SPATIOTEMPORAL MODELING OF INCIDENT CASES, ACCESS TO HEALTHCARE AND THE COSTS OF CERVICAL CANCER IN ADDIS ABABA, ETHIOPIA

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LIST OF PAPERS

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V. Tariku Shimels, Biruck Gashawbeza, Teferi Gedif Fenta. The Economic Burden of Cervical Cancer in Addis Ababa: A Matched Case-Control Study. 2024 (Under review)

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ABBREVIATIONS AND ACRONYMS

AAU	Addis Ababa University
CA	Conjoint Analysis
CI	Confidence Interval
COI	Cost of Illness
CSA	Central Statistical Agency
CVM	Contingent valuation Method
CVI	Content Validity Index
CVR	Content Validity Ratio
DCE	Discrete Choice Experiment
ETB	Ethiopian Birr
FCM	Friction Cost Method
FIGO	International Federation of Gynecology and Obstetrics
FMOH	Federal Ministry of Health
GC	Gynecologic Cancers
HCT	Human Capital Theory
HIV	Human Immune Virus
HPV	Human Papilloma Virus
ICU	Intensive Care Unit
IQR	Inter Quartile Range
IRB	Institutional Review Board
LISA	Local Indicators of Spatial Autocorrelation
LMICs	Least and Middle Income Countries
MAUP	Modifiable Area Unit Problem
MEI	Medicare Economic Index
OLS	Ordinary Least Square
QALY	Quality Adjusted Life Year
QGIS	Quantum Geographic Information system
QoL	Quality of Life
SMD	Standardized Mean Difference
SPHMMC	Saint Paul's Hospital Millennium Medical College
SPIRHR	Saint Paul's Institute for Reproductive Health and Rights
STDM	Spatiotemporal Data Mining
TASH	Tikur Anbessa Specialized Hospital
TB	Tuberculosis
US	United States
USD	United States Dollar

VIA	Visual Inspection with Acetic Acid
WTP	Willingness To Pay

ABSTRACT

Background: Cervical cancer is an evolving public health problem of women world-wide. Low and middle-income countries like Ethiopia are gravely affected owed, mainly, to their poor health infrastructure. This study aimed to understand the spatiotemporal dynamics of cervical cancer incidence in Addis Ababa over the last decade, assesses patients' access to healthcare services, and examines the economic burden associated with the disease.

Methods: The project employed a mixed-methods approach, incorporating ecological, cross-sectional, and matched case-control designs. Data for the spatiotemporal analysis came from the Addis Ababa cancer registry and Ethiopian Statistics Service. This ecological study was conducted from September to November 2023. Analytical tools included R, QGIS, GeoDa, and SAGA GIS with Bayesian tests were applied to identify hotspots and spatial autocorrelation. Age-standardized incidence rates were calculated to evaluate temporal trends in Joinpoints regression. A cross-sectional assessment, using KoboCollect app-based patient interviews, on access to healthcare services was performed at two public oncology centers from July to August 2023, involving histopathologically confirmed cervical cancer patients. Data was analysed in Amos v.26 and SPSS v.26 software. The matched case-control design was conducted to measure the economic impacts of cervical cancer, and spanned from July to September 2023 using interviewer-administered questionnaires and medical records. Data analysis was entered in Epi Info v.7.2.5.0 and analysis conducted using SPSS and R, with statistical significance set at $p < 0.05$ at 95% confidence interval.

Findings: Between the period 2012 and 2021, 2,435 cervical cancer cases were reported in Addis Ababa. Spatial analysis revealed significant clustering in certain sub-cities such as Nifas Silk Lafto, Bole, and Yeka subcities while global Moran's I also suggested a statistically significant geographic disparity in 2018 (z score>1.96). The findings uncovered a temporal increase in age-standardized incidence rate (ASIR), with annual percentage changes from 4.2% in Bole (95% CI: 2.5-6.0) to 13.5% in Kolfe Keraniyo (95% CI: 5.87-21.76). Of the total 391 patients surveyed on healthcare access, the mean age was 50.3 years. Over half could access general medical services, medications, and radiotherapy, while only 11.5% reported financial accessibility in objective assessments. Essential medications were out of stock 58.6% of the time, yet diagnostic services were largely available (95.1%). A multivariable regression revealed that perceived access of patients to healthcare was influenced by factors including unemployment (AOR: 0.19, 95% CI: 0.08-0.46), low average monthly income (AOR: 0.19, 95% CI: 0.10-0.35), lack of CBHI coverage (AOR: 4.16, 95%

CI: 1.76-9.85), presence of social support (AOR: 3.80, 95% CI: 1.96-7.41), and poor dietary practices (AOR: 2.36, 95% CI: 1.28-4.35). The analysis on economic burden of 932 participants (466 cases and 466 controls) showed substantial financial impacts, with average annual expenses of 3,196.27 INT$ in the first year and 2,235.86 INT$ subsequently. Direct medical costs were highest, averaging 2,638.05 INT$ in the first year and 1,898.02 INT$ thereafter. Among the predictors of higher total annual costs included larger household size, comorbidities, lack of social support, poor dietary habits, year of treatment initiation, and advanced cancer stage of cancer.

Conclusions: Addis Ababa recorded 2,435 new cases of cervical cancer from 2012 to 2021, with marked geographic disparities in sub-cities such as Nifas Silk Lafto, Bole, and Yeka, which suggests potential areas of disease concentration. ASIR trends indicate a rising prevalence in selected areas. Healthcare access showed variability; over half reported adequate access to services, though affordability remains a concern. Socioeconomic factors, such as low income and employment type, influenced perceived access to healthcare of patients, while CBHI coverage, social support, and dietary habits were associated with better access perceptions. The financial burden of cervical cancer remains significant, indicating the need for enhanced public health measures, including vaccination, early detection, and expanded affordable healthcare services to reduce the impact of cervical cancer in Addis Ababa.

Keywords: Access to healthcare services, cervical cancer, economic burden, spatiotemporal analysis, Addis Ababa, Ethiopia

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GLOSSARY OF TERMS AND CONCEPTS USED IN THE STUDY

Modeling

In this study, the concept "modeling" refers to the systematic analysis and representation of spatial and temporal patterns related to cervical cancer incidence. It involves using geostatistical methods, spatial clustering techniques, spatial interpolation, and temporal trend analysis to identify patterns, dependencies, and trends over space and time during the decade, 2012 to 2021**.**

Access to healthcare services

The phrase pertains to the comprehensive evaluation of healthcare access for patients with cervical cancer, utilizing both objective and subjective methods. Objective assessments included observation checklists, patient exit interviews and reviews of medical records. Subjectively, it involved patients' perceptions of their ability to obtain follow-up medical care, which may include treatments like medications, radiotherapy, surgery, and consultations that a diagnosed cervical cancer patient requires. This evaluation is confined to patients whose medical care needs are established and does not extend to those until the tertiary prevention phase (access to screening, precancerous diagnosis, or educational services in the community). Perceptions of accessibility were measured across six key dimensions: accessibility, availability, acceptability, affordability, accommodation, and awareness. These dimensions will be assessed using a five-point Likert scale, where one represents ‘absolutely disagree’ and 5 ‘absolutely agree.’ An average score above the mean was categorized as 'adequate access' and below as 'poor perception to access.'

Cost of illness

The term economic impact, cost of illness or economic burden, as used in the text, encompasses the various expenses incurred by patients with cervical cancer. These costs include diagnosis, imaging, medical treatments, consultations, transportation, sick leave, absenteeism, and disability. These expenses can be direct or indirect and can, as well, be of medical or non-medical.

Physical exercise

Physical exercise, also known as physical activity, was measured based on the recommendations set by the US Physical Exercise Advisory Committee (PAGAC, 2018) and the American Cancer Society (ACS) (Rock et al., 2020) as well as the World Health Organization (WHO) (WHO, 2018) that patients with chronic illness, particularly those with cancer patients could accommodate engaging in moderate exercise. Accordingly, a patient needs to engage in 150-300 minutes of moderate exercise or 75-100 minutes of vigorous

physical activity per week. Considering these recommendations, we assessed patients' engagement in physical activity. We would classify them as ‘good’ (when the patient satisfies either of the above two recommendations) or ‘poor’ when it is not.

Current history of dietary practice

As defined in the guidelines by the American Cancer Society (Rock et al., 2020) the dietary recommendation for cancer patients entails taking foods that are high in nutrients in amounts that help them get to and stay at a healthy body weight, a variety of vegetables (dark green, red, and orange, fiber-rich legumes (beans and peas), and others, and fruits, especially whole fruits in a variety of colours, as well as whole grains. In the meantime, it is advised that patients reduce or limit red and processed meats, sugar-sweetened beverages, highly processed foods, and refined grain products. This study used these criteria to classify patients' dietary practices as ‘good’ (when they report practicing any combination of the recommended diets) or ‘poor’ (when they report practicing high-risk diets or do not have access to a recommended diet at all).

Current use of excess alcohol

This is defined based on a participant's response to the question, ‘Do you currently drink excess alcohol (more than one bottle a day)?’ as established by the American Cancer Society guidelines (Rock et al., 2020).

Current use of cigarettes

According to the World Health Organization (WHO, 2018), this term refers to whether respondents report using either smoked or unsmoked cigarettes during the data collection.

Current use of khat or other stimulant substances

This is determined based on whether a participant reports using khat or other stimulant substances, such as hashish or ganja, during the data collection period.

Accessibility (objective measure)

The objective measure of access to healthcare services to be considered in this project employed indirect methods to count on the distance and time it takes to access the required healthcare services. The WHO recommends that a health service be accessible within 5 kilometres (KM) of a patient's home (WHO, 2015). This is also equivalent to a primary healthcare service or health facility being available within an hour's walking distance. Otherwise, the patient population is considered underserved, and this method has been employed in other Sub-Saharan countries (Dos Anjos Luis and Cabral, 2016; Huerta Munoz

and Källestål, 2012). In this way, we assessed the geographic accessibility of clinical, laboratory tests, imaging diagnoses, radiotherapy, and surgical services at the selected public and private outlets.

Availability (objective measure)

This indicator was applied mainly related to accessibility and affordability. The WHO defined it as the proportion of health facilities that have a core set of relevant essential medicines available and affordable on a sustainable basis (WHO, 2018). Though the term is often utilized for the availability of essential medicines, it can also be used to assess other key healthcare services and readiness measures such as cancer diagnosis, guidelines, and trained personnel (Terefe Gelibo 2017). In this study, we utilized secondary and tertiary care services available to patients with cervical cancer, including surgical interventions, radiotherapy, diagnostic and imaging services, and palliative care as stipulated in the National Cancer Control Plan of Ethiopia (FMOH, 2015). As there was no specifically defined list of antineoplastic drugs for cervical cancer, we considered a few lists of tracer drugs that are frequently prescribed at the health facilities for this group but were also mentioned in the essential drug list of Ethiopia (EFDA, 2020). Therefore, the availability of any of the core drugs, cisplatin, carboplatin, bleomycin, paclitaxel/docetaxel, rituximab, bevacizumab, and gemcitabine during the data collection period at the health facilities with an affordable price was considered to qualify availability.

Affordability (objective measure)

Three major inputs were considered to compute the affordability of medicines according to the WHO's recommendation (WHO, 2018). These are the defined daily dose (DDD), the national poverty line (NPL) for Ethiopia, and the wage of the lowest-paid unskilled government worker (LPGW wage). The calculation of affordability was as follows: 1) Because of the diversity in need of services and treatments in this group, estimated cumulative monthly expenses for medicines and bundle of services received were converted to daily costs, added to the NPL for Ethiopia which is 7184 Birr at the 2015/2016 estimation (19.95 Birr/day), (Mekasha and Tarp, 2021) and 2) was divided by the LPGW wage i.e 24.67 Birr. Health insurance coverage (if any) was deducted from the numerator. As such, affordability identifies how much (if any) extra daily wages are needed for an individual who earns the LPGW wage to be able to purchase medicine or get a medical service. This ratio is then transformed into a binary variable where medicine is affordable when zero extra daily wages are required to purchase it, and it is not affordable otherwise.

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CHAPTER ONE: INTRODUCTION

1.1 Background

Within the healthcare context, access is measured in terms of supply of services, affordability, physical accessibility, and acceptability (Gulliford et al., 2002). A more comprehensive perspective to encompass the broader aspects of access can also include elements about the structural features of the healthcare system, such as availability; features of individuals, such as preferences, taste, and information (Mooney, 1983; Haddad, 1992) and financial, organizational, and professional factors (Dutton, 1986). Nonetheless, as healthcare service delivery is not a homogenous product characterized as a single service, the precise meaning of having access remains vague (Daniels, 1982). More precisely, it also depicted the link between specific patient and organizational dimensions (Penchansky and Thomas, 1981). This conception labels access in 5As-availability, accessibility, accommodation, affordability, and acceptability. Furthermore, factors that could be considered thus pertain to supply-side features of health systems and features of populations and to process factors describing how access is realized (Levesque et al., 2013).

Cervical cancer is one of the most common public health problems in women, for which a severe disparity in access to healthcare services is frequently reported (McDonald et al., 2017; Amin et al., 2020; Newmann and Garner, 2005). With an estimated 570,000 cases and 311,000 deaths in 2018, the disease remains the fourth most common cancer cause of morbidity and mortality among women (Sung et al., 2021). About 80% of all cervical cancer cases and 90% of deaths occur in resource-limited settings, with the sub-Saharan Africa region accounting for the leading burden (Bray et al., 2018). Of the many possible contributors to this figure, the Human Immune Virus (HIV) is the one often mentioned, as nearly 20% of cervical cancer cases in the region are reported to be attributed to it (Ibrahim Khalil et al., 2022).

Despite the availability of predetermined risk factors in the emerging incidence of cervical cancer, such as HIV/AIDS (Wassie et al., 2021) and Human papillomavirus (HPV) (Crosbie et al., 2013), studies on the space-time autocorrelation are critical. Connected to this and other hypotheses, reports suggest cervical cancer exhibited a dynamic geographic dependence and changing incidence rate over time (Thongsak et al., 2016; Tafadzwa et al., 2021).

Apart from the recommended prevention measures available and readily provided in most of the primary setups, including primary prevention (vaccination with the human papillomavirus (HPV)) and secondary prevention (screening), there are also diverse management approaches

(tertiary prevention) of confirmed cases depending on the stage of cancer, age, and performance status. These may include simple hysterectomy, radical hysterectomy, radiotherapy, or radiation combined with either surgery or chemotherapy, among others (Somashekhar and Ashwin, 2015). However, the question of access to healthcare services remains a challenge, particularly in sub-Saharan Africa. In addition to the low level of knowledge and awareness, facilities for the prevention and treatment of cervical cancer in the region were reported to be inadequate (Anorlu, 2008), necessitating the need for implementing active policies similar to others in HIV, tuberculosis (TB), and malaria.

A multitude of factors may interplay in the access of patients to healthcare, including poor cervical cancer screening, lack of awareness and knowledge of cervical cancer, biological factors such as poor nutrition; infections with human immunodeficiency virus (HIV), TB, and malaria; socioeconomic and socio-cultural factors with political inequities (Ntekim, 2012). Further, challenges related to the health system, psychological (fear of recurrence, negative social attitude, and distress associated with the side effects of treatments), and economic factors were identified as the barriers to women's access to healthcare (Tadesse, 2015).

Geographic distribution and access to healthcare services could directly link with the cost of illness (COI) in most chronic diseases, implying that higher costs inhibit patients' access to healthcare services (Holman, 2020; Hussey et al., 2014). The costs of illness following cervical cancer also accounted for a remarkable portion of the disease's burden in the broader population in general and in this population in particular. According to a report in the United States (US)(Mariotto et al., 2011), the average annual medical cost of cervical cancer varies widely depending on the phase of treatment. For example, the average cost of care during the last year of life could be as high as $118,000 for patients younger than 65 and as high as $79,000 for those older than 65. A study in Ethiopia revealed that the mean outpatient cost per patient for cervical cancer was $407.2, of which the direct outpatient cost accounted for the largest share (Hailu and Mariam, 2013).

In Ethiopia, the incidence and mortality were about 22.3 and 16.8 per 100,000 women populations, respectively (Sung et al., 2021). Nearly 6,300 new cases are reported to be diagnosed annually. At the same time, about 4,884 women die from the same disease each year, making it the second most common and second most deadly cancer among this group in the country (Begoihn et al., 2019).

Given its growing incidence, inquiry for a combination of management modalities, catastrophic costs of illness, and patients' reduced quality of life, much data and organized

evidence needs to be included in most developing settings, particularly Ethiopia. Hence, this project aims to close information gaps observed on the geographic distribution, trend, access to health services, the associated economic burden, and experience of cervical cancer patients in Addis Ababa. As most of the incident cases attending hospitals in Addis Ababa are supposed to have passed through the cancer registry center, measuring the level of access to healthcare services of this population, the costs borne by the illness and treatment, and the experience of patients with it would serve as an essential source of evidence to estimate the burden of the disease in the city at its broadest surface.

1.2 Statement of the problem

Cervical cancer causes a devastating health outcome in women of all age groups, potentially leading to maternal morbidity and mortality. Although the disease can be prevented and treated effectively, most notably when it is detected at an early stage (stages I and II), there is a growing disparity in women's access to essential healthcare services. The problem gets even worse when more than eight in ten women diagnosed with and nine in ten women who die from cervical cancer live in a low-middle-income country (Ginsburg et al., 2017). Compared to women in high-income nations, those in low-and middle-income countries have a 35% higher average life risk of cervical cancer globally (Echelman and Feldman, 2012). The average age at diagnosis was reported to be 53 years, ranging from 44 years (Vanuatu) to 68 years (Singapore), and the average age at death from cervical cancer was 59 years, ranging from 45 years (Vanuatu) to 76 years (Martinique) both reported globally (Arbyn et al., 2020). The figure changes significantly in low-income countries, such as Ethiopia. According to a study conducted at Gandhi Memorial Hospital, 49.4% of the patients tested positive for visual inspection with acetic acid (VIA), 42% of those with low-grade lesions, and 60% of those with high-grade lesions were aged 30–39 (Mekuria et al., 2021). This, too, may indicate that the disease accounted for a more significant proportion of reproductive and productive-age women.

The width and depth of the effect of illness in cases of cervical cancer may not be measured very easily. However, several implications can be counted. From one perspective, it can be viewed in light of patients' depleted quality of life. Poor access to healthcare services may worsen patients' morbidity in life, thereby impairing their survival and increasing disability to function generally in life. These may include body image, self-esteem, relationships with partners, and sexual and reproductive issues (Herzog and Wright, 2007). A study that evaluated 12 East African countries revealed that women's access to maternal healthcare services was only 43% (Minyihun and Tessema, 2020). On the other hand, the increasing cost

following illness could be catastrophic and often not manageable for most patients. A study in Kenya, for example, highlighted those patients with cervical cancer suffered from financial challenges for their medication, travel, and diagnosis costs as their top expenses (Owenga and Nyambedha, 2018).

While assessing the problem with the current study context, a range of factors are reported to contribute to the catastrophic outcomes of cervical cancer. The study by Minyihun and Tessema (2020) figured out that poor household income, lack of access to health facilities, education, and residence were the main factors affecting maternal healthcare access in East Africa (Minyihun and Tessema, 2020). Furthermore, cultural practices (early marriage, polygamy, multiple parity), education, residence, system-based and practitioner delays, high costs of treatment, and side effects of medications have been documented as frequent challenges (Tadesse, 2015). Another study has also reported that having multiple sexual partners, being positive for Human Immunodeficiency Virus (HIV), having a history of STI, and initiation of sexual intercourse at an early age were factors associated with cervical cancer (Mekuria et al., 2021).

