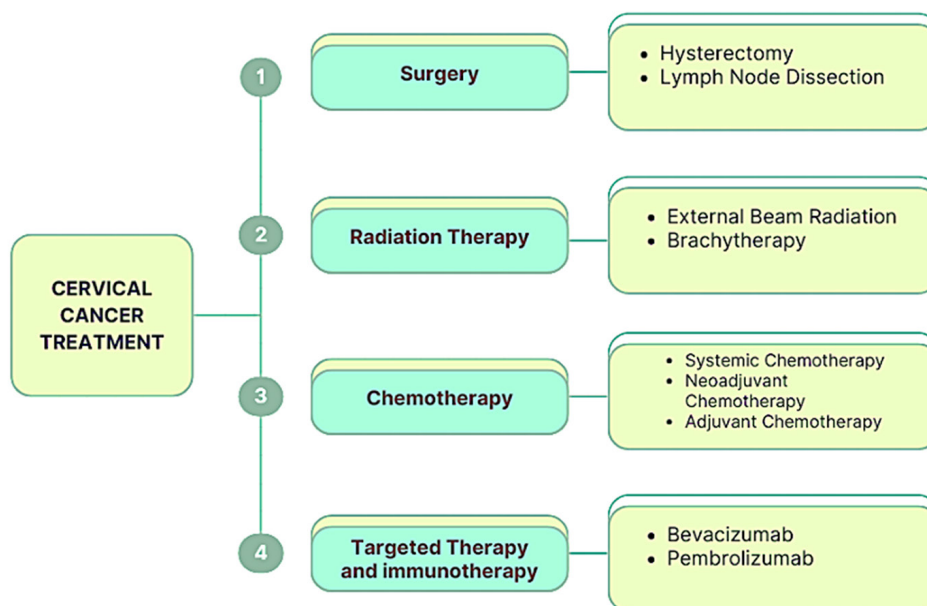


Fig. 1. Cervical cancer treatment options.

These vaccines are designed to prevent infection with certain types of HPV, including those that are associated with cervical cancer and other HPV-related cancers. HPV vaccination has been proven to significantly reduce the incidence of cervical cancer by preventing infections with high-risk HPV types. This prevention has a substantial impact on the overall cost of treating and managing cervical cancer [19]. In addition to preventing cervical cancer, HPV vaccination also reduces the incidence of other HPV-related cancers, such as anal, vulvar, vaginal, penile, and oropharyngeal cancers.

#### *Economic evidence for cervical cancer prevention and treatment*

Overall, 114 studies were identified through electronic databases. We analyzed 20 studies that met our inclusion criteria (Table 1). Most of the studies ( $n = 9$ ) used the cost-effectiveness pharmacoeconomic method [20–28]. The studies vary in settings; many of them are conducted in middle and low-in-

come countries. The objective of these studies was to assess the cost-effectiveness of HPV vaccination. A pharmacoeconomic evaluation using cost-utility analysis was performed to compare HPV vaccination and screening in Indonesia [29]. A systematic review conducted in 2017 summarizes the health-economic studies of HPV vaccination in Southeast Asian countries. The studies included in this review consider factors such as vaccine costs, disease prevention, and the long-term economic impact of vaccination programs [30]. Other therapeutic approaches are analyzed using the cost-benefit [31] and cost-utility methods [32, 33]. Three studies evaluate the budget impact and economic burden of cervical cancer [34–36]. Four of the analyzed studies use cost of illness methodology [7, 37–39].

Incremental Cost Effectiveness Ratios (ICERs) for HPV screening methods, such as HPV testing as a primary screening tool for cervical cancer, have generally been found to be cost-effective. HPV testing has demonstrated improved sensitivity for detecting high-grade cervical intraepithelial neoplasia