Most studies have tried to address the prevalence and factors associated with the disease in local (or facility-based) studies. The designs considered may not enable one to visualize the absolute magnitude of the disease. Specifically, the questions of access to health/medical care, the population's cost of illness, and the experience of patients have yet to be evaluated in a broader geographic context. Moreover, while very crucial, the spatiotemporal pattern of the disease has never been assessed in the country. Answering these questions would offer the depth of evidence needed for health authorities and policymakers to make timely decisions and policy interventions. In this regard, different sets of social, economic, clinical, and health system-related factors could be tested and speculated to potentially influence access and total costs of illness in cervical cancer. On top of this, the costs of illness borne by cervical cancer will be examined extensively and compared with other costs of illness. Finally, the disease's spatial distribution and temporal trend are particularly interesting in this study. By doing so, all incidence cases from 2012 through 2021 would be examined for spatiotemporal autocorrelation patterns at city, sub-city, and woreda levels. Furthermore, small areas of potentially high clusters would be identified and mapped for action.

1.3 Rationale of the study

Cervical cancer remains a significant public health challenge globally, particularly in low- and middle-income countries, where it causes a substantial burden in terms of morbidity and

mortality. In Ethiopia, and specifically in Addis Ababa, the prevalence of cervical cancer is alarmingly high, yet comprehensive data on its epidemiology and impact are either sparsely available or lacking. This study was prompted by the urgent need to address this knowledge gap, with the goal of discovering its up-to-date magnitude, enhancing the effectiveness of health interventions, and improving outcomes for affected women.

The rationale for focusing this study on the urban context of Addis Ababa stems from several key considerations: (1) high incidence and mortality rates: Addis Ababa, as a major urban center in Ethiopia, reports higher incidence rates of cervical cancer compared to rural areas (Abate, 2015). The urban setting also presents unique challenges and opportunities regarding healthcare access and delivery that are crucial for effective disease management and prevention. (2) Limited data on spatial and temporal trends: There is a lack of detailed data on how cervical cancer cases are distributed across different sub-cities and woredas within the city and how these trends have evolved over the past decade. Understanding these patterns can provide a vital step for targeted public health interventions. (3) Access to healthcare services: variability in the accessibility and quality of healthcare services within the city affects early detection and timely treatment of cervical cancer. Studying perceived and realized access to these services helps identify critical barriers and facilitators in healthcare delivery. (4) Economic burden: The financial impact of cervical cancer on patients, families, and the broader health system in Addis Ababa remains poorly understood. An economic analysis is necessary to inform cost-effective disease management and prevention strategies. (5) Policy and implementation gaps: Existing health policies may not adequately address the specific needs of cervical cancer patients in an urban setting. This study aimed to provide evidence-based recommendations that can shape more effective health policies and programs.
By addressing these specific areas, the study attempts to provide a comprehensive overview of the cervical cancer landscape in Addis Ababa, which, in turn, offers a deep insight that can drive policy changes and improve clinical practices. Ultimately, the findings are expected to contribute to the reduction of cervical cancer incidence, improve access to treatment of patients with the disease, and enhance the quality of life for women with the disease in the capital and beyond.

1.4 Scope of the study

The scope of this study encompassed the key dimensions necessary to provide a comprehensive understanding of cervical cancer within the urban context of Addis Ababa, Ethiopia. Initially, we performed a global and comprehensive systematic literature search and meta-analysis of treatment delay and its association with survival. Informed by this, the

project aimed to examine the spatial distribution and temporal trends of cervical cancer incidence in Addis Ababa, along with patients perceived and realized access to healthcare services. Furthermore, the study has evaluated the economic burden associated with cervical cancer, focusing on direct medical and nonmedical costs, as well as indirect costs related to lost productivity and other societal impacts.

By encompassing a broad spectrum of factors, from clinical and health system-related aspects to socioeconomic and cultural influences, the study aimed to provide a detailed understanding of the distribution of the disease across woredas (the lowest administrative units) and sub-cities within Addis Ababa. It explored trends over the past decade, assessed the perceived and realized access of patients to treatment modalities, and evaluated the economic burden associated with cervical cancer in this specific urban setting.

Including all incident cases from across the city over the past ten years and patients from the largest referral hospitals during the study period was considered a critical development. This approach was designed to reveal the magnitude of the problem and the factors associated with its treatment and costs in the urban context of Ethiopia. This comprehensive scope helped ensure that the study captured a broad spectrum of experiences and conditions affecting cervical cancer patients in the city, providing valuable insights that can inform future healthcare policies and interventions.

1.5 Significance of the study

This study is deemed to present a precise and focused understanding of the spatial distribution and temporal trend of cervical cancer cases, patients' perceived access to healthcare services, the costs borne by cervical cancer (total costs, direct medical and nonmedical costs, and indirect costs); and the experience of patients living with the disease in an urban context of Ethiopia. It also delivers information on associated factors that may elucidate a potential link between access and the economic burden of the disease. The population considered the study design protocol to be employed, and the context would make the study unique, especially in the developing settings proposed to answer this poorly researched but highly relevant topic. The inclusion of all patients from the largest and referral hospitals, as well as those attending in a private setting, will also help to represent the more excellent image of the problem that all patients with cervical cancer in Addis Ababa face. Hence, addressing the specific objectives of this project will provide up-to-date evidence on the burden of the problem under question.

The findings of this study help healthcare authorities, especially the Federal Ministry of Health (FMOH) and other partners and policymakers, identify key areas to focus on for

preventing and reducing complications among cervical cancer patients. They guide the prioritization of resource allocation for prevention and management efforts and encourage multidisciplinary approaches. Based on the study's results on spatial clustering, access to care, and illness costs, recommendations are made to support the delivery of targeted and high-quality healthcare services, helping to achieve women's cancer control goals and improving care for this vulnerable population.

The study also adds to scientific knowledge by mapping cervical cancer incidence in Addis Ababa, exploring perceived healthcare access, assessing the economic burden of the disease, and identifying associated factors within the Ethiopian context. Identifying the main cost drivers for patients helps policymakers design strategies to optimize resource use and reduce the overall cost of illness for patients and society. The approaches used in this study serve as a model for future research on similar healthcare issues, especially chronic illnesses, in various regions of the country.

1.6 Structure of the dissertation

The dissertation starts with a title page, followed by acknowledgement, list of papers, table of tables, table of figures, abbreviations and acronyms, abstract, list of appendices, and glossary of terms. Chapter one, the introduction, sets the stage by providing background information on cervical cancer, stating the problem, outlining the study's rationale, defining the scope, explaining the significance, and describing the structure of the dissertation. Under chapter two, we added the literature review, which surveys existing cervical cancer literature and discusses theoretical and conceptual frameworks. More importantly, the literature review has encompassed a systematic search of available evidence on the association between treatment indications and survival in the same population. Chapter three deals with the study objectives and research questions. Chapter four, the methodology, detailed the philosophical considerations, research design, study area, population and sampling methods, data collection methods, data analysis techniques, and ethical considerations. Chapter five presents the results using various data presentations and analyzes these findings in detail. Chapter six, the discussion, strength, and limitation section, interprets the results, covers the implications, and acknowledges the study's limitations. Finally, chapter seven concludes with a summary of findings, conclusions based on these findings, recommendations for future actions, and suggestions for areas for future research. The References section lists all sources cited, and appendices include supplementary materials that support the research.

CHAPTER TWO: LITERATURE REVIEW

2.1 Cervical cancer: brief etiology, epidemiology, and its management modalities

Cervical cancer is a malignant tumour originating at the cervix's junction between the outer squamous cell layer and inner columnar cell lining (Saleh et al., 2020). It includes ten major histopathologic subtypes as classified by the World Health Organization: squamous cell carcinoma, adenocarcinoma, clear cell adenocarcinoma, adenosquamous carcinoma, serous carcinoma, glassy cell carcinoma, adenoid basal carcinoma, adenoid cystic carcinoma, undifferentiated carcinoma, and small cell carcinoma (Jhingran A, 2003). Squamous cell carcinoma is the predominant subtype, making up about 75% of cases, followed by adenocarcinoma, which accounts for 10% to 25% of cases (Pirog et al., 2018).

Globally, cervical cancer is the fourth most common cancer among women (Torre et al., 2017; Bray et al., 2018) and accounts for 22.2% of all cancers in Sub-Saharan Africa (Anorlu, 2008), also making it the leading cause of cancer death in the region. In Ethiopia, it is the second most common and deadly type of cancer among women (Begoihn et al., 2019).

Treatment options for cervical cancer include a combination of chemotherapy and radiotherapy or surgery (Candelaria et al., 2006). Radiotherapy and radical surgery are particularly effective for the disease's locally advanced stages (IB, IIA) (Landoni et al., 2017). Incorporating chemotherapeutic agents like cisplatin, carboplatin, and hydroxyurea into treatment regimens has demonstrated superior outcomes over radiotherapy (Keys et al., 1999) or chemotherapy alone (Rose et al., 2007).

2.1.1 The association between delay in treatment modalities and outcome

Relying on findings from earlier primary studies, the results under this section present the comprehensive systematic review and meta-analysis which offers an updated understanding of the existing evidence regarding the impact of treatment delays on patient outcomes. The primary aim was to compile data and elucidate the potential effects that such delays might have on key health outcomes, particularly of overall survival (OS) and disease-free survival (DFS), in patients diagnosed with cervical cancer. This detailed examination seeks to explore how delays between diagnosis and the initiation of treatment modalities like surgery, radiotherapy, and chemoradiotherapy can affect the progression and prognosis of the disease. The rationale behind this systematic literature search and review was to demonstrate the link between treatment delays and patient outcomes and identify the principal factors contributing to these delays, especially in patients with confirmed diagnoses. This investigation is intended to provide actionable insights and guide the focus of our subsequent research efforts to

address these challenges. The results for this review were developed and reported according to the PRISMA-2020 guideline (Page et al., 2021), registered on the international register of systematic review protocols PROSPERO (Schiavo, 2019) (Registration number: CRD42022299689), and has been published (Shimels et al., 2022). The details of the published review article can be found in the appendix (Paper I).

2.1.1.1 Overall survival

We performed a systematic review and meta-analysis of available literature with defined eligibility criteria to answer one of the main questions: 'What is the association between delay in treatment indications and overall survival in patients with cervical cancer?' The overall survival (OS) was assessed across 11 comparison groups, focusing mainly on the effects of treatment delays. A subgroup analysis of a five-year follow-up after radiotherapy indicated that a four-week delay in treatment commencement was associated with a 1.27 times higher chance of mortality risk from any cause (HR: 1.27; 95% Confidence Interval [CI]: 1.12-1.45). However, similar delays in the initiation of concurrent chemoradiotherapy (CCRT) (HR: 1.31; 95% CI: 0.76-2.23) and surgery (HR: 0.96; 95% CI: 0.60-1.54) did not show a statistically significant association with mortality risk compared to the treated groups. Furthermore, the exact duration of delay did not influence mortality risk during a three-year follow-up period (HR: 0.76; 95% CI: 0.44-1.32) (Paper I: Figure 1).

Several factors could contribute to the observed results, especially in the treatments where no statistically significant connection was found. On the other hand, no statistically significant mortality risk was detected when comparing the delayed and treated groups under combined chemoradiotherapy. And, nor did a relatively shorter follow-up period reveal any significant differences in mortality estimates. It was noted also that over 86% of patients in studies by Noh and his colleagues (Noh et al., 2022) and Matsuo et al. (Matsuo et al., 2021) were diagnosed with squamous cell carcinoma (SCC) at similar stages, with the latter study excluding patients who had waiting times beyond one year, potentially masking the impact of delayed treatment on survival outcomes. The fact that patients with SCC were observed with better OS and DFS that those with adenocarcinoma has been documented by Hu et al. (Hu et al., 2018). In Ramey et al.'s study (Ramey et al., 2018), despite the majority of patients (85%) undergoing chemoradiation therapy, the risk of treatment delays from the expected treatment start date was reported to be lower in this group compared to those receiving only radiotherapy.

On a different note, the risk of mortality from any cause over five years among patients treated for surgery, either on schedule or delayed showed no statistically significant variation. A study within this subset indicated that a waiting time of 4 or 8 weeks had no substantial effect on overall survival. Upon additional exploration, this finding seems likely since patients in this group were in the early stages of cancer (stages IA-IIB) and have undergone either radical or primary hysterectomy. Research suggests that early-stage cervical cancer can effectively be managed with minimal complications through either type of hysterectomy. Specifically, Raspagliesi and Bogani (Raspagliesi and Bogani, 2019) showed that the five-year overall survival rate following radical hysterectomy can reach up to 90%.

Waiting time is an additional rate limiting factor which could significantly influence disease progression, with further contributors like comorbid conditions potentially affecting mortality risks differently across patient groups. For example, those receiving immediate treatment might inherently be at higher risk or exhibit more severe clinical symptoms, contributing to their outcomes. Unfortunately, this variable was not extensively evaluated as the studies reviewed did not consistently report on such an additional factor.

As an expansion to the waiting time, a paradox exists in the literature where patients with shorter intervals between diagnosis and treatment initiation often report worse outcomes (Castelo et al., 2023; Lopez-Cedrún et al., 2019). While it was not feasible to assess further confounders such as tumor aggressiveness or cancer cell proliferation rates in this analysis, it is plausible that patients presenting with more severe symptoms were prioritized for earlier treatment but ultimately had poorer prognoses. This suggests that quicker referral and treatment initiation, while seemingly beneficial, may correspond to more advanced disease stages at diagnosis.

2.1.1.2 Disease-free survival

In the second objective of our systematic review and meta-analysis, we attempted to observe the relationship between treatment delay and disease-free survival (DFS) in patients with cervical cancer. Of the challenges was that no sufficient literature covered on this topic. As depicted in figure 2 of paper 1, only two studies met our inclusion criteria and were analyzed for their five-year follow-up outcomes. The analysis showed that a four-week delay in starting radiotherapy was associated with a 1.72 times increased risk of disease relapse (HR: 1.72; 95% CI: 1.25-2.35). In contrast, a similar delay in surgery did not demonstrate a statistically significant difference in disease-free survival over five years (HR: 0.89; 95% CI: 0.75-1.04). These findings repeat the results obtained from the overall survival analysis, suggesting that

common factors such as heterogeneity among studies, the small number of studies, and the waiting-time paradox may influence these outcomes (Paper I: Figure 2).

While this comprehensive systematic review primarily focused on assessing the effects of a 4-week delay in treatment initiation, it also has incorporated an extended waiting time of 8-weeks in the analysis. Furthermore, a meta-regression was conducted to explore various variables of interest derived from the primary studies. Numerous factors, including the well-documented waiting-time paradox, might have influenced the outcomes, all showing challenges in establishing a minimal wait time for treatment initiation in this patient population (see paper I for the details of these findings).

Given this context, delays in treatment can be precipitated by several contributors, which are often specific to the local context, such as in Ethiopia. Apart from those evaluated in this review, key factors linked directly to delays in treatment for patients with cervical cancer include the lack of spatial data on case clustering, which is crucial for resource allocation, insufficient access to essential healthcare services for managing cervical cancer, and a limited understanding on the economic burden of the disease, which all are vital for informing both prevention (primary and secondary) and early management (tertiary prevention) as well as palliative care interventions. The subsequent coverage of literature, therefore, relies on these specific areas as essential inputs to the next steps in the project.

2.2 Spatiotemporal analysis and mapping of cervical cancer incidence

2.2.1 Spatial data analysis

Spatial analysis or statistics is a geographic analysis that employs mathematical techniques and geometry to explain the topological patterns of a phenomenon. Therefore, while geographic information systems (GIS) allow us to study and understand real-world processes by developing and applying manipulation, analysis criteria, and models and to carrying out integrated modelling, spatial analysis serves as a key component of GIS enabling one to model vector-based and raster data through a sophisticated tool (Raju, 2021). The application of GIS mapping in health programs monitoring and displaying performance indicators has been documented in various sources (Robin et al., 2019; Makanga et al., 2016).

Spatial analysis in GIS involves three types of operations namely: attribute query, also known as non-spatial (or spatial) query (including features with tabular presentations), spatial query (features that require any spatial processing and are based on a location data), and the generation of new data sets from the original database. The scope of spatial analysis ranges

from a simple query about the spatial phenomenon of interest through complicated combinations of attribute queries, spatial queries, and alterations of original data (Raju, 2021). The spatial auto-correlation function in GIS is an important dimension whereby the dependency of observations is tested in space. The concept of spatial autocorrelation was proposed by Tobler in the first geography law: "Everything is related to everything else, but nearest things are more related than distant things" (Tobler, 1970). It shows the correlation between a series of points on a map of an observation for different shifts in space or time. Generally, large pairs of points close to each other have a lower variance (i.e., are better correlated) than pairs of points at larger separation (Jossart et al., 2020). With this, autocorrelation quantification enables us to uncover existing spatial relationships and gain insight into the spatial behaviour of the phenomenon of interest. The typical spatial methods applied in health research include mapping of disease incidence, clustering techniques, diffusion studies, and identification of risk factors through map comparisons and regression analysis (Gesler, 1986).

2.2.2 Spatiotemporal analysis

A temporal analysis is a metric of chronological observations of an event that reveals its trend over time. When added to the metric of space, it accounts for a geographic space with a time sequence. Spatial and temporal modelling, also known as spatiotemporal data mining (STDM), is an emerging field that combines both concepts of space and time. This novel concept proposes using methods for analysing event-based data, trajectories, time series, spatial maps, and raster data. Some of the main STDM tasks are clustering, anomaly detection, frequent pattern mining, relationship mining, change detection, and predictive learning (Ferreira et al., 2020).

2.2.3 Challenges of spatiotemporal analysis

Some questions unique to the combined use of spatial and temporal methods still need to be answered. It is also important to note that many of these still need a single solidified answer or solution, as identified through the literature. The spatiotemporal data analysis requires that both temporal and spatial correlations be considered. Assessing data's temporal and spatial dimensions adds significant complexity to the data analysis process for two major reasons: 1) the continuous and discrete changes of spatiotemporal objects' spatial and non-spatial properties, and 2) the influence of correlated spatiotemporal objects on one another. A key issue, therefore, arises when including space and time in a single model (Griffith, 2021).

The accepted thinking is that space is a two-dimensional flat layer with unlimited directionality: North-South-East-West and everywhere in between, while time is a unidirectional measure and can only move in one direction – forward. As a result, most of the current GIS tools are designed to handle this intuitive understanding. An alternative argument has been proposed for the long-held conception of space and time (Qiang and Van de Weghe, 2019). Accordingly, spatiotemporal techniques and visualizations need rethinking and rescaling to represent linear time in the third dimension of space (z-axis).

In addition to the timescale, another limitation that uniquely arises from spatial data patterns is the modifiable areal unit problem (MAUP) (Wong, 2009). Also known as the "ecological fallacy," these related concepts represent the issues associated with the potential disconnection between the scales of processes and the scales of spatial data used to represent them (Li et al., 2018). As a result, the investigator can get completely different answers depending on whether space is assessed by states, zip codes, or census tracts and whether time is assessed by year, day, or minute. Different spatial and temporal definitions can do the same analysis, and the results can lead to entirely different answers. Therefore, depending on how the investigator defines the data, they may get exciting but spurious patterns. One of the solutions suggested is acknowledging its presence and conducting multiscale and multi-zonal systems analyses to show the range of possible results (Wong, 2009).

2.2.4 Spatial and spatiotemporal mapping of cervical cancer

Globally, certain studies have presented the spatial or spatiotemporal pattern of cervical cancer. This suggests that GIS has been paramount in detecting and mapping cervical and other cancers. According to a report on the application of spatial analysis in China, the method can display the distribution of cancer cases. It can use spatial analysis methods and scanning statistical techniques to obtain key areas of cancer incidence. These results can provide data and key areas for formulating regional public health policies and recommendations for cancer screening and the rational allocation of health resources (Wan et al., 2020). Most of these studies were based on national or district-level cancer registry centers, as incidence studies should be from a relatively stable population and have a high profile of epidemiologic recording. The spatial study by Beyer et al. (Beyer et al., 2022) in Uganda highlighted that population-based cancer registry data and geospatial mapping can be used in low-resource settings to support cancer prevention and control efforts and to create the potential for research examining geographic factors that influence cancer outcomes.

The combination of spatial and temporal analysis was enhanced in many of the reported findings in the literature. In fact, multiple covariates models have been implemented in some of these studies as well to help identify potential factors with spatial autocorrelation (Zhao et al., 2017; Teixeira et al., 2019; Roche et al., 2015). Considering the details, it has been shown by Zhao et al. (2017) that cervical cancer incidence exhibited trends by religion over time indicate differences in sexual habits, lifestyle, and religion-associated culture between Muslims and Buddhists and suggesting divergent risk factor profiles for these groups. The high incidence rates in Sadao and Hat Yai are likely explained by the main road to Malaysia, which runs across these two areas and has frequent commercial sex trade. Female sex workers should be targeted as a vulnerable population for screening efforts to address this continuing burden of cervical cancer (Zhao et al., 2017).

Similarly, a spatiotemporal analysis of cervical cancer in Thailand showed that the risk of cervical cancer has decreased over time, but in some localities, there was a higher risk than in the major province of Chiang Mai. Accordingly, the authors recommended promoting cervical cancer screening coverage in all areas, especially where access is complex and/or for women of lower socioeconomic status (Thongsak et al., 2016). A similar trend in the incidence of cervical cancer has also been reported by a study in Brazil, especially for women aged 45 years and older and those with squamous cell carcinoma (Teixeira et al., 2019).

On the contrary, a similar design and method employed to assess the incidence of cervical cancer among HIV/AIDS-positive women in South Africa revealed an opposite trend. The results showed an increase in incidence of cervical cancer in what they call ‘affluent municipalities’ to mean those with better availability of healthcare facilities. The authors also justified this rise to be attributed to better access to health care in more affluent areas, which could result in better diagnosis and detection of cases (Tafadzwa et al., 2021).

2.3 Access in healthcare: definitions and conception

Access is a latent concept encompassing interrelated but distinct health policy and service delivery dimensions. According to Penchansky and Thomas, access comprises at least four elements: availability, accessibility, accommodation, affordability, and acceptability (Penchansky and Thomas, 1981). Later, Gulliford et al. expanded on the concept, highlighting that the extent to which a population gains access depends on the financial, organizational, social, or cultural barriers that limit the utilization of services (Gulliford et al., 2002). The authors argue that access measured in terms of utilization depends on the affordability, physical accessibility, and acceptability of services and not merely supply adequacy.

According to the United Nations (UN) Committee on Economic, Social, and Cultural Rights (CESCR, 2000), the concept of access to essential healthcare services has been defined in aspects of individuals' freedom as well as entitlements to attain unrestricted privileges of health. This they claimed is regarded as a fundamental component of human rights. It has documented a set of social, economic, and political dimensions that should be considered when thinking about health. Further, the committee interpreted health as an inclusive right extending not only to timely and appropriate health care but also to the underlying determinants of health, such as access to safe and potable water and adequate sanitation; an adequate supply of safe food, nutrition, and housing; healthy occupational and environmental conditions; and access to health-related education and information, including on sexual and reproductive health. It was also mentioned that though the precise application of each element depends on the conditions prevailing in a particular state party, four basic main dimensions exist, namely: 1) availability; 2) accessibility (non-discrimination, economic accessibility, and information accessibility); 3) acceptability; and 4) quality.

A related notion in healthcare access emphasizes the need to view this concept at its micro-, meso-, and macro-levels when deciding treatments, health strategies, and policies (Sawatzky et al., 2021). At the micro-level, individual patient-level inputs gain more weight to inform routine healthcare practices (Greenhalgh et al., 2018). On the other hand, access in this context could be conceived as if individuals have access to medical care (Hoseini-Esfidarjani et al., 2021). At the meso-level, the focus is on using such data for decisions made by healthcare managers and administrators for quality improvement, performance monitoring, reimbursement, and accreditation (Greenhalgh et al., 2018). At the macro level, access is about a population having the opportunity to use healthcare services (Gulliford et al., 2002). Hence, the implications of patient-reported outcomes lead to governments' decisions for health policy purposes (Black and Tan, 2013).

2.3.1 Measuring access to healthcare

Measuring access to healthcare as a latent outcome is complex due to the nature of the ingredient variables, as defined above. Using indicators offers a quick way of tracking how well a society is discharging its responsibilities for the organization and health care delivery. According to the earlier theory by Elinson (1974) on socio-medical arenas of health, socio-medical indicators reflect both objective conditions and social values. They are policy-oriented, serving as mobilizing agents for socio-political pressures concerned with raising the overall level of health of the population (Elinson, 1974).

On the other hand, proxy terms of access, such as utilization, should be applied to measure realized access in health equity. However, utilization is influenced by the supply and demand for services, which makes it distinct so that individual attributes such as preferences, tastes, and information would affect their potential to consume it (Mooney, 1983). Therefore, access is more related to having an opportunity for unrestricted supply and functions regardless of whether the access is reached. However, the notion that utilization is based on individuals' need for care, also known as "demand for healthcare," continues to be criticized because it does not stand alone in this regard, and other factors interact to influence it (Feldstein, 1966; Mason et al., 2019). That demand is a derived need arising from the fundamental demand for good health, which is required for consumption and investment purposes (Grossman, 1972).
The National Academies of Sciences, Engineering, and Medicine (NASEM, 2018) also documented the following, arguing that utilization could arise as a result of other drivers and apart from a need to do so: *''Many factors affect healthcare utilization independently of need and are reflected in differences, some of which are remediable, among population groups. Some of these factors are related to biological or environmental differences among groups, such as disproportionate residence in polluted environments, access to healthy food and adequate housing, and education associated with effective healthcare use. Others are related to differences in access, such as health insurance coverage or income needed to obtain services; ease of obtaining services; and discriminatory practices of providers''*

As much interest has recently been conferred on using precise measurement tools when evaluating healthcare access populations, experts in the field have proposed mechanisms that comprise diverse dimensions. In this sense, studies agree that there is a clear consensus regarding the meaning of access and that it is characterized by multidimensionality, hence the need for methods that address these dimensions (Gulliford et al., 2002; McIntyre et al., 2009; Levesque et al., 2013).

To summarize this session, let us focus on four progressive developments in accessing healthcare that closely align with this topic. However, it is worth mentioning that though slightly differing ways of assessing access have been noted across the sources consulted, particularly those on which the following paragraphs focused, the foundations of all falls on the perspective of common and selected dimensions.

The first approach was proposed using two sequential methods, one of which is a development or improvement over the other, interestingly of the oldest concept of access. According to Penchansky and Thomas's definitions, access is optimized by accounting for its

different dimensions: accessibility, availability, acceptability, affordability, and adequacy in service design, implementation, and evaluation (Penchansky and Thomas, 1981). Saurman (2016) has added "awareness" to this definition, arguing that one cannot perceive or consume a health service without literacy or awareness of its benefit (Saurman, 2016).

The second development was the one devised by the UN Committee on Economic, Social, and Cultural Rights (CESCR, 2000). In this document, healthcare access has been conceived to cover such facets as a) availability, b) accessibility (non-discrimination, economic accessibility, and information accessibility), c) acceptability, and d) quality.

The third approach, which closely relates to the previous versions, was proposed by Levesque and his colleagues (Levesque et al., 2013). Accordingly, access was conceptualized into the following five aspects of accessibility, namely: 1) Approachability, 2) Acceptability, 3) Availability and accommodation, 4) Affordability, and 5) Appropriateness. In the same vein, five corresponding abilities of populations were defined in this framework, namely: 1) the ability to perceive, 2) the ability to seek, 3) the ability to reach, 4) the ability to pay, and 5) the ability to engage.

Lastly, Hoseini-Esfidarjani and colleagues have devised a relatively simple but comprehensive tool (Hoseini-Esfidarjani et al., 2021). This psychometric instrument has been reported to be tested and discriminately able to address perceived access to healthcare services. It comprises the following six components: availability, accessibility, acceptability, affordability, accommodation, and awareness.

2.3.2 Barriers to access to healthcare

There are three primary barriers to healthcare access: structural, financial, and cognitive (Santalahti et al., 2020; Brusnahan et al., 2022). Structural barriers are impediments to medical care directly related to health care providers' number, type, concentration, location, or organizational configuration. The distance to the health facility and time spent on travel also account for a significant proportion of this barrier (Carrillo et al., 2011). On the other hand, financial barriers are the other set of barriers that restrict access, either by inhibiting the ability of patients to pay for needed medical services or by discouraging physicians and hospitals from treating patients of limited means (Drainoni et al., 2006). Personal and cultural barriers may also inhibit people who need medical attention from seeking it or, once they obtain, care (Adugna et al., 2020). On the contrary, policy development, improved physical accessibility, public disability awareness, and parental support are some of the key facilitators

to accessing healthcare services, especially in low and middle-income settings (Adugna et al., 2020).

2.3.3 Determinants of access to healthcare

Studies have reported on numerous factors that positively or negatively influence populations' healthcare access. A study conducted in Uganda reported that healthcare access was affected by health need-related factors, such as self-reported NCDs, severity of illness, mobility limitations, and enabling factors, such as household wealth status and earning wages (Wandera et al., 2015). The following are selected characteristics that significantly impact the access or utilization of health as a commodity.

2.3.4 Income level

Income exhibits a negative correlation with the risk factors for chronic illnesses, such that households that have lower family income have higher rates of heart disease, stroke, diabetes, or hypertension and have four or more common chronic conditions (Jayathilaka et al., 2020). Poor people remain in the vicious cycle of this problem because they lack the financial capability to access healthcare for their ill health needs. The increasing burden of such chronic diseases is disproportionately in low-resource settings, which may impose a significant financial burden on households, particularly those in low and middle-income countries (LMICs) compared to developed nations (Murphy et al., 2013). Whereas poverty is identified as the main intensifier of poor health accessibility, its effect might be worsened when it augments the affordability of other structural barriers, such as geographic accessibility (Russell et al., 2013).

2.3.5 Health insurance coverage

Quite older in its conception and coming into effect, health insurance coverage is recommended to be among the potential enabling factors that trigger patients' engagement in preventive and curative health (Tipirneni et al., 2018). Similarly, a large cohort-based analysis of multiple insurance options revealed that individuals with private insurance were more likely to report poor access to care, higher costs of care, and less satisfaction with care compared with individuals covered by publicly sponsored insurance programs, suggesting that public health insurance options may provide more cost-effective care than private options (Wray et al., 2021).

2.3.6 Gender

Even though the scope of assessment seems to rest on a female population, studies suggest that there exists a considerable gender disparity in terms of accessing healthcare resources, particularly in developing and middle-income settings (Minyihun and Tessema, 2020; Bintabara et al., 2018; Neyazi et al., 2022; Zhang, 2022). Numerous reasons were documented for poor access in this population. For instance, a study in Malawi suggested that women were less likely than men to secure community-sourced healthcare financial aid and more likely to underutilize necessary healthcare (Azad et al., 2020). A report from Tanzania highlighted those women without health insurance, those belonging to the poorest class according to the wealth index, those who had not attended any formal education, and those who were not employed for cash each year with increasing age. Those who were divorced, separated, or widowed were associated with greater problems in accessing healthcare (Bintabara et al., 2018). Sometimes, women's poor access to healthcare services might not be attributed merely to biological differences but also to the general access to healthcare and lack of diagnostic inputs (Mariani et al., 2017).

The burden of disparity, however, is not limited to low-income countries. A study that assessed 9164 older people in the US revealed that women had greater healthcare needs but were less likely to have hospital stays, physician visits, and median hospital visits (Cameron et al., 2010). A cross-national analysis of 49 European countries showed a greater correlation between female poetical representations. It decreased maternal and neonatal mortality, as well as lower rates of health equity disparities between men and women (Reeves et al., 2022). A study conducted in the urban setting of Beijing also illustrated that despite the total number of facilities meeting the standards recommended by the WHO, the spatial distribution of healthcare facilities is imbalanced, and women's healthcare encompasses both physical and psychological health (Zhang, 2022). In Canada, it was reported that women sought physician consultations for both mental and physical healthcare services (Thompson et al., 2016).

In Ethiopia, reports show that cultural and social predispositions play a role in women's health and affect gender equality, for example, preference for sons (Weber et al., 2019). A time-series survey of married women in the country also revealed that there was a slight decrease in the autonomy of women for decision-making between 2005 and 2011 (18.7% vs. 17%, respectively) and a slight increment to 19% in 2016 (Asabu and Altaseb, 2021). One of the factors that contributed might be women's involvement in healthcare service delivery. A recent systematic review revealed that participation and membership in women's development

teams (WDTs) positively minimize maternal death and improve child immunization service use, as well as a source of information to mothers (Yitbarek et al., 2019).

2.3.7 Advanced age

In addition to other socio-demographic patient factors, age may be a determinant that alters the physical and psychological capacity to choose healthcare. A study among the elderly populations of China showed that older women (>=75 years) were at a disadvantage in accessing medical care (Zhang et al., 2018). The study has shown that inadequate access to care had slightly greater consequences for the physical, cognitive, and overall survival status of older women in China than older men. A study from Somalia reported that there is no age-wise difference in seeking primary healthcare, which is most characterized by maternal and child health (Ahmed, 2020). This finding might be biased for generalization due to the outcome of interest considered (maternal and childcare) and the composition of participants (representation beyond 45 years was only 6%). In line with this, women are also vulnerable to diverse social and economic constraints (Walters, 2004; Bekele, 1980) linked to their health status. A qualitative study in Western Australia highlighted several themes that explain what older women experience in homelessness. These included safe accommodation; financial insecurity; experience of trauma and abuse; stigma, embarrassment, and fear of being judged; the health impact of not fulfilling their role as a family nurturer; mental health; complex interaction of physical and mental health issues; healthcare costs; and the need for ongoing psychosocial and healthcare support once housed (Sutherland et al., 2022).

2.4 Economic burden

2.4.1 Defining the concept

The term "cost of illness" (COI), also known as "burden of disease" (BOD) or "economic burden," refers to the various aspects of costs incurred and financial distress that a country, region, community, or even individuals face (Jo, 2014). Depending on the methods employed, the cost category would broadly lie in the incidence or prevalence aspect of a disease and its impact on longevity, morbidity, or even quality of life (QoL) of patients (Whang et al., 2021). Further extensions in cost of illness measurement could address financial losses in direct and indirect expenditures resulting from premature death, disability, or injury due to the corresponding disease and/or its comorbidities (Jo, 2014; Sorato et al., 2022).

2.4.2 Approaches to measure economic impact

The human capital theory (HCT): From the economic viewpoint, the term "capital" refers to one of the factors of production employed in the conversion of resources into valuable

goods or services (Blair, 2011). With this, humans take charge of all economic behaviors, including transactions, consumption (mainly in a market of goods), and production (in a market of inputs or factors of production). Therefore, it can be recognized that human capital is one of the production factors or inputs that can generate additional values by employing it in a production process, which makes it the center of development and modernization (Cinnirella and Streb, 2017). The understanding that human capital is viewed as a resource rest on two classifications. 1) human capital could be viewed as an input in the production process generated by or along with other production factors such as financial capital, land, machinery, natural resources, and labor hours. 2) Secondly, human capital can be viewed as the investment target through formal and informal education and training that formulate knowledge, skills, competency, and experience embodied in an individual. The COI study focuses on the latter definition of human capital, the individual's productivity in a society (Jo, 2014).

Despite being widely used by many researchers to estimate indirect costs, the HCT is criticized for its bias in intellectual formation and education as a sole basis for productivity and wages. According to Marginson (2019), the human capital theory fails the test of realism due to its weaknesses in method, use of a single theoretical lens, and closed system modelling, and that it imposes a single linear pathway on the complex passage between heterogeneous education and work (Marginson, 2019). An additional critique of HCT is that, depending on current socioeconomic status, certain groups are assigned a higher value than others, which may cause a statistical bias that leads to spurious estimation results (Hodgson et al., 1982; Drummond, 1992).

Friction cost method (FCM): The second approach to HCT is the friction-based costing of indirect costs. This approach estimates the value of human capital when another person from the unemployment pool replaces the present value of a worker's future earnings until the sick or impaired worker returns or is eventually replaced. Hence, the friction cost (initial disruption costs plus training costs) is limited to the illness, injury, or premature death of the short-term period defined as the "friction period' (Jo, 2014). The FCM will estimate a lower cost than the human capital method in the long run. For example, according to a study in the Netherlands, the medium-term macroeconomic consequences of absence from work and disability reduce national net income by an additional 0.8%. These estimates are considerably lower than estimates based on the traditional human capital approach, but they better reflect the economic impact of illness (Koopmanschap et al., 1995).

Nonetheless, the method is criticized for being based on implausible assumptions unsupported by neoclassical economic theory that might apply with difficulty and diminishing indirect costs (Johannesson and Karlsson, 1997; Brouwer and Koopmanschap, 2005). Another criticism of this model is that leisure is treated as having no value. Instead, it is considered value in terms of quality-adjusted life years (QALYs), as generally in economic evaluation (Brouwer and Koopmanschap, 2005). Furthermore, this approach is criticized for being utilized rarely as it requires extensive data. When firms use their reserved labor inputs to replace impaired workers during friction, calculating the productivity losses will be far more challenging (Rothermich and Pathak, 1999).

Willingness to pay method (WTP): The WTP method measures the amount an individual is eager to pay to reduce the probability of illness or mortality (Hodgson et al., 1982). Various methods exist to determine and estimate an individual's WTP, such as conducting surveys, examining the extra wages for precarious jobs, and examining the demand for products that lead to greater health or safety (Hirth et al., 2000). They are collectively called "conjoint analysis (CA)," and the contingent valuation method (CVM) is the most commonly used among CA methods (Venkatachalam, 2004). Through hypothetical survey questions, CVM is designed to elicit utility and determine an individual's maximum WTP for some good that usually has no market price (Klose, 1999). Recently, the discrete choice experiment (DCE) method has been used more frequently in CA, which provides opportunities for evaluating process effects and non-health outcomes in addition to traditional QALY analysis. The DCE technique is an attribute-based measure of benefit based on the assumptions that, firstly, alternatives (goods or services) can be described by their characteristics (attributes), and secondly, an individual's valuation (i.e., benefit, utility, satisfaction, or preference) depends upon the levels of these attributes (Clark et al., 2014). In a DCE study, individual respondents are offered a series of choice sets and asked to choose between two or more alternatives in each choice set. The choice observed is assumed to reveal an underlying (latent) utility function. The DCE approach combines random utility theory with consumer theory, experimental design theory, and econometric analysis. The WTP method is usually characterized by higher estimates of the value of life than the human capital approach attempts to ameliorate these problems (Hirth et al., 2000).