**Table 1.** Pharmacoeconomic studies related to prevention and treatment of cervical cancer

Author, Year of publication	Country	Type of pharmacoeconomic evaluation	Compared alternatives
Usher <i>et al.</i> , 2008 [20]	Ireland	Cost-effectiveness	HPV vaccination
Annemans <i>et al.</i> , 2009 [21]	Belgium	Cost-effectiveness	Quadrivalent vaccine
Ezat and Aljunid, 2010 [22]	Malaysia	Cost-effectiveness	HPV vaccination
Praditsithikorn <i>et al.</i> , 2011 [31]	Thailand	Cost-benefit	Policy implementation and prevention and control of cervical cancer
Kostinov and Zverev, 2012 [23]	Russia	Cost-effectiveness	HPV vaccination
Setiawan <i>et al.</i> , 2015 [24]	Indonesia	Cost-effectiveness	HPV vaccination
Agapova <i>et al.</i> , 2015 [34]	Ireland	Cost analysis, Markov modelling	Cytology and co-testing
Guerrero <i>et al.</i> , 2015 [32]	Philippines	Cost-utility	Screening and vaccination
Liu <i>et al.</i> , 2016 [7]	Canada	Cost of illness	–
Setiawan <i>et al.</i> , 2016 [29]	Indonesia	Cost-utility, Markov modelling	Vaccination and screening for HPV
Cheikh <i>et al.</i> , 2016 [37]	Morocco	Cost of illness	–
Tay <i>et al.</i> , 2018 [25]	Singapore	Cost-effectiveness	School – based HPV vaccination campaign
Jiang <i>et al.</i> , 2019 [26]	China	Cost-effectiveness	9-valent HPV vaccine
Castañon <i>et al.</i> , 2019 [33]	UK	Cost-utility	HPV testing
Setiawan <i>et al.</i> , 2020 [35]	Indonesia	Budget impact analysis and Markov modelling	HPV vaccination
Wu <i>et al.</i> , 2020 [38]	China	Cost of illness	–
Vale <i>et al.</i> , 2021 [27]	Brazil	Cost-effectiveness	Cytology against HPV screening
Ibáñez <i>et al.</i> , 2021 [36]	Spain	Cost analysis	Cervical cancer screening
Wondimu <i>et al.</i> , 2022 [28]	Ethiopia	Cost-effectiveness	quadrivalent and nonavalent human papillomavirus vaccines
Lebanova <i>et al.</i> , 2023 [39]	Bulgaria	Cost of illness	–

(CIN) compared to traditional Pap smears, leading to earlier detection and prevention of cervical cancer [40].

### Costs associated with cervical cancer

Cervical cancer imposes both direct medical and non-medical costs, contributing to the economic burden on individuals, healthcare systems, and society as a whole (Fig. 2). Understanding these direct medical and non-medical costs is crucial for conducting comprehensive pharmacoeconomic analyses. Evaluations aim to assess the cost-effectiveness of interventions, considering both the economic impact on healthcare systems and the financial burden on patients and their families. Reducing the overall burden of cervical cancer includes not only improving treatment outcomes but also addressing the economic challenges associated with the disease [41].

#### Direct Medical Costs

- **Treatment Costs:** This includes expenses related to medical procedures, surgery, chemotherapy, radiation therapy, targeted therapy, immunotherapy, and other interventions used in the treatment of cervical cancer.
- **Hospitalization Costs:** Expenses related to hospital stays, which may be necessary for surgeries, recovery, or intensive treatments.

- **Diagnostic Costs:** Costs associated with diagnostic procedures such as biopsies, imaging (MRI, CT scans), and laboratory tests.
- **Medication Costs:** The cost of pharmaceuticals used in treatment, including chemotherapy drugs, targeted therapies, and supportive medications.
- **Follow-up Care Costs:** Regular follow-up visits, imaging, and tests to monitor the patient's condition and detect any potential recurrence.
- **Palliative Care Costs:** If required, the costs associated with palliative care and pain management.

#### Direct Non-Medical Costs

- **Travel Expenses:** Costs related to transportation to and from medical appointments, including fuel, public transportation, or lodging for patients who need to travel for treatment.
- **Accommodation Costs:** For patients who require treatment away from their home, accommodation expenses may be incurred.
- **Caregiver Costs:** The economic impact on caregivers, including potential lost income due to time spent caring for the patient.
- **Productivity Loss:** Direct non-medical costs also encompass the economic impact of reduced productivity or absence from work for both patients and their caregivers.