2.4.3 Context-specific reports on costs of illness in cervical cancer

A prevalence-based cost-of-illness study of gynaecologic cancers (GCs) was carried out in Iran in 2014 (Sargazi et al., 2022). This study followed a similar methodology to ours, except that it was not matched with controls. It found that the total cost of GCs in Iran was estimated

at $51 million in 2014. The direct costs were $32 million, and indirect costs were $19 million of the total annual cost. The total cost of ovarian cancer was the highest among the three cancers.

A similar study was conducted in Eswatini to evaluate the annual cost of illness following cervical carcinoma. The study estimated that the total annual cost of cervical cancer was $19 million (with a range of $14 million to $24 million). It was also highlighted that direct costs represented the majority at 72% ($13.7 million). Further information from this report showed that managing invasive cervical cancer was the main cost driver, with costs attributable to treatment for the International Federation of Gynaecology and Obstetrics stage III (FIGO III) and FIGO IV representing $1.7 million and $8.7 million, respectively (Ngcamphalala et al., 2021).

A population-based survey in Ontario aimed to identify the main cost drivers and predictors of increased costs (Liu et al., 2016). All patients with cervical cancer diagnosed between 2005 and 2009 in the province of Ontario were propensity-score matched to 5 non-cancer controls on birth year, income quintile, rurality, comorbidities, and patterns of healthcare utilization pattern during the two years before cancer diagnosis. The results of this matched study revealed that the total incremental costs for managing cervical cancer were $362 in the pre-diagnosis phase, $15,722 in the initial phase, $3924 per year in the continuing phase, and $52,539 in the terminal phase. Inpatient care accounted for 34%, 28%, and 52% of total healthcare costs in the initial, continuing, and terminal phases.

An incidence-based approach was conducted to estimate the cost of illness among cases of locally advanced invasive cervical cancer in Bangkok (Katanyoo et al., 2021). The cost was calculated for five years, starting with the treatment initiation. Direct medical costs were extracted from the hospital database. The cost of two-dimensional techniques and three-dimensional conformal radiation therapy was calculated separately. As per the findings, the economic burden for newly diagnosed locally advanced cervical cancer patients in Thailand in 2018 was approximately US $129 million and US $131 million for using two-dimensional and three-dimensional conformal radiation therapy, respectively. Costs from recurrence and mortality were estimated to account for 70% of all total costs. A study in Japan reported a time-dependent increment in the costs and mortality of the population from 1996 to 2011. The cost of illness was estimated to have increased by 66%, from 96.1 billion yen in 1996 to 159.9 billion yen in 2011 (Hayata et al., 2015).

Few studies have been conducted on the costs of illness in Ethiopia. The study done at Tikur Anbessa Hospital (TASH) revealed that the mean outpatient cost per patient was $407.2 (Median = $206.9) per the 2012-2013 estimate (Hailu and Mariam, 2013). In this report, the direct outpatient cost (Mean = $334.2) takes the largest share compared with the indirect counterpart ($150). The outpatient cost for half of the respondents falls between $93.7 and $478. The mean inpatient cost for hospitalized patients was $404.4. The average direct inpatient cost was $329 (74% medical costs and 26% nonmedical costs).

Though not specific to cervical cancer, a study on the average cancer-related expenditure has been conducted in Northwest Ethiopia. Accordingly, the findings suggest that the mean cost of cancer illness among adult patients was US$ 1103.7 ± 33.2, and the median cost was US$ 951.0 with an interquartile range (IQR) of 822.1 (Hagos A, 2020). A similar study was done at Hawassa Specialized Hospital to determine the costs and drivers of different cancer diagnoses. On average, $209.99 was spent on treatment for each cancer patient. Of these, medication costs are the highest ($20.77, IQR = 0.53-112.56) of the direct medical costs, and transportation costs are the highest ($58.33, IQR = 22.0-131.67) of indirect medical costs. Outpatients paid $147.37 (IQR = 84.42-240.50), while inpatients paid $245.16 (IQR = 147.64-439.20). The patients lose about 55.99% of their average annual income (Bona et al., 2021).

2.4.4 Factors affecting costs of illness

The cost of illness in healthcare can be affected by many patient factors that may encompass beneficiaries' broader demographic, socioeconomic, and clinical and functional characteristics (Li et al., 2021). The study that covered periods between 2003 and 2010 in Korea showed that health spending was mainly associated with the proportion of the elderly population. However, the Medicare Economic Index (MEI) showed an inverse association (Han et al., 2013). A study carried out in Brazil in 2020 on the common factors potentially determining average costs documented that the average overall monthly cost for patients was positively correlated with the occupation ($p = 0.021$) and origin ($p = 0.038$) variables, and no statistically significant relationship was noted for other characteristics (Araújo, 2020).

According to reports in Ethiopia, hospital admission costs account for the higher proportion. For example, the study by Hailu and Mariam (2013) indicated that for every additional day of inpatient hospital stay, there is a daily incremental inpatient cost of $4.2 (Hailu and Mariam, 2013). A study from Northwest Ethiopia has assessed, using a linear regression, the potential factors associated with the costs of different cancers in adults. Such factors as urban residency

(β= 0.147; 95%CI: 0.047, 0.246), distance (β = 0.0007; 95%CI: 0.0002, 0.001; p<0.001), marital status (β = 0.125; 95%CI: 0.037, 0.212), higher education (β = 0.318; 95%CI: 0.202, 0.435), purchasing drugs from private facilities (β = 0.134; 95%CI: 0.026, 0.243), most affluent households (β = 0.320; 95%CI: 0.143, 0.496) (Hagos A, 2020). According to the findings of a study conducted at Hawassa University Comprehensive Hospital, outpatients pay $0.92 less than inpatients (P<0.001, 95%CI:0.72-0.34), and the cost increases by $0.2 for patients from Oromia (Bona et al., 2021).

As we consider other chronic illnesses, age could also be recognized as an essential prognostic factor that would determine yearly cumulative medical expenditure. A study reported that a 65-year-old with a chronic severe illness spends $1,000 to $2,000 more per year in health care services than a similar adult without the condition. However, cumulative Medicare payments are only modestly higher for the chronically ill due to their shorter life expectancy (Joyce et al., 2005).

2.5 Theoretical framework

2.5.1 Five A's healthcare access framework

As first proposed by Penchansky and Thomas, this concept of access to healthcare embraces five main dimensions, denoted as 'A's'. These are: availability, accessibility, affordability, acceptability, and accommodation (Penchansky and Thomas, 1981). Our model comprised to define and test these elements in the context of cancer treatment centers in Ethiopia. Availability refers to the presence of healthcare services and resources, such as medical staff, treatment options, and facilities are readily reachable, preferably, in an hour distance of walk, and which might determine healthcare access even more than demand-side factors (Anselmi et al., 2015). On the other hand, accessibility focuses on the geographic location of health services and the ease with which patients can reach them (Tanou et al., 2021). This emphasizes on the travel distance and transportation barriers that patients face. As an important factor of healthcare access from demand-side perspective (Zavras, 2020), affordability measures the costs of care, including fees for services, treatments, and associated expenses, as well as the patient's ability to pay or receive financial assistance. Acceptability of healthcare services is the fourth dimension of access component that addresses the compatibility of healthcare services with patient preferences, values, and cultural or social expectations (Latif, 2020; Sekhon et al., 2017). Finally, the component 'accommodation' pertains to the organization of healthcare services in such a way that patients are able to ascertain supply side arrangements, including appointment scheduling, facility hours, as well as the availability of supportive services, such as interpreters or wheelchair access, to ensure

that care is accessible when needed (Haggerty and Levesque, 2017; Levesque et al., 2013). Within our project's assessment, the five A's framework addresses a comprehensive structure of both the demand- and supply-side factors relevant in assessing healthcare access perception by patients.

2.5.2 Andersen's healthcare utilization model

One of the oldest known theories in measuring access to healthcare is Andersen's behavioural Healthcare Utilization Model (Andersen and Newman, 1973; Kehrer, 1972). It provides a set of dimensions of the healthcare system and patient behaviours, such as the characteristics of the health system, changes in medical technologies, and the assessment of individual determinants of health. Since its first development, the following revisions have been incorporated into the model. Priorities, enabling, and need factors were considered for healthcare service utilization. In the 1970s, it was highlighted that the model added on additional factors such as population characteristics (those factors in phase 1) along with health system factors were important, leading to health service uptake, which, in turn, brought about patient satisfaction. In the behavioral model from the 1980s to 1990s, it was important to embrace factors such as personal health practices and the environment as integral to the elements in the earlier models. The last model also revealed that the earlier factors would be linked with outcome factors, such as perceived health status, evaluated health state, and consumer satisfaction, which, in turn, could influence predisposing, need, and enabling factors in the loop (Andersen, 1995).

According to a recent systematic review, the common factors included the age of the patient, education level, gender, marital status, and employment condition as predisposing factors, while income level, coverage (status) of health insurance, and residence as enabling factors (Alkhawaldeh et al., 2023). This review emphasized the main determinants of healthcare utilization into three primary components, which are also relevant to our study: predisposing characteristics, enabling resources, and perceived need.

Predisposing characteristics include demographic factors such as age and gender and social structure variables like education, ethnicity, and cultural beliefs that influence individuals' propensity to use healthcare services. The enabling resources encompass both personal and community resources; these are factors that facilitate or hinder healthcare access, such as income, insurance coverage, availability of healthcare providers, and transportation. Perceived need refers to the subjective and objective need for medical services, which can drive the decision to seek care. We have assessed patient and health system attributes that relate to both

the perceived and realized access behaviors. This included how patients perceive accessibility, affordability, accommodation, availability, and awareness of different treatments at the health facilities. Andersen's model is beneficial in assessing disparities in healthcare access and utilization, making it a valuable tool for studies aimed at improving healthcare delivery and addressing inequities in health outcomes, such as those seen in cervical cancer treatment practices in the respective settings.

2.6 Conceptual framework

The conceptual model for this project was developed based on a comprehensive literature review and an integrated synthesis of relevant theoretical frameworks. It illustrates the spatial and temporal patterns, access to healthcare services, and the economic burden associated with cervical cancer. These outcomes are grounded in the 5 A's of Healthcare Access and Andersen's Behavioral Model, which encompass a range of clinical, sociodemographic, economic, and behavioral factors. The economic burden is further categorized into direct costs (both medical and non-medical), indirect costs, and intangible costs. Figure 1 integrates these variables to provide a structured, theory-driven perspective on how individual beliefs, behaviors, and systemic healthcare access challenges interact to influence the management and outcomes of cervical cancer.

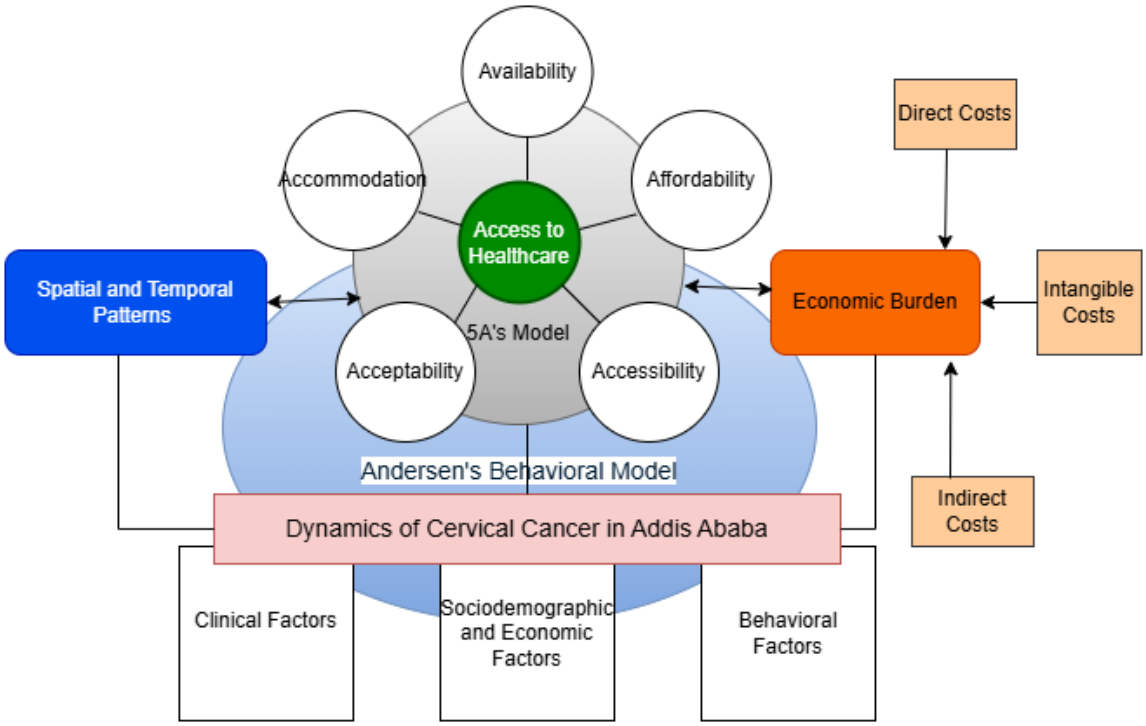


Figure 1: Conceptual model of the study on the spatiotemporal modeling, access to healthcare services and economic burden of cervical cancer in Addis Ababa, Ethiopia

CHAPTER THREE: OBJECTIVES AND RESEARCH QUESTIONS

3.1 General objective

- To model the spatial and temporal dynamics of cervical cancer incidence, estimate its associated cost, and evaluate healthcare service accessibility in Addis Ababa, Ethiopia

3.2 Specific objectives

The specific objectives of the study were to:

- Model the spatial and temporal patterns of cervical cancer incidences in Addis Ababa from 2012 to 2021
- Evaluate healthcare service accessibility for cervical cancer patients in Addis Ababa
- Investigate factors influencing healthcare access in the study area
- Examine the economic burden of cervical cancer in the study area
- Identify predictive factors of annual total costs associated with cervical cancer

3.3 Research questions

The following questions were crucial to the scope of this project:

1. What are the spatiotemporal patterns of cervical cancer incidence in Addis Ababa from 2012 to 2021?
2. What is the level of access to healthcare services for cervical cancer patients in Addis Ababa?
3. What factors are associated with perceived good access to healthcare services for cervical cancer patients in Addis Ababa?
4. What is the economic burden of cervical cancer on patients and their families in Addis Ababa?
5. What are the predictors of the annual total costs incurred by patients for accessing cervical cancer healthcare services?

CHAPTER FOUR: METHODOLOGY

4.1 Philosophical stance: Ontological, epistemological, and axiological considerations

Ontology is a branch of philosophy that studies the state of being (Maedche, 2002). Conversely, epistemology explores the methods of acquiring knowledge, examining how we know what we know and identifying who qualifies as a knower. It is a philosophical branch concerned with understanding the foundations and scope of knowledge, justification, explanation, and wisdom, questioning the nature of these concepts and the capacity of a knower to grasp them (Buckland and Chinn, 2015). Axiology, another crucial philosophical component, deals with the study of values and ethics, particularly concerning their role and influence within the research process, including how values shape the relationships among paradigms, methodologies, and methods (Zaidi and Larsen, 2018). The following paragraphs cover on a brief overview of the philosophical stance considered in this study.

From an ontological stance, the study primarily explores the nature of existence or reality concerning human understanding, mainly focusing on cervical cancer's positivist (objective) viewpoints concerning its ontology and treatment-related phenomena. In the management of cervical cancer, the ontological perspective significantly shapes how the disease is conceptualized and, subsequently, how both providers and patients approach it. This perspective grapples with fundamental questions about what constitutes the essence of cervical cancer to providers, patients, and the community. For instance, is cervical cancer merely a biological and physiological condition, or does it also encompass broader social and psychological dimensions that influence treatment outcomes and access that can be known? Consequently, the ontology in this study posits that cervical cancer is a medical condition with available treatment options, wherein access to healthcare can be objectively assessed, and patients' perceptions of access and the actual costs of management can be precisely quantified.

From a strictly biological viewpoint or objective ontology, cervical cancer might be viewed as a series of cellular abnormalities and genetic mutations that are proliferated molecularly and immunologically by human papillomavirus (HPV) (Wolf and Ramirez, 2001; Balasubramaniam et al., 2019). This perspective leads to treatments focused primarily on the physical removal of cancer cells, using methods such as surgery, chemotherapy, or radiation therapy. It prioritizes molecular and pharmacological research aimed at understanding and

interrupting the biological pathways of cancer development. Advanced and precise methods employing nanoparticles are recently evolving (Verma et al., 2023).

In general, adopting an objectivist ontological approach, the researcher views cervical cancer primarily as a physical condition that is influenced quantifiably by various psychological, social, and environmental factors. This perspective considers how social determinants such as socioeconomic status, healthcare accessibility, educational levels, and cultural beliefs about the disease and its treatments affect the prevalence and management outcomes of cervical cancer. This implies that effective management strategies should encompass more than just medical treatments. They should also include community engagement, educational initiatives, psychological support, and policies designed to enhance access to care and preventive measures, underlining the importance of a holistic approach to managing cervical cancer.

From an epistemological perspective, this study considers positivist and critical epistemologies as central to its approach. According to adherents of positivism, knowledge should be grounded in empirical evidence and quantitative data where truth is separate from human consciousness (Berryman, 2019). They emphasize the importance of clinical trials, epidemiological studies, and other quantitative research methods that provide statistical evidence of effectiveness. In the context of our study, this positivist approach supports the development and validation of methods to assess the extent of access accurately, perceptions of healthcare access, and actual costs and burdens of the disease, striving for objectivity and reproducibility in findings. Conversely, a critical epistemology involves scrutinizing the broader social, economic, and political contexts that impact cervical cancer management. This standpoint encourages an exploration of how social determinants of health, such as poverty, education, and healthcare resource availability, contribute to disparities in cervical cancer outcomes.

In managing cervical cancer, axiological considerations influence the research agenda and clinical practices. Axiology, the study of values and ethics, significantly impacts the prioritization, conduct, and application of research within the medical community. Values such as patient dignity, autonomy, and equity play crucial roles in determining how different aspects of cervical cancer management are emphasized, ranging from the accessibility of screening programs to the treatment options and the protocols for obtaining patient consent. Ethical values are essential in ensuring that research and treatment uphold the rights and well-being of individuals. These values guide practices such as obtaining informed consent, maintaining patient confidentiality, and providing care to minimize harm while maximizing

benefit. Additionally, axiological considerations are instrumental in shaping how research findings are interpreted and implemented, ensuring that ethical standards are met throughout the process.

4.2 Methods

4.2.1 Study area and setting

The study was conducted in Addis Ababa, the capital city of Ethiopia, centrally located at geographic coordinates 9°2'N latitude and 38°45'E longitude. Covering an area of 540 square kilometers, Addis Ababa stands at an average elevation of 2400 meters above sea level (Berhe et al., 2017). According to the 2007 National Population and Housing Census (CSA, 2007), Addis Ababa's population was 2,739,551, growing at an annual rate of 3.8%. By 2021, projections suggested the population had increased to 3,773,999, with the highest numbers recorded in the Kolfe Keranyo, Yeka, Nifas Silk Lafto, and Bole sub-cities, respectively (CSA, 2021). A 2014 report indicated there were 12 public hospitals in Addis Ababa (Asemahagn, 2014), and according to the report by Bekele and his colleagues (Bekele GE, 2018), six of these hospitals, along with 103 health centers, were managed by the city administration. Nair et al. (2011) documented 25 private hospitals in the city (Nair et al., 2011). However, a later study in 2018 reported an increase, indicating 13 public and 32 private hospitals in Addis Ababa (Kasahun et al., 2020) (Figure 2).

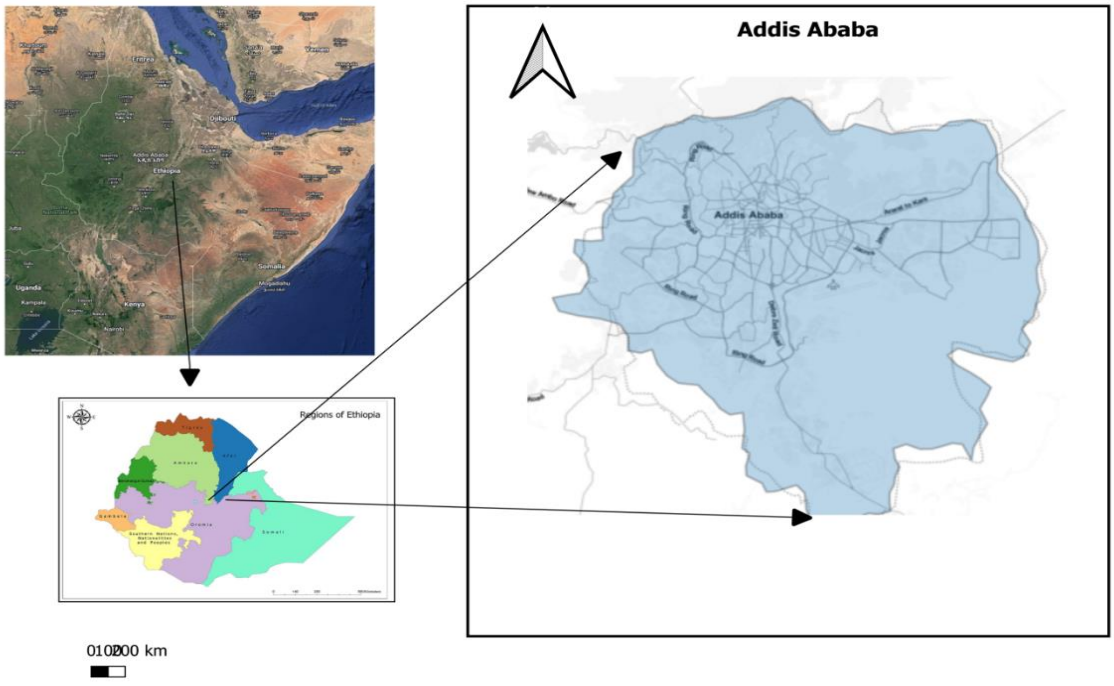


Figure 2: Depiction of the study area based on Google Maps and Global Administrative Areas Map (GADM)

Whereas spatiotemporal mapping of incident cases covered the entire city, study settings for the remaining objectives focused on the main public oncology centers in Addis Ababa. Saint Paul's Hospital Millennium Medical College (SPHMMC) and Tikur Anbessa Specialized Hospital (TASH). The two public hospitals are the country's top referral units, delivering specialized and comprehensive healthcare services and medical training. SPHMMC was established in 1969 by the German Evangelicals and is currently administered under the Federal Ministry of Health of Ethiopia (FMOH). In addition to the health professionals' training, it delivers a diverse set of healthcare services with 392 beds, an annual average of 200,000 patients, and a catchment population of over 5 million (Gebreweld A, 2018). Currently, it also provides chemotherapy services to patients diagnosed with cervical cancer. Similarly, TASH is the country's oldest and largest referral hospital, with 700 beds, managed under Addis Ababa University. Apart from rendering training in many health disciplines, it delivers health services to patients referred from all over the country. The hospital provides both inpatient and outpatient oncology services. The oncology services encompass radiology, chemotherapy, surgery, and chemoradiotherapy (TASH, 2020).

4.2.2 Study design and period

Throughout this study project, we employed a mixed-methods study design. Initially, an ecological design utilizing space-time analysis with time series data was implemented to examine the spatiotemporal incidence of cervical cancer from the years 2012 to 2021. Subsequently, a cross-sectional study design was used to evaluate the perceived and realized access to healthcare services among patients diagnosed with cervical cancer in the city. Lastly, the economic burden of cervical cancer and its incremental costs were compared to a control group of known hypertensive patients using a matched case-control design. The study was conducted from January 1 to November 30, 2023.

4.2.3 Populations

4.2.3.1 Source population

The source population for this study varied based on the specific objectives being addressed. For the spatial mapping and temporal analysis of cervical cancer, the source population included all females residing in Addis Ababa during the review period. For the other study objectives, the source population consisted of all women diagnosed with cervical cancer who were visiting the selected public hospitals in Addis Ababa, Ethiopia.

4.2.3.2 Study population

The study population for analyzing the incidence of cervical cancer in the study area comprised all newly diagnosed cases from 2012 to 2021 that were reported to the Addis Ababa cancer registry center. For the other objectives, the study population included all patients with a confirmed diagnosis of cervical cancer who had started treatment in the selected settings and met the inclusion criteria.

4.2.4 Inclusion and exclusion criteria

Table 1: Inclusion and exclusion criteria of individual studies

Study	**Inclusion Criteria**	**Exclusion Criteria**
1. Spatiotemporal Analysis of Cervical Cancer Incidence	- Women diagnosed with cervical cancer between 2012 and 2021. - Cases registered in the Addis Ababa Cancer Registry. - Patients with complete geographic information (kebele or sub-city level).	- Cases with missing or incomplete geographic data. - Duplicate records or inconsistencies in diagnostic information. - Cases diagnosed outside the study period (before 2012 or after 2021).
2. Healthcare Access Study	- Adult women (aged 18 and above) diagnosed with cervical cancer. - Patients who sought healthcare services at participating hospitals or clinics in Addis Ababa. - Those who provided informed consent to participate in the survey.	- Women under 18 years of age. - Patients with cognitive impairments affecting survey participation. - Individuals who refused or withdrew consent. - Cases diagnosed outside Addis Ababa or treated outside the city.
3. Economic Burden Study (Matched Case-Control Design)	- Cervical cancer patients (cases) diagnosed within the study period, matched 1:1 with controls on age and socioeconomic status. - Controls selected from the same community or healthcare facility. - Participants who incurred	- Cases and controls with incomplete cost data. - Participants who received financial support from charities or special programs. - Controls with a history of cervical cancer or major chronic

	healthcare-related costs (direct or indirect).	illnesses. - Participants who did not seek any healthcare services during the study period.

4.2.5 Sample size and sampling technique

4.2.5.1 Sample size estimation

The required sample size varied based on the specific research questions and designs previously outlined. For spatiotemporal dynamics, no minimum sample size calculation was necessary; instead, all eligible incidence cases reported during the review period of January 1, 2012, through December 31, 2021, were included for spatial mapping and temporal trend analysis.

For the study objective concerning the perceived and realized access of patients to healthcare, the following considerations were made due to the need for previous reports on the topic and with the aim of increasing the sample size. The single proportion formula was utilized with specific assumptions: (i) the probability of patients perceiving adequate healthcare service was set at 50% (P=0.5), (ii) a 95% confidence level (α=5%) was established, and (iii) a margin of error was set at 5%. These parameters necessitated a minimum of 385 study participants.

In the third objective, costs (total, direct, and indirect) and the incremental cost of illness were compared using a matched case-control design, i.e., cervical cancer patients and controls (patients without cervical cancer). These cases were matched based on age, admission classification (inpatient/outpatient), hospital, and follow-up period. As population or sample mean estimates and standard deviations related to the proposed research question were unavailable, a minimum standardized mean difference (SMD) of costs was assumed to be 0.2. The SMD, also known as Cohen's d or effect size, identifies three levels of measurement: 0.2, 0.5, and 0.8 or more, which Cohen (2013) categorizes as small, medium, and large effect sizes, respectively (Cohen, 2013). The following formula was used to determine the minimum sample size required.

$$n=2[\frac{Z\frac{\alpha}{2}+Z\beta}{ES}]^2$$

Which:

$$ES=\frac{\mu 1-\mu 2}{\sigma}$$

And, where:

n=required sample size per group

Zα/2=standard normal z-value for a significance level **α**=0.05 (two-tailed), which is 1.96

Zβ=standard z-value for a power of 80%, which is 0.84

A minimal cost standardized mean total cost difference of 20% is assumed, with **ES**=0.2 Considering a 20% for non-complete data

Combining the above:

N *final*=2n

=942 participants

4.2.5.2 Sampling techniques

No samples were recruited for the first objective, as previously implied. The inclusion of selected hospitals for subsequent objectives was decided purposely based on the population under study, patient flow, and availability of healthcare inputs. Cases were included consecutively, considering current registries in the cancer clinics, patient' flow, and eligibility criteria. All patients had to adhere to their follow-up schedules throughout the study period. Controls were included from similar wards (when appropriate) or outpatient units at the same hospitals during the same follow-up periods.

4.2.6 Data collection instruments, procedures, and quality assurance

4.2.6.1 Data collection instruments and process

4.2.6.1.1 Spatiotemporal modeling and mapping cervical cancer incidence

The data required for this section was extracted from the Addis Ababa cancer registry database, including information on patients' age, date of confirmed diagnosis, test method, cancer stage, history of treatment initiation, sub-city, *woreda/kebele*, and report date. Additional data on the yearly age-grouped population and sub-city, as well as *the city's woreda/kebele*-level projected population, were obtained from the Ethiopian Statistics Service (ESS) for the years under review. A structured data abstraction format was prepared to

account for these variables and their associated data. The extracted and calculated data were then entered into the geospatial analysis software for further processing and analysis.

4.2.6.1.2 Access to healthcare services

Quantitative data were collected using a structured interviewer-administered questionnaire prepared based on an extensive literature review. Multiple dimensions of psychometric tools, as proposed in the literature, were used to help measure access to healthcare services in various contexts (Levesque et al., 2013; Hoseini-Esfidarjani et al., 2021; CESCR, 2000; Saurman, 2016; Penchansky and Thomas, 1981). This modification to define access evolved progressively, and this study adopted the latest version consisting of six components: availability, accessibility, acceptability, affordability, accommodation, and awareness (Hoseini-Esfidarjani et al., 2021). The original instrument consisted of 30 items using a five-point Likert scale. In addition to perceived access to healthcare services, data on socio-demographic characteristics, clinical profiles, and objective access measures (including accessibility, availability, and affordability) were captured through exit interviews and observation checklists. After completing a verbal informed consent process, selected participants were invited to participate in the interviews (Appendix I and II).

4.2.6.1.3 Cost of illness

The data collection format for the cost of illness was developed following a review of the literature on cancer (Hailu and Mariam, 2013; Bona et al., 2021; Hagos A, 2020) and other chronic illnesses (Bermudez-Tamayo et al., 2017; ADA, 2008; Yang et al., 2012). The instrument was designed to capture data on direct medical and non-medical costs and indirect costs that patients incurred in the past 3 months preceding the interview date. Data on direct costs were collected retrospectively using a bottom-up approach involving individual patient records and face-to-face interviews. The locally validated MD Anderson symptom inventory (MDSAI) tool was employed to capture the patient-reported inventory of common symptoms among cases (Anshabo et al., 2016).

The cost of illness was estimated at market prices and net salary or wages. Indirect costs were estimated using the human capital theory (HCT) approach (van den Hout, 2010), which considers the income patients or their companions (relatives or caregivers) would lose due to morbidity at the hospital, home, or other health settings. Thus, patient productivity loss and absenteeism costs were estimated by interviewing about the number of days the patient or the companion had lost. The daily average per capita net earnings were used for working participants, while the market price of daily wages was considered for laborers, housekeeping

staff, students, or homemakers, as previously employed in other studies (Xie et al., 2008). Productivity losses for retired or over 60 women were not considered, as the human capital approach is based on market earnings. Although a third category of costs, called 'intangible' costs, exists within the cost of illness domain, these were not evaluated in this study because intangible costs—related to subjective experiences of pain, suffering, and helplessness—are difficult to quantify monetarily. Although willingness to pay might be an important measure of intangible costs (Xie et al., 2008), this approach was excluded for ethical reasons in this population. All costs were measured and reported in any of the Ethiopian Birr (ETB), international dollars (INT$), and United States Dollar (USD) as appropriate in studies and rated during the review or study period. Since all costs are assumed to have been incurred within one year, no discount was applied (Appendices IV and VI).

4.2.6.2 Data quality assurance

Quality assurance was a central step in generating rigorous and reliable findings in the research, passing through established protocols, formats, and analysis processes. The following measures were considered to ensure the quality of the data collected in this project.

4.2.6.2.1 Use of well-designed protocol and consistent formats

This study was conducted according to the procedures and principles detailed in the methods section. The data collection instrument was developed by reviewing existing literature and incorporating various variables pertinent to the study. The questionnaires were prepared in English, translated into Amharic, and back translated into English to ensure linguistic consistency.

4.2.6.2.2 Qualified data collectors and training

Experienced health professionals, including nurses and general practitioners, were employed for data collection. The data collectors received training on research ethics, patient privacy, and confidentiality of the data collected.

4.2.6.2.3 Supervision, rigorous data handling, and reducing bias

To ensure the integrity of the data collected, appropriate preventative measures were implemented at all stages, with a particular focus on the data collection phase. Continuous supervision was maintained throughout all fieldwork processes to minimize potential errors. Cost data were collected for the previous 90 days to reduce recall bias. Close monitoring was conducted, and accuracy and completeness were rigorously checked during data collection. Additionally, to avoid biases, such as social desirability bias, confirmation bias, observer bias,

or selection bias, during assessing access to healthcare services, it was ensured that data collectors were not employed at the respective oncology clinics.

4.2.7 Validity and reliability of the instrument

An emphasis on the validity and reliability of the instrument used in the data collection was ensured using many approaches employed sequentially. The steps outlined in the guidelines by (Tsang et al., 2017) and (Yusoff MSB, 2021) were adhered to in the adaptation and validation process of the questionnaire. Generally, all instrument development activities went through five main steps: instrument design and adaptation, translation, validity tests of the draft instrument, piloting, and psychometric evaluation of the construct. The appropriate qualitative or quantitative methods employed, the steps followed, and the required inputs are described below.

4.2.7.1 Instrument design and adaptation

The study instrument was developed to assess patient characteristics (socio-demographic, behavioural, clinical), objective outcomes (access and illness costs), and perceived healthcare access from patient perspective. Based on existing literature and expert input, components underwent content validation by specialists, adapting psychometric constructs from (Hoseini-Esfidarjani et al., 2021). Adaptations included tailoring accessibility constructs for the secondary healthcare context, revising terms like "accessibility" to "reachability," and modifying items to reflect regional religious and cultural diversity.

4.2.7.2 Translation and validity testing

The tool was translated into Amharic via forward-backward translation to ensure conceptual accuracy. Content validity was assessed qualitatively and quantitatively through a 3-point Likert scale, calculating content validity ratio (CVR) and index (CVI). Face validity was assessed with a 5-point Likert scale, and an item impact score of ≥1.5 indicated retention.

4.2.7.3 ***Pilot testing***

A pilot test with 30 participants evaluated face validity, flow, and completion time. Internal consistency (Cronbach's alpha) was also used to test reliability score of items.

4.2.7.4 ***Psychometric evaluation***

Construct validity, assessed through confirmatory factor analysis (CFA), focused on factorial validity across six domains of healthcare access. Model fit indices included TLI, NFI, and RMSEA. Reliability was confirmed using Cronbach's alpha, with ≥0.7 indicating acceptable internal consistency.

4.2.8 Variables

4.2.8.1 Dependent variables

The dependent variables were the spatial and temporal incidence of cervical cancer in Addis Ababa, the level of access to healthcare services, and the cost of illness following cervical cancer. Access to healthcare (perceived and realized) was measured as a composite variable across six latent dimensions: accessibility, acceptability, affordability, availability, easiness of accommodation, and awareness. The cost of illness was evaluated in three broader categories: total costs (a summation of direct and indirect costs), direct medical costs, and indirect costs. Direct medical costs included: i) payments made at hospitals for medicines, laboratory services, physiotherapy, follow-up visits, ICU stays, and surgeries; ii) services obtained outside of hospitals, such as visits to specialists and primary care doctors, nursing care, and access to a community pharmacy; or iii) services from traditional healers. Direct non-medical costs comprised i) travel to and from hospitals and traditional healers, ii) payments made for foods or supplements, and iii) fees for paid caregivers.

4.2.8.2 Independent variables

Socio-demographic and economic characteristics: included in the study were marital status, education, occupation, religion, average monthly income, place of residence, number of family members, supportive people nearby, distance from the current health facility, and age, among others.

Clinical characteristics: These included the presence of comorbidity, the name of comorbidity, symptoms inventory scores, time since cervical cancer was first diagnosed, time since treatment began, cancer stage, history of cancer screening, and history of HPV vaccination.

Lifestyle, dietary, and substance use-related variables: included current history of dietary practices, physical exercise (categorized as adequate vs. inadequate), current history of alcohol intake, current history of smoking cigarettes or using tobacco products, and current history of Khat consumption.

Health facility or system-related variables: included the number and type of health facilities, coverage of health insurance, geographic location, accessibility, availability, and affordability of healthcare services.

4.2.9 Epidemiologic approach and perspective

For the cost study, a prevalence-based approach was used to evaluate the economic impact of cervical cancer on society per patient per year. The analysis took a societal perspective, accounting for all associated expenses. These included direct medical costs such as medications, diagnostics, supplies, hospitalization, and physician consultations; direct non-medical costs, including transportation, food, and caregiver expenses; and indirect costs, which covered lost earnings due to job absenteeism and productivity reductions incurred by caregivers.

4.2.10 Data processing and analysis

After being checked, cleaned for completeness, and coded manually, the quantitative data were entered into Microsoft Excel and exported to R studio programming version 4.2 for analysis. Both descriptive and inferential statistics were employed for data analysis.

The spatiotemporal trend of cervical cancer incidence was visualized in the integrated quantum geographic information system (QGIS) version 3.36 and R programming version 4.2 package. A descriptive statistical analysis was carried out to describe the study context and population. A direct age-standardization was performed using the Segi's World standard population (Segi, 1960). Age groups were estimated using a five-year group age classification. Geocoding of locations was executed in QGIS utilizing the OpenStreetMap (OSM) provider. For missing geographic coordinates, the nearest neighbor imputation was performed using R. Subsequently, GeoDa software version 1.2.2 was utilized to visualize the spatial distribution of cervical cancer hotspots and cold spots across 99 geographic locations. The Local Indicators of Spatial Autocorrelation (LISA) using local Moran's I was applied, employing the Bayesian Empirical Test with a significance threshold of $p<0.05$. Weight matrix estimation was conducted using the block method. To address locations with minimal or absent values, spatial interpolation was performed using the System for Automated Geoscientific Analyses (SAGA) GIS version 9.3.2 software. The best fitting model, whether spherical, cubic, or Gaussian, was determined based on the results of semivariogram analysis conducted for each year's data. Subsequently, the universal kriging method was employed to interpolate and map values at unknown locations. The spatial dependence of cervical cancer across the study area was estimated using Global Moran's I statistic. Finally, temporal trends of incident cases and rates across sub-cities and age groups were analyzed using the Joinpoint trend analysis software from the National Cancer Institute (NCI, 2023). The appropriate number of joinpoints, which best describe the underlying structure of the data, was determined using the Bayesian information criterion (BIC). The results were presented as

annual percent changes (APC) in incidence rate per 100,000 women-years. Statistical significance was considered at $p<0.05$.

Descriptive statistics illustrated participants' profiles and validated the instrument. At the same time, structural equation modeling (SEM) was employed to present model fitness indices, a standardized correlation matrix, and the structure of the construct. Given the violation of normality assumptions, measurements were compared against bootstrapped estimates with confidence intervals and standard errors of the sample. Known group validity was confirmed using Student's t-test (for two-grouped variables) and one-way analysis of variance (one-way ANOVA) for variables with more than two categories. The estimates in the t-test were based on the second row (assuming unequal variances), while the post-hoc pairwise comparison in ANOVA utilized Dunnett's T3 calculation (Dunnett, 1980). The computation of divergent validity was estimated using the methods proposed by (Henseler et al., 2015). Apart from presenting univariate and bivariate descriptions of participant attributes, access to healthcare and associated factors were modeled in binary logistic regression. The bivariate and multivariable regression models were employed at $p\leq0.2$ and $p<0.05$ statistical significance, respectively, and their 95% confidence intervals. Model assumption tests, including homoscedasticity and multicollinearity diagnosis, were performed. The Hosmer and Lemeshow test(R) assessed the global model goodness of fit.

The cost data entry was done using Epi-Info v.7.0 and exported to computer languages, namely MS-Excel, Statistical Packages for Social Sciences (SPSS) (George and Mallery, 2019), and R for additional cleaning, re-coding, transformation, and modeling. Data analysis and presentation, including percentages, means, and standard deviations, were done using descriptive statistics. In the matched case-control study, each cervical cancer patient (case) was matched 1:1 with a non-cancer control based on age (± 5 years) and socioeconomic status, ensuring comparability by controlling for potential confounders. To analyze the economic burden, a Paired t-test was used to compare the mean costs between matched pairs, accounting for the dependency created by matching. The incremental cost model was expanded to include a bootstrapping of 1000 samples due to the data's right-skewed non-normal distribution to handle uncertainties. As the overall expense was likewise typified by positively skewed data with outliers, we fitted Tukey's biweight regression model to evaluate the variables related to the yearly total expenditures of illness from cervical cancer. In addition to conducting diagnostic tests for the model, we have verified if the robust model outperforms the ordinary least square (OLS) method. The reports presented the analysis

results using tables, charts with percentages, and numbers. Statistical significance was established at $p<0.05$ and a 95% confidence interval.

4.2.11 Ethical considerations

The study was conducted with strict adherence to ethical considerations, having obtained approval from the Institutional Review Boards (IRBs) of Saint Paul's Hospital Millennium Medical College (SPHMMC: Ref.no: PM23/284), Addis Ababa University, College of Health Sciences, School of Pharmacy (ERB/SOP/543/15/2023) and the College of Health Sciences at Addis Ababa University (055/23/SoP). The study instruments were translated into Amharic, the official working language in the country. Informed consent was a cornerstone of our approach, ensuring that all participants were fully aware of the study's aims, procedures, potential risks, and benefits before their involvement. Participation was voluntary, with assurance given that individuals could withdraw at any time without any repercussions. For the data accessed from the cancer registry, anonymization was ensured by removing all patient identifiers, including names, addresses, and personal health information. Access to the dataset was restricted to authorized personnel [SA] working at the center to maintain confidentiality. Additionally, a formal data sharing agreement was signed with the Cancer Registry Center, outlining the scope of data usage exclusively for this study's objectives. All data handling procedures were designed to minimize risks and safeguard sensitive information.

CHAPTER FIVE: KEY FINDINGS

This study investigates cervical cancer in Addis Ababa from 2012 to 2021, focusing on its epidemiological profile, spatiotemporal dynamics, healthcare access, and economic burden. Chapter four presents key findings in several sections: Section 5.1 outlines the demographic and clinical characteristics of participants, providing context for the affected population. Section 5.2 analyzes spatiotemporal dynamics, identifying changes in local and global incidence patterns over the decade. Section 5.3 examines patients' access to healthcare, differentiates between realized and perceived access, and explores influencing factors. Section 5.4 then assesses the economic impact of cervical cancer, detailing patient costs and incremental expenses over three months and annually and identifying predictors of these costs.

5.1 Profile of cases and study participants

This section summarizes the combined analysis of participant profiles from three distinct studies—spatiotemporal dynamics of incidence cases, access to healthcare services, and the economic burden of cervical cancer in Addis Ababa—as outlined below for each study.

5.1.1 Spatiotemporal dynamics of cervical cancer study

From January 1, 2012, to December 31, 2021, 2,435 cases of cervical cancer were reported after excluding 6 cases with incomplete location data. Case numbers ranged from a low of 191 in 2013 to a high of 287 in 2021. The diagnosis was primarily based on histology (92.3%), with fewer cases diagnosed by cytology (3.6%) and clinical examination or ultrasound (2.2%). The mean age of cases was 51.8 years (S.D. ±12.4), with ages spanning 20 to 99. Cancer staging data was largely unavailable (77.3%), but among reported stages, most cases were stage IIB (6.6%). Spatial analysis used nearest neighbor imputation for missing values across 41 locations. Geographic coordinates for all woredas in Addis Ababa were assigned using OpenStreetMap in QGIS, producing 325 valid geocoded points, which were then mapped to 99 polygon features representing the city’s administrative units.

5.1.2 Access to healthcare services study

In this study, 391 patients participated, including six above the minimum sample size. The average age was 50.3 years (SD = 12.2), ranging from 22 to 89. The mean monthly income was 4,960.8 ETB (SD = 4,046.3), ranging from 0 to 50,000 ETB. Most participants were 50 years or younger (60.9%), lived above the extreme poverty line (58.6%), were married (57.5%), and were literate (62.1%). Additionally, 42.4% had no formal education, 32.7%

were housewives, 77.7% had CBHI coverage, 57.3% lacked social support, and 83.9% belonged to households with five or fewer members (Table 2).

Table 2: Socio-economic profile of patients with cervical cancer in Addis Ababa, Ethiopia (n=391).

Variable	Label	Frequency	Percent
Age (Yrs.)			
	50 or less	238	60.9
	>50	153	39.1
Average monthly income of the household			
	3567 ETB or less	162	41.4
	>3567 ETB	229	58.6
Marital status			
	Single	20	5.2
	Married	225	57.5
	Widowed	76	19.4
	Separated or separated	70	17.9
Able to read and write			
	Yes	243	62.1
	No	148	37.9
Education level			
	No formal education	166	42.4
	Primary education (grades 1-8)	109	27.9
	Secondary education (grades 9-12)	75	19.2
	Tertiary education (University or college)	41	10.5
Occupation			
	Housewife	128	32.7
	Private employee	121	30.9
	Government employee	29	7.4
	Jobless	74	18.9
	Others*	39	9.9
Community-based health insurance coverage			
	Yes	304	77.7
	No	87	22.3
Presence of social support			
	Yes	167	42.7
	No	224	57.3
Household size			
	Five or less	328	83.9
	>5	63	16.1

*Includes merchants, students, housemaid, farmer

5.1.3 Economic burden of cervical cancer study

The study included 932 participants, split evenly into 466 cases and 466 controls, 53.6% affiliated with St. Paul's Hospital and the rest from Tikur Anbessa Specialized Hospital. The mean age was about 52 years for both groups, with more cases (58.2%) aged 52 or younger than controls (48.3%). Most participants were married (74.7% cases; 69.5% controls), and literacy rates were similar (69.7% cases; 71.5% controls). Cases were concentrated in Addis Ketema (14.4%) and Kolfe Keranio (13.5%), while the highest percentage of controls was in Lideta (15%) and Addis Ketema (14.8%). Most were housewives (55.8% cases; 46.6% controls), and 68.9% of cases and 61.4% of controls accessed community support. Most lived in households of five or fewer members (79.6% cases; 86.3% controls). The average monthly household income was 5656.6 ETB (102.8 USD) for cases and 5404.9 ETB (98.3 USD) for controls, with over 60% above the poverty line. Community-based health insurance covered medical expenses for 70.0% of cases and 67.4% of controls (see Table 3).

Table 3: Sociodemographic and economic characteristics of study participants, Addis Ababa, Ethiopia (N=932)

Variable	**Category**	**Cases (n=466)**		**Controls (n=466)**	
		Frequency	**Percent**	**Frequency**	**Percent**
Hospital					
	SPHMMC	250	53.6	250	53.6
	TASH	216	46.4	216	46.4
Age (yrs.)					
	52 or less	271	58.2	225	48.3
	>52	195	41.8	241	51.7
Marital status					
	Married	348	74.7	324	69.5
	Widowed	67	14.4	70	15.0
	Others*	51	10.9	72	15.5
Able to read and write					
	No	141	30.3	133	28.5
	Yes	325	69.7	333	71.5
Level of education	No formal education	174	37.3	176	37.8
	Primary and middle school (grades 1-8)	142	30.5	117	25.1
	High school (grades 9-12)	89	19.1	88	18.9
	Tertiary level (College or University)	61	13.1	85	18.2
Sub-city					
	Addis Ketema	67	14.4	69	14.8

	Akaki Kality	30	6.4	32	6.9
	Arada	31	6.7	30	6.4
	Bole	23	4.9	27	5.8
	Gulele	38	8.2	47	10.1
	Kirkos	37	7.9	41	8.8
	Kolfe Keranio	63	13.5	44	9.4
	Lemi Kura	56	12.0	22	4.7
	Lideta	37	7.9	70	15.0
	Nifas Silk	41	8.8	52	11.2
	Yeka	43	9.2	32	6.9
Occupation					
	Government employee	64	13.7	80	17.2
	Private employee	64	13.7	76	16.3
	Merchant	33	7.1	46	9.9
	Housewives	260	55.8	217	46.6
	Others**	45	9.7	47	10.1
Presence of social support	No	145	31.1	180	38.6
	Yes	321	68.9	286	61.4
Number of members in the household	Five or less	371	79.6	402	86.3
	>5	95	20.4	64	13.7
Average monthly income of the household	≤3567 ETB or 65US$	180	38.6	175	37.6
	>3567 ETB	286	61.4	291	62.4
Source of funding for medical expense***	Health insurance	326	70.0	314	67.4
	Self	157	33.7	170	36.5
	Aid or social support	11	2.4	7	1.5
	Relatives or friends	29	6.2	31	6.7

**Includes separated, divorced or singles; **includes housemaids, jobless, students, retired or farmers; ***does not consider a combination of sources. The sum of percentages may exceed 100.*

5.2 Spatiotemporal dynamics of cervical cancer incidence and its trend from 2012 to 2021

5.2.1 Local spatial clustering of new cases

Assessment of hotspots and coldspots from 2012 to 2021 reveals dynamic spatial patterns in cervical cancer incidence across subcities in the study area. In 2012, 30 high-high cluster woredas were identified primarily in Nifas Silk Lafto, Kirkos, Yeka, Gulele, Lideta, Kality, and Addis Ketema subcities, while the majority of woredas (n=61) were classified as coldspots surrounded by other coldspots (low-low) (Figure 3A).

The trend continued in 2013 with a similar proportion of woredas (n=26) exhibiting high-high clustering compared to the previous year, while the number of low-low clustering areas remained consistent (Figure 3B). By 2014, high clusters of cases expanded to Nifas Silk Lafto, Addis Ketema, Gulele, and Akaki subcities, with most locations maintaining coldspot characteristics (Figure 3C).

In 2015, the number of high-high spots diminished significantly (n=2), mainly localized in Nifas Silk Lafto and Kirkos subcities. Conversely, certain woredas in Nifas Silk Lafto, Akaki, Yeka, and Kolfe Keraniyo subcities emerged as high cluster areas surrounded by low cluster woredas, while others were identified as low-low or non-significant spots (Figure 3D). Subsequent years saw fluctuations in clustering patterns. In 2016, an increase in high-high clusters was observed in various sub cities, while other areas remained predominantly coldspots or non-significant (Figure 3E).

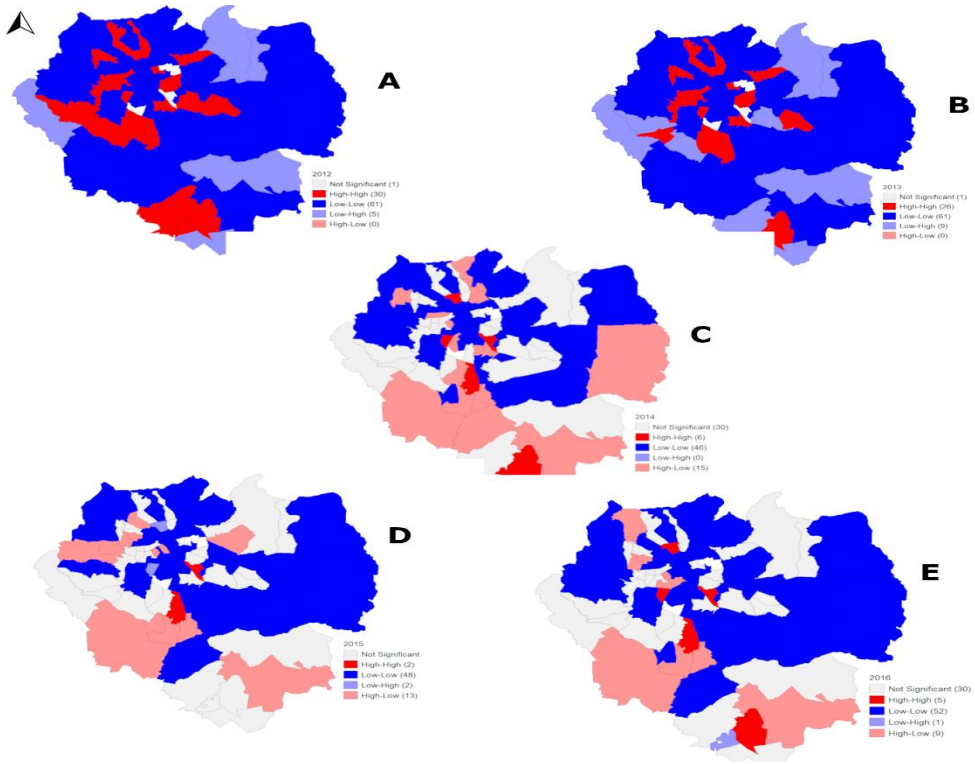


Figure 3: Clusters of reported cervical cancer cases in Addis Ababa from 2012 to 2016

This variation with minor changes persisted through 2017, 2018, and 2019 (Fig. 4A-C). By 2020, spatial patterns began to stabilize, with distinct sub-cities exhibiting high-high clusters, while most woredas showed low-low or non-significant dependence (Fig. 4D). In 2021, high-high clusters declined alongside a rise in high-low clusters, yet most areas were categorized as non-significant or low-low clusters (Fig. 4E).

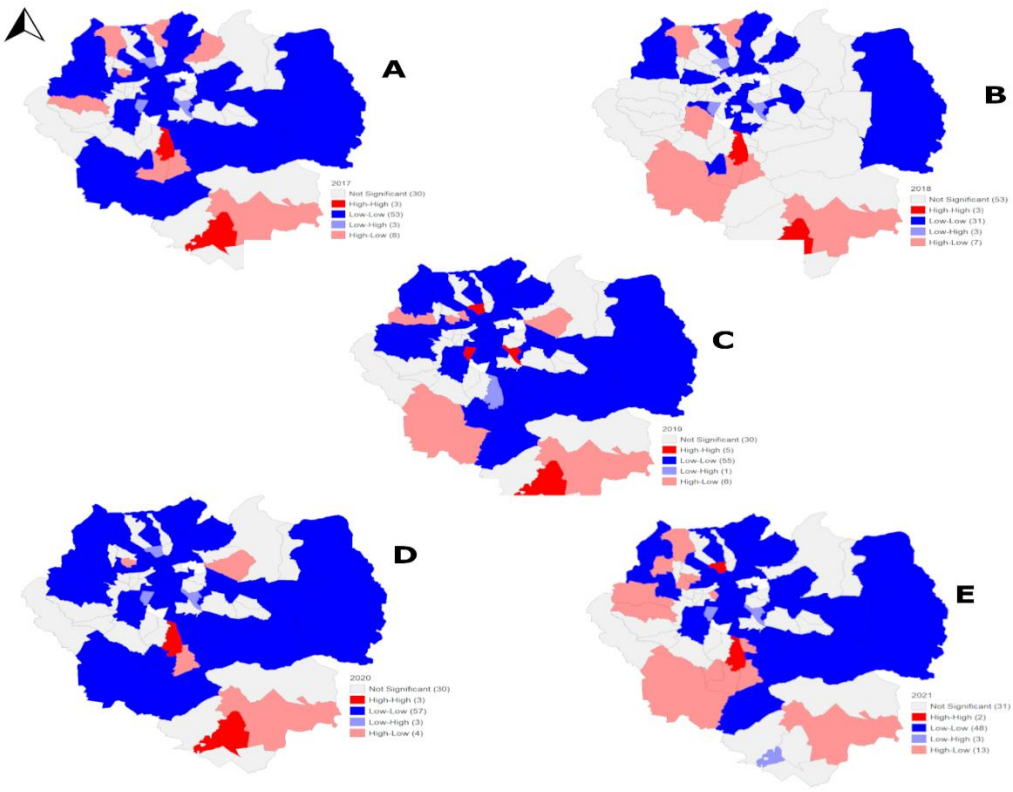


Figure 4: Clusters of reported cervical cancer cases in Addis Ababa from 2017 to 2021

5.2.2 Global spatial autocorrelation of cases with space and time

From 2012 to 2021, Universal Kriging interpolation revealed a distinct spatial distribution of new cervical cancer cases across Addis Ababa, showing significant positive spatial autocorrelation (Moran's I: 0.947–0.989). In 2012, the highest incidence clusters (z score > 0.80) were concentrated in western Kolfe Keraniyo and Nifas Silk Lafto, while areas like Kirkos, Lideta, and Yeka showed moderate Clustering (z score 0.64–0.80; Fig. 5A). By 2013, high-incidence areas shifted southward into Nifas Silk Lafto, Kolfe, and Akaki Kality (z score > 0.92; Fig. 5B). In 2014, clusters expanded to Bole, Yeka, Gulele, and Kolfe Keraniyo, with z scores above 1.0 in these regions (Fig. 5C).

In 2015, the strong clusters emerged in Akaki Kality, Bole, and Yeka (z score > 1.0), while adjacent areas showed moderate level of clustering (z score 0.80–1.0; Fig. 5D). This high-moderate clustering persisted in 2016 across woredas in Nifas Silk Lafto, Kolfe, Gulele, Yeka, and Bole (Fig. 5E).

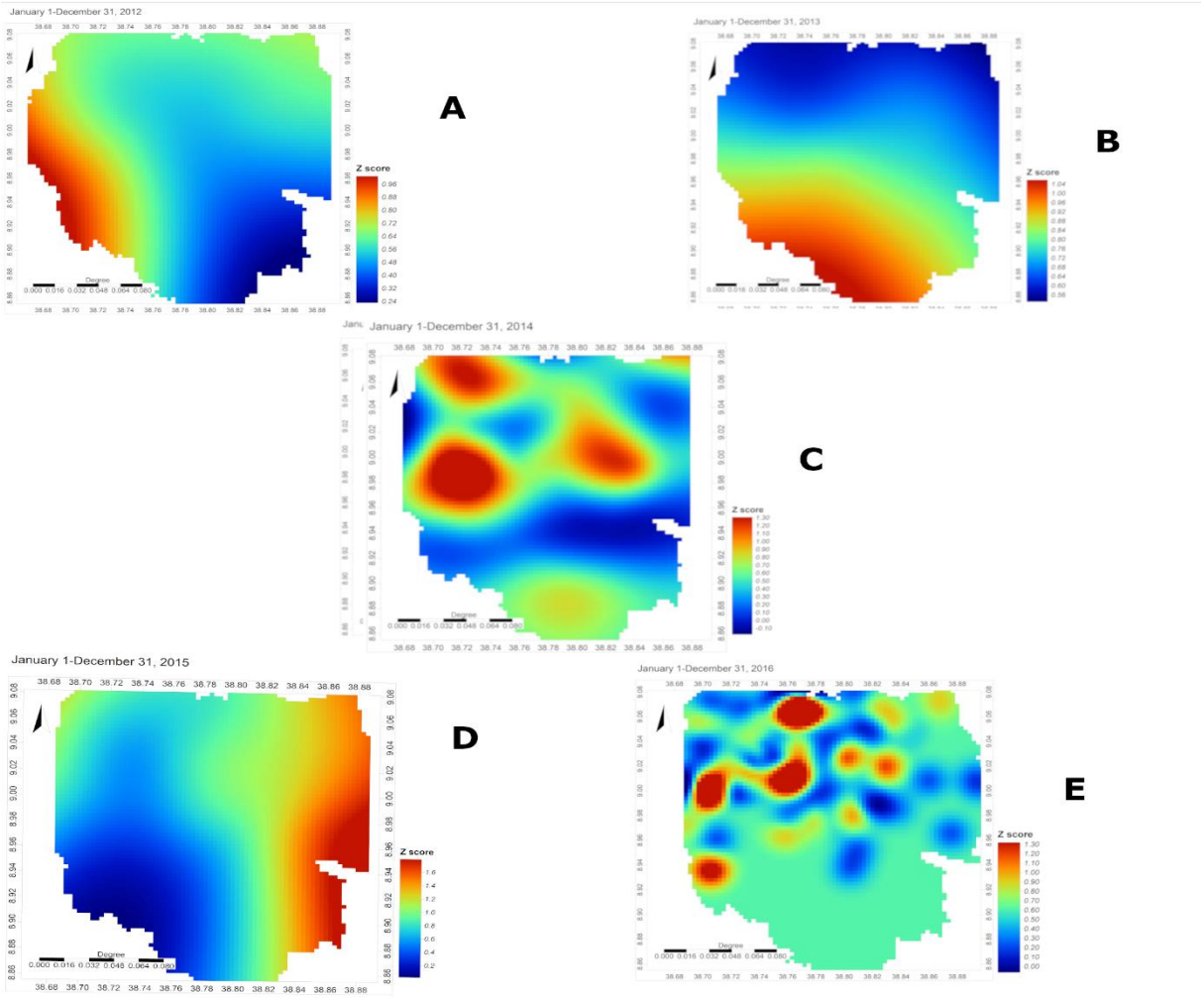


Figure 5: Global clustering of cervical incident cases in Addis Ababa from 2012 to 2016

From 2017 to 2018, clustering intensified, with Bole, Nifas Silk Lafto, and Kolfe showing z scores above 1.0 (Figs. 6A and B). Particularly, a statistically significant autocorrelation (z score>1.96) was recorded in 2018 in the sub cities, Nifas Silk Lafto, Bole, Kirkos and parts of Gulele and Yeka (Figure 6B). In 2019 and 2020, high clusters remained consistent across several sub-cities (z score > 1.0; Figs. 6 C and D), with similar patterns in 2021, underscoring ongoing hotspots in these areas (Fig. 6E).

In summary, although many woredas exhibited strong case clustering from 2012 to 2021, as indicated by high and positive Global Moran's I values, statistically significant spatial autocorrelation at $p<0.05$, was observed only in 2018.

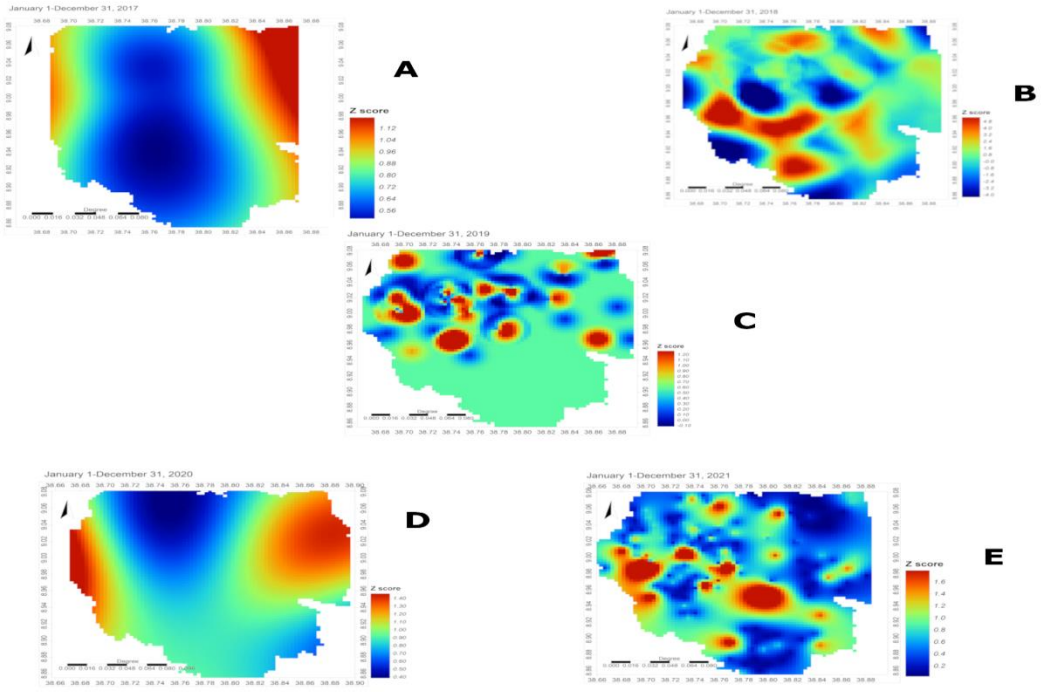


Figure 6: Global clustering of cervical incident cases in Addis Ababa from 2017 to 2021

5.2.3 Incidence rate of cervical cancer in the city

From 2012 to 2021, the age-standardized incidence rate (ASIR) of cervical cancer in Addis Ababa remained stable, ranging from 19 per 100,000 women-years in 2013 to 26 in 2016. Sub-city analysis showed that Kirkos had an ASIR of 33 in 2012. In 2013, Gulele, Nifas Silk Lafto, and Bole each reported an I.R. of 23. Arada recorded an ASIR of 26 in 2014, while Yeka's ASIR rose to 32 in 2015 and remained steady through 2016. Gulele's ASIR increased to 32 in 2017, Bole's to 24 in 2018, and Kolfe Keraniyo reached 30 in 2019. In 2020, Bole saw an ASIR of 33; Akaki Kality recorded the highest rate at 39 in 2021 (Table 4).

Table 4: Incidence rate of cervical cancer per100000 women-years by year and sub-city in Addis Ababa, Ethiopia, 2012 to 2021

Year	Akaki Kality	Nifas Silk Lafto	Kolfe Keraniyo	Gulele	Lideta	Kirkos	Arada	Addis Ketema	Yeka	Bole	Addis Ababa
2012	26	27	14	26	31	33	23	20	29	17	24
2013	14	23	14	23	15	22	17	18	19	23	19
2014	16	21	18	16	22	19	26	22	20	19	20
2015	21	20	11	25	18	30	20	22	32	30	23
2016	21	28	27	19	27	29	30	18	32	26	26
2017	23	25	21	32	28	26	13	17	22	20	22
2018	22	23	27	22	19	23	10	21	21	24	22
2019	28	29	30	21	17	15	27	19	23	27	24
2020	24	24	27	18	18	11	17	20	25	33	23
2021	39	29	18	21	21	27	13	18	29	25	24

5.2.4 Trend analysis of age-specific incidence rates and count of cases

Figure 7 illustrates the trends in age-specific counts (A) and incidence rates (B) of cervical cancer from 2012 to 2021. Consistent with data in Tables 1 and 2, new cases have notably increased among individuals aged 45 to 74, particularly from 2018 onward (Fig. 7A). However, the age-standardized incidence rate per 100,000 women-years has remained relatively stable since 2017, following a peak in 2016. The 45 to 74 age groups have consistently recorded the highest incidence rates per 100,000 women-years throughout the study period (Fig. 7B).

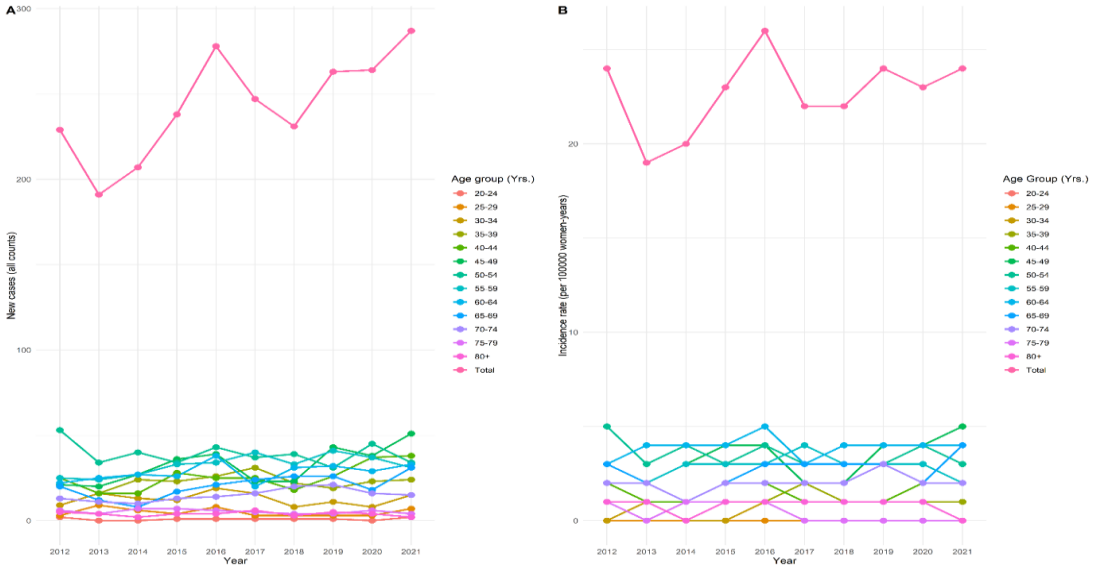


Figure 7: Trend line depicting age-specific count and IR of cervical cancer from 2012 to 2021

5.2.5 Time series analysis of incidence rates by sub-city and year

The joinpoint regression analysis revealed variable trends in cervical cancer incidence rates across sub-cities. Akaki Kality and Nifas Silk Lafto showed trend reversals in 2014, while Kolfe Keraniyo experienced a change in 2019. Akaki Kality saw a significant rate decrease (10.62% APC from 2012 to 2014), followed by nearly 10% increase until 2021. Kolfe Keraniyo had a notable rise (13.54% APC from 2012 to 2019), then a sharp decline (18.06% APC from 2019 to 2021). Other sub-cities displayed stable trends with no joinpoints. Bole sub-city consistently increased by 4.2% APC from 2012 to 2021 (Fig. 8).

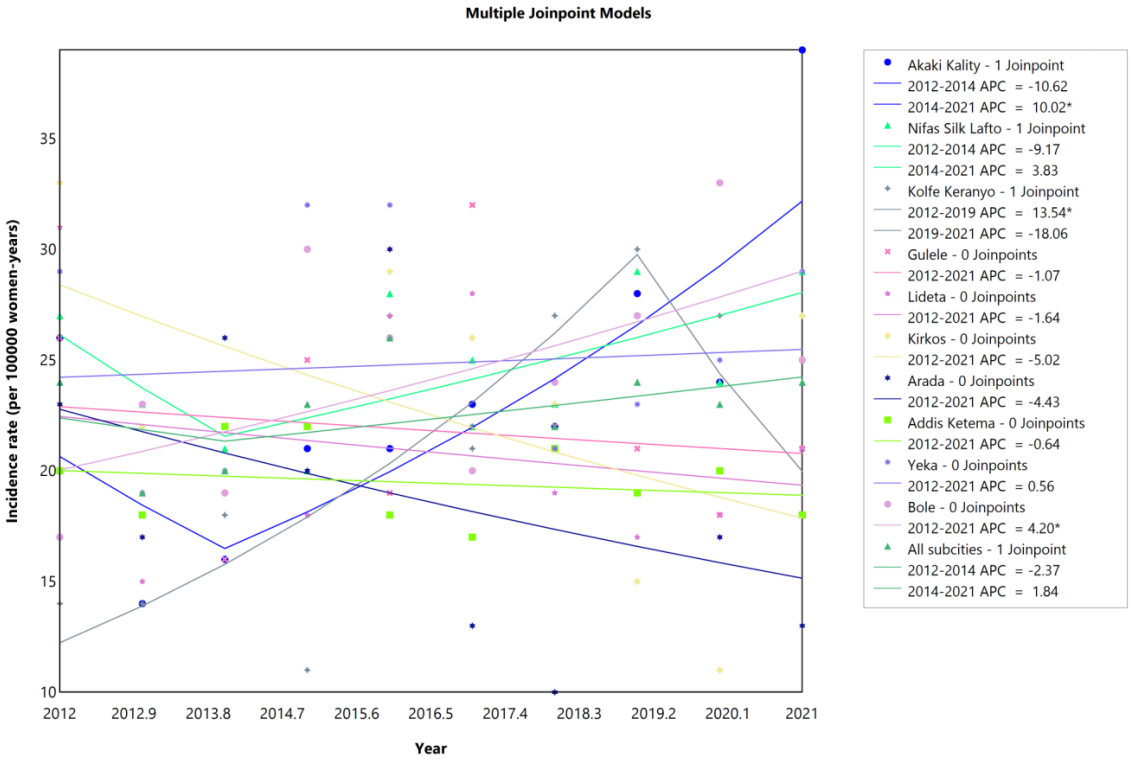


Figure 8: Joinpoint regression of cervical cancer incidence rates (per 100,000 women-years) across sub-cities in Addis Ababa, 2012-2021

5.3 Patients' access to healthcare services

5.3.1 The data collection instrument

Quantitative data were collected using a validated structured questionnaire developed through a comprehensive literature review. The questionnaire contained 68 items, with nine focused on objective measures of healthcare service access and 19 assessing patient perceptions. The remaining items gathered patients' socioeconomic, behavioral, and clinical characteristics. A five-point Likert scale was used (1 = strongly disagree to 5 = strongly agree). All questions were designed and uploaded to the KoboToolbox server. Data collection involved exit interviews using KoboCollect or ODK Collect tools. Detailed information on the instrument, including validation, model fitness indices, and a structural equation model (SEM), can be found in the published article listed at the end of this document (Paper III).

5.3.2 Realized access

The assessment of realized access to healthcare services focused on accessibility, availability, and affordability. Geographic access was measured by patients' travel time to reach the nearest health facilities. Results showed that general medical services were accessible to 221 patients (56.5%), medications to 224 patients (57.3%), laboratory diagnostics to 223 patients

(57.0%), imaging diagnostics to 222 patients (56.8%), and radiotherapy services to 218 patients (55.8%). Among patients without Community-Based Health Insurance (CBHI) (n=87), only 10 (11.5%) found the services affordable. Availability analysis of essential anticancer medicines indicated that 229 patients (58.6%) experienced unavailability at least once in the past three months. In contrast, basic diagnostic services were generally available (n=372, 95.1%), and surgical and palliative care services were consistently accessible at the facilities.

5.3.3 Perceived access and associated factors

Key findings from the assessment of perceived access to healthcare services revealed that two-thirds of patients rated their access as good. Inpatients were about 80% less likely than outpatients to perceive good access (AOR=0.2; 95%CI: 0.06-0.67)). Additionally, merchants, farmers, students, and housemaids reported lower perceptions of access than housewives, with adjusted odds ratios of 0.19 and 0.30, respectively. Patients with incomes below the extreme poverty line had an 81% lower likelihood of perceiving good access (AOR=0.19; 95%CI: 0.10-0.35). In contrast, those without Community-Based Health Insurance (CBHI) were 4.16 times more likely to perceive good access (AOR=4.16; 95%CI: 1.76-9.85), while patients with social support were 3.8 times more likely to perceive good access (AOR=3.81; 95%CI:1.96-7.41). Interestingly, patients with poor dietary practices were also more likely to perceive good access to healthcare services (AOR=2.36; 95%CI: 1.28-4.35) (Table 5).

Table 5: Factors associated with perceived good access to healthcare services among patients with cervical cancer in Addis Ababa, Ethiopia (n=391)

Variable	**Category**	**Perceived access to healthcare services**		**COR**	**95%CI for COR**		**AOR**	**95% CI for AOR**	
		Poor (n)	**Good (n)**		**Lower**	**Upper**		**Lower**	**Upper**
Service classification	Outpatient	103	264	Ref			Ref		
	Inpatient	19	5	0.10	0.04	0.28	0.20*	0.06	0.67
Marital status	Single	4	16	Ref			Ref		
	Married	64	161	0.63	0.20	1.95	1.35	0.28	6.58
	Widowed	24	52	0.54	0.16	1.79	3.40	0.60	19.25
	Separated or divorced	30	40	0.33	0.10	1.10	1.33	0.25	7.14
Able to read and write	Yes	56	187	Ref			Ref		
	No	66	82	0.37	0.24	0.58	0.93	0.46	1.86
Occupation	Housewife	29	99	Ref			Ref		
	Private employee	25	96	1.13	0.62	2.06	0.50	0.20	1.27
	Government	4	25	1.83	0.59	5.69	0.66	0.15	2.89

	employee								
	Jobless	46	28	0.18	0.10	0.33	0.19*	0.08	0.46
	Others**	18	21	0.34	0.16	0.73	0.30*	0.11	0.84
CBHI coverage***	Yes	111	193	Ref			Ref		
	No	11	76	3.97	2.03	7.80	4.16*	1.76	9.85
Household's average monthly income	≤3567 ETB	92	70	0.12	0.07	0.19	0.19*	0.10	0.35
	>3567 ETB	30	199	Ref			Ref		
Number of family members	Five or less	96	232	1.70	0.98	2.96	1.43	0.66	3.07
	>5	26	37	Ref			Ref		
Presence of social support	Yes	33	134	2.68	1.68	4.26	3.81*	1.96	7.41
	No	89	135	Ref			Ref		
Dietary habit	Poor	41	164	3.09	1.97	4.83	2.36*	1.28	4.35
	Good	81	105	Ref			Ref		
Age category (Yrs.)	50 or less	52	186	3.02	1.94	4.70	1.91	0.89	4.14
	>50	70	83	Ref			Ref		
Life style	Poor	76	197	1.66	1.05	2.61	1.01	0.52	1.94
	Good	46	72	Ref			Ref		

**Includes merchants, students, housemaids, and farmers; ***Community-based health insurance

5.4 Economic burden of cervical cancer

5.4.1 Distribution of all costs during the past 90 days

Table 6 presents cost differences between cases and controls over the past 90 days. Cases incurred higher direct medical expenses at hospitals, averaging 148.31 ± 240.24 INT$ for drugs, 71.23 ± 121.25 INT$ for imaging, and 44.47 ± 91.49 INT$ for hospital stays. Controls primarily spent 41.66 ± 60.20 INT$ on drugs and 29.15 ± 27.12 INT$ on laboratory diagnoses. Outside hospitals, cases spent 114.07 ± 274.62 INT$ on diagnostic services, while controls focused on consultations (33.66 ± 102.36 INT$). Travel costs averaged 28.38 ± 47.38 INT$ for cases and 14.19 ± 17.22 INT$ for controls, and productivity loss due to absenteeism was 36.69 ± 120.31 INT$ for cases and 14.05 ± 99.83 INT$ for controls.

Table 6: Description of all costs in INT$ incurred by the study participants during the previous three months, Addis Ababa, Ethiopia (N=932)

	Cases		Controls	
Direct medical costs incurred at the current hospitals				
Cost object	**Mean**	**SD**	**Mean**	**SD**
Hospital visits	6.46	11.91	5.53	4.37
Laboratory diagnosis	38.36	63.88	29.15	27.12
Imaging services	71.23	121.25	14.41	34.95
Drugs	148.31	240.24	41.66	60.20
Hospital stay	44.47	91.49	1.95	11.69
Intensive care unit or emergency stays	1.54	23.43	0.41	7.18
Surgery	10.26	31.74	0.00	0.00
Nursing or palliative care services	10.78	46.83	8.17	44.19
Total	331.40		101.28	
Direct medical costs incurred outside the current hospitals				
Services related to any or a combination of consultation, follow-up, or admission	95.29	431.37	33.66	102.36
Services received related to any diagnosis (laboratory, C.T. scan, MRI, x-ray, ultrasound)	114.07	274.62	23.54	72.90
Traditional practitioner	14.36	57.06	9.52	51.04
Spiritual leader or care provider	7.84	57.78	1.51	12.24
Total	231.55		68.23	
Direct non-medical costs				
Travel	28.38	47.38	14.19	17.22
Food or supplementation	10.92	22.36	5.12	13.31
	4.29	44.11	1.62	12.16
Total	43.59		20.93	
Indirect costs				
Productivity loss/absenteeism	36.69	120.31	14.05	99.83
Productivity loss caregiver	32.78	94.44	11.58	107.91
Total	69.47		25.63	

5.4.2 Incremental costs during the past 90 days

In the first year after treatment initiation, cases incurred significantly higher mean direct medical costs, averaging 659.51 INT$ (±635.91) compared to 169.18 INT$ (±249.15) for

controls, resulting in a mean difference of 490.33 INT$ (95% C.I.: 404.99-575.63). Overall annual costs for cases were also higher, with a mean total of 799.09 INT$ (±815.90) versus 206.26 INT$ (±276.43) for controls, leading to an incremental cost difference of 592.83 INT$ (95% C.I.: 485.21-700.51), significant at p<0.001. In the subsequent period, cases continued to show higher expenditures, with direct medical costs of 474.51 INT$ (±704.19) versus 176.41 INT$ (±187.58) for controls and a total average cost of 558.99 INT$ (±747.09) compared to 234.60 INT$ (±363.39) for controls, resulting in an incremental total cost of 324.39 INT$ (95% C.I.: 213.65-435.05), also significant (p<0.001) (see Table 7).

Table 7: Incremental costs in INT$ incurred by the study participants during the previous 90 days, Addis Ababa, Ethiopia (N=932)

Time frame	Cost category	Cases	Controls	Mean Difference (95% C.I.)	p-value
		Mean (S.D.)	Mean(SD)		
First-year	Direct medical costs	659.51(635.91)	169.18(249.15)	490.33 (404.99-575.63)	p<0.001
	Direct non-medical costs	49.75(121.69)	19.53(33.36)	30.22(14.52-46.06)	p<0.001
	Indirect costs	89.83(225.17)	17.55(27.39)	72.28(43.89-100.65)	p<0.001
	Total costs	799.09(815.90)	206.26(276.43)	592.83(485.21-700.51)	p<0.001
Post first year	Direct medical costs	474.51(704.19)	176.41(187.58)	298.10(200.86-395.29)	p<0.001
	Direct non-medical costs	38.14(34.82)	23.35(24.67)	14.79(9.08-20.43)	p<0.001
	Indirect costs	46.34(124.30)	34.84(298.21)	11.50(-31.52-54.51)	p<0.001
	Total costs	558.99(747.09)	234.60(363.39)	324.39(213.65-435.05)	p<0.001

5.4.3 Drivers of total annual cost in cancer care

The main cost drivers in cancer care are diagnosis and treatment, which account for the largest expenses across both the first year and post-first year phases. In the first year, diagnosis costs are the highest, averaging INT$1548.16 (±SD INT$1946.87), followed by treatment costs at INT$1004.18 (±SD INT$1403.45). Post-first year, diagnosis costs remain significant at INT$1020.91 (±SD INT$2344.55), with treatment costs averaging INT$796.26 (±SD INT$1001.36). Indirect costs such as lost productivity also contribute notably, especially in the first year (INT$359.23, ±SD INT$900.72), although they decreased in the post-first year. Direct non-medical costs, such as transportation, are relatively smaller but still

impactful, averaging INT$199.00 (±SD INT$486.77) in the first year and reducing to INT$152.52 (±SD INT$139.27) afterward (Table 8).

Table 8: Major cost drivers in INT$ of cancer care by phase and time frame in Addis Ababa, Ethiopia

Time frame	Care phase and associated costs	Base case mean(±SD)	Sensitivity analysis range	
			Lower (-20%)	Upper (+20%)
First year	Diagnosis costs	1548.16 (1946.87)	1238.53	1857.79
	Treatment costs	1004.18(1403.45)	803.34	1205.02
	Nursing and palliative care	39.30(215.04)	31.44	47.16
	Direct non-medical costs	199.00(486.77)	159.20	238.80
	Indirect costs	359.23(900.72)	287.38	431.08
Post-first year	Diagnosis costs	1020.91(2344.55)	816.73	1225.09
	Treatment costs	796.26(1001.36)	637.01	955.51
	Nursing and palliative care	47.38(150.04)	37.90	56.86
	Direct non-medical costs	152.52(139.27)	122.02	183.02
	Indirect costs	185.33(497.17)	148.26	222.40

5.4.4 Annual incremental costs

Outpatient cases had mean annual total costs of 2597.37 (±2940.43) INT$, while inpatient cases incurred significantly higher costs of 5766.57 (±5498.89) INT$, resulting in a non-significant mean difference of -3169.20 INT$ ($p < 0.060$). Among controls, outpatient costs averaged 856.11 (±1247.24) INT$, compared to 1319.56 (±1803.56) for inpatients, with a non-significant difference of -463.46 INT$ ($p= 0.270$). Outpatient cases had significantly higher costs than outpatient controls (MD = 1741.27 INT$, $p = 0.001$), and inpatient cases exceeded inpatient controls (MD = 4447.01 INT$, $p= 0.023$). In the first treatment year, direct medical costs for cases averaged 2638.05 (±2543.64) INT$ versus 676.78 (±996.71) for controls, with a significant incremental cost of 1961.27 INT$ ($p<0.001$). In subsequent years, cases continued to report higher direct medical costs, averaging 1898.02 (±2816.72) INT$, leading to an incremental total cost of 1297.39 INT$ ($p<0.001$) (Table 9).

Table 9: Annual incremental costs in INT$ incurred by the study participants, Addis Ababa, Ethiopia (N=932)

Time frame	Cost category	Cases	Controls	Mean Difference (95% C.I.)	p-value
		Mean (S.D.)	Mean(SD)		
First-year	Direct medical costs	2638.05(2543.64)	676.78(996.71)	1961.27(1619.97-2302.58)	p<0.001
	Direct non-medical costs	198.99(486.78)	77.83(133.38)	121.16(58.08-184.25)	p<0.001

	Indirect costs	359.23(900.74)	70.24(109.51)	288.99(175.53-402.46)	p<0.001
	Total costs	3196.27(3263.62)	824.85(1105.69)	2371.42(1940.87-2802.03)	p<0.001
Post first year	Direct medical costs	1898.02(2816.72)	705.68(750.26)	1192.34(803.50-1581.20)	p<0.001
	Direct non-medical costs	152.52(139.26)	93.45(98.70)	59.07(36.36-81.81)	p<0.001
	Indirect costs	185.32(497.17)	139.34(1192.87)	45.98(-126.28-218.02)	p<0.001
	Total costs	2235.86(2988.37)	938.47(1453.54)	1297.39(854.59-1740.26)	p<0.001

5.4.5 Predictors of annual total cost

A Tukey's biweight regression analysis identified key predictors of higher annual total costs. The refined model excluded less impactful variables and removed nine outliers, achieving a residual standard error (RSE) of 1,332.04, improved from 1,881.64 in the ordinary least squares (OLS) model. Significant predictors included an increase of 492.82 INT$ for households with more than five members ($p = 0.016$), an additional 834.96 INT$ for patients with comorbid conditions ($p < 0.001$), and a rise of 627.48 INT$ without social support ($p = 0.001$). Poor dietary habits added 740.27 INT$ ($p < 0.001$), while the first year of treatment increased costs by 967.72 INT$ ($p < 0.001$). Patients diagnosed at an advanced cancer stage incurred an extra 1,324.12 INT$ annually compared to those diagnosed early ($p < 0.001$) (Table 10).

Table 10: Predictors of annual total cost in INT$ among patients with cervical cancer in Addis Ababa, Ethiopia (n=457)

Variables	Estimate	Std. Error	t value	Pr(>|t|)
(Intercept)	-7.0739	222.0823	-0.032	0.974604
Age >52 years	210.0943	173.9764	1.208	0.227847
Not able to read and write	-222.0755	200.9696	-1.105	0.269753
Employed to any organization	33.6234	218.5482	0.154	0.877799
Merchant	453.9785	354.6270	1.280	0.201163
More than five members in the household	492.8157	204.1674	2.414	0.016194*
Concomitant chronic comorbidity	834.9642	167.9186	4.972	9.49e-07*
Absence of social support	627.4826	184.6109	3.399	0.000738*
Poor physical activity	224.2978	177.8559	1.261	0.207932
Poor dietary habit	740.2696	185.9441	3.981	8.02e-05*
In the first year of starting treatment	967.7256	184.4599	5.246	2.42e-07*
Advanced-stage of cancer	1324.1189	246.4117	5.374	1.25e-07*
Symptomatic per MDASI rating	39.7220	205.9067	0.193	0.847116
Admission to the inpatient	860.8666	590.0070	1.459	0.145255
Days of hospitalization in the past 90 days	92.0729	55.3280	1.664	0.096797
Days from diagnosis to treatment initiation	0.6230	0.9276	0.672	0.502154

*statistically significant

CHAPTER SIX: DISCUSSION, STRENGTHS AND LIMITATIONS

6.1 Discussion

This study adopts an integrated approach to understanding cervical cancer dynamics by examining spatiotemporal patterns, healthcare access barriers, and economic burden. The three sub-studies are inherently linked, providing a comprehensive and cumulative understanding of the disease. The spatiotemporal analysis identified geographic clusters and temporal trends of cervical cancer incidence over the decade 2012 to 2021, highlighting potentially high-cluster areas and vulnerable populations. Building on this, the healthcare access study explored actual and perceived level of access to healthcare services and associated factors revealing disparities in availability, affordability, and acceptability of services. These access challenges were further linked to the economic burden study, which quantified the financial impact on patients, demonstrating how inadequate access contributes to high out-of-pocket expenses and indirect costs. Collectively, these interconnected studies reveal a cyclical relationship where spatial disparities and access barriers exacerbate the economic burden, leading to delayed diagnosis and poorer outcomes.

As per the spatiotemporal analysis results, the number of newly diagnosed cases in Addis Ababa was high, with 229 cases reported in 2012 compared to 131 in Shijiazhuang, China (Wen et al., 2019). The analysis of spatial autocorrelation within sub-cities revealed significant clustering of cases, indicating that geographic factors influence cervical cancer distribution, consistent with findings from Saudi Arabia and Thailand (Al-Ahmadi and Al-Zahrani, 2013; Thongsak et al., 2016). Additionally, research in South Africa showed higher cervical cancer incidences among HIV-positive individuals in areas with better healthcare access (Tafadzwa et al., 2021). We noted that the findings from the spatiotemporal analysis identified high-cluster sub-cities with elevated cervical cancer incidence rates. However, it is important to interpret these clusters with caution, as residing in these areas does not necessarily imply an increased individual risk of developing cervical cancer. Addis Ababa is characterized by interconnected socio-economic and demographic similarities across sub-cities, including shared healthcare infrastructure, cultural practices, and mobility patterns. These factors contribute to the diffusion of risk and access to resources across geographic boundaries. Therefore, the observed clusters may reflect differences in screening uptake, healthcare access, or reporting practices rather than a direct risk associated with residence. Additionally, high-incidence clusters could be influenced by population density, healthcare-seeking behavior, or historical differences in public health interventions. These contextual factors highlight the need for targeted public health strategies that address systemic access

barriers rather than solely focusing on geographic residence. From the interpolated results, we also noted that there was no statistically significant spatial autocorrelation except in 2018.

It was found in the current study that age-standardized incidence rates (ASIR) of cervical cancer in Addis Ababa remained slightly stable throughout the review period. As yet, the figures were substantially higher as compared with those from Shijiazhuang, China, and Shexian County in rural China which could be linked with regional disparities that, in turn, could be associated with differences in healthcare infrastructure, HPV prevalence, and socioeconomic factors (Wen et al., 2019). Given that Ethiopia's is in its lower income status potentially hindering effective prevention and treatment, the steady increase in IR indicates the ongoing impact of the disease on women's health in the country.

Sub city-level disparities were notable, with Akaki, Bole, and Kolfe Keraniyo showing a varying trend in cancer incidence estimates. This could be attributed to factors, such as demographic changes, healthcare access, and HIV prevalence, particularly in Bole sub city, which has the highest HIV rates (EPHI, 2023). Equally important is the socioeconomic status of populations across sub-cities which can play a marked role in affecting healthcare access and lifestyle behaviors that, in turn, contribute to cancer risk. In addition, it was noted that rise in cervical cancer risk among individuals aged 45 to 74 years was apparent, which might be correlated with prolonged HPV infections that can lead to cancer. This trend suggests the need for continued monitoring and intervention strategies to address HPV-related risk factors (Ersado, 2021).

The study evaluated perceived and realized access to healthcare services for cancer patients, guided by frameworks focused on interim cancer care. Findings indicated that fewer than half of the patients (55% to 57%) had access to essential healthcare services, such as medical consultations, medications, laboratory diagnostics, imaging, and radiotherapy, highlighting a significant access gap. There was a concordance between patients reporting higher access levels and those perceiving good access to healthcare. However, challenges like a shortage of oncologists, oncology nurses, and radiotherapy technologists were noted as growing concerns (Haileselassie et al., 2019), contrasting with a U.S. report where only 6% of cancer survivors reported access issues (de Moor et al., 2016).

Cost evaluations revealed that only 11.5% of patients could afford healthcare services, lower than Rwanda's 20% affordability for anticancer medications (Rurangwa et al., 2023). While essential diagnostic services were consistently available (95% of the time), essential anticancer medications were out of stock for 41% of patients, aligning with Rwandan public

hospitals but falling short of the WHO's 80% availability target (Nanthamongkolkul and Hanprasertpong, 2015).

Our study also showed that nearly two-thirds of cervical cancer patients in Addis Ababa perceived their access to healthcare services at good level despite facing significant barriers. As documented elsewhere, such perceptions could be shaped by personal experiences and external factors like the availability and professionalism of healthcare providers (Bourque and Loiselle, 2022). In this context, inpatients, individuals with incomes below the extreme poverty line, and various occupational groups (e.g., unemployed, merchants, students) were less likely to perceive good access, probably attributed to the high treatment costs and inadequate infrastructure. In the contrary, women outside the scheme of a community-based health insurance, those with poor dietary adherence or habits, and those receiving social support reported to better perceived access. This paradox regarding insurance may emanate from unmet expectations among insured patients. Social support enhances communication with healthcare providers and positively affects perceptions of access (Guan et al., 2021).

The aim in the last paper of our project was to understand the costs of cervical cancer in Addis Ababa, comparing these costs to matched hypertensive controls. Accordingly, direct medical costs for cervical cancer patients mainly included medications, imaging diagnostics, and hospital stays, highlighting the high expenses of oncology care. The results also revealed that there was no notable differences between outpatient and inpatient expenses ($p=0.060$) despite high cost burden among inpatients. This could likely be due to a smaller inpatient sample size considered in the study. However, hospitalization costs were significantly higher for cervical cancer cases compared to controls, likely due to more frequent emergency admissions and visits (Peerenboom et al., 2024).

The analysis highlighted significant challenges related to the availability and high costs of medications, which create barriers to effective cancer management and increase financial strain on patients. Nearly three-fourths of cancer patients in Addis Ababa experience catastrophic health expenditures (Kasahun et al., 2020). Outpatient expenses were largely driven by imaging services, emphasizing the importance of diagnostic imaging in ongoing cancer management (Paudyal et al., 2023).

The estimated average annual total expenses for cervical cancer patients were nearly four times higher than those for controls, with a slight decrease after the first year of treatment. This pattern reflects the typical intensive resource use during initial treatment, including comprehensive diagnostics and aggressive therapies. Implementing subsidized treatment

programs, such as voucher systems or sliding fee scales, will reduce out-of-pocket expenses for patients, especially in high-incidence areas. Public-private partnerships (PPPs) can expand diagnostic and treatment capacities by collaborating with private healthcare providers, enhancing access to advanced technologies and specialized oncology care. Community-based health education programs tailored to local cultural beliefs and practices will help address stigma and encourage early detection and prevention.

Key factors influencing these costs included household size, comorbid conditions, and the cancer stage at diagnosis. Larger households and comorbidities were linked to higher costs, likely due to more complex care needs (Ma et al., 2023; Ding et al., 2020). Advanced-stage diagnoses led to more intensive treatments, often requiring frequent hospitalizations. Additionally, patients lacking social support and those with poor dietary habits incurred higher healthcare costs, highlighting the impact of social and lifestyle factors on cancer management. Poor diet may worsen conditions, resulting in more intensive interventions and elevated costs (McCullough and Islami, 2021).

6.2 Strengths of the study

The strengths of this study on the spatiotemporal dynamics of cervical cancer, access to healthcare, and economic burden in Addis Ababa, are substantial and far-reaching. By examining not only the incidence and spatial distribution of cervical cancer but also the access to healthcare and economic impacts, the study offers a holistic view that is essential for effective public health planning and intervention. This broad scope allows