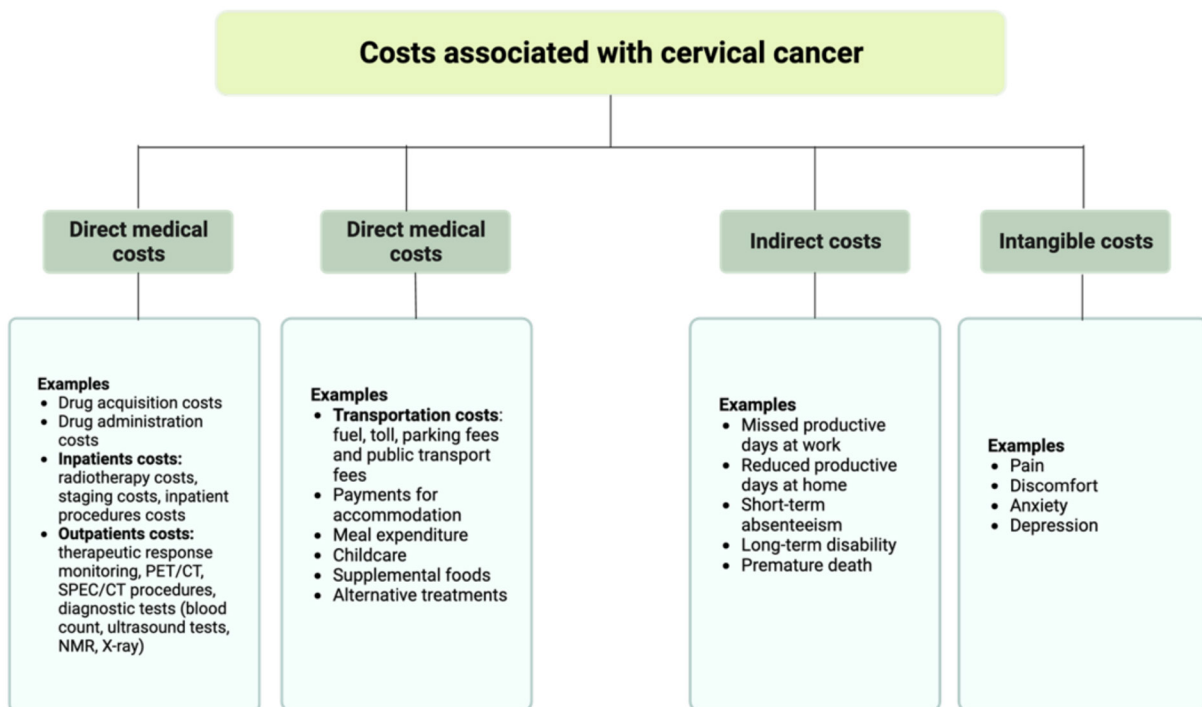


Fig. 2. Costs associated with cervical cancer treatment.



- *Counseling and Support Services*: Costs associated with psychological support services, counseling, and other support mechanisms.

#### *Indirect costs*

Indirect costs refer to the economic impact of the disease that extends beyond direct medical expenses. These costs encompass various factors that can affect individuals, families, and society as a whole. Here are some key components of the indirect costs associated with cervical cancer:

- *Productivity Loss*: Cervical cancer may lead to absenteeism and reduced productivity in the workplace due to treatment-related side effects, recovery periods, and medical appointments. Caregivers, often family members or friends, may also experience productivity loss as they may need to take time off work to provide support and care.
- *Premature Mortality and Disability*: Premature mortality resulting from cervical cancer deprives the workforce of potentially productive individuals, leading to lost economic contributions. Disability caused by the disease, or its treatment can result in long-term or permanent work limitations, impacting a person's ability to earn a living.
- *Impact on Caregivers*: Family members or friends who take on the role of caregivers may experience economic strain due to reduced work hours, career interruptions, or the need to hire additional help.

It is important for individuals diagnosed with cervical cancer to consult with a multidisciplinary healthcare team, including gynecologic oncologists, radiation oncologists, medical oncologists, and other specialists. The treatment plan should be tailored to the specific characteristics of the cancer and the patient's overall health [42]. Additionally, prevention through HPV vaccination and regular screenings such as Pap smears and HPV tests is crucial for early detection and treatment. Patients should discuss potential side effects, long-term effects, and the overall prognosis with their healthcare team to make informed decisions about their treatment.

Bulgaria has witnessed a significant incidence of illness and death resulting from cervical cancer, coupled with low coverage in immunization. During the years 2018–2020 in Bulgaria, the cumulative loss of life amounted to an estimated total of 20,446 years, attributed to cervical cancer [39]. There is a necessity to reconsider the approach to disease prevention, emphasizing a reassessment of strategies

involving compulsory screening and immunizations [43]. Healthcare professionals in Bulgaria are cognizant of the concerning levels of cervical cancer occurrence and mortality within the nation. Nonetheless, a lack of robust communication and collaboration between policymakers and frontline healthcare personnel has resulted in an insufficient flow of information about existing programs. The absence of a clear health policy about screening is identified as a primary barrier to the effective implementation of a comprehensive screening initiative [44].

## CONCLUSIONS

Cervical cancer management is an ongoing research area. There is a need for improvement of the prevention and information campaigns for cervical cancer awareness, especially in the developing countries. Pharmacoeconomic studies utilize various methods and study perspectives. They show the economic impact of the disease and the cost effectiveness of novel therapies. HPV vaccination has a broader public health impact by reducing the transmission of the virus within the population. This, in turn, helps to decrease the overall burden of HPV-related diseases, leading to improved public health outcomes. Studies have shown that the economic benefits of HPV vaccination extend beyond healthcare cost savings. Preventing HPV-related diseases contributes to increased productivity and improved quality of life for individuals and their families. It's important to note that the cost-effectiveness of HPV vaccination may vary by region and healthcare system. Additionally, ongoing research and public health efforts aim to improve vaccination coverage rates and address challenges related to access, equity, and awareness.

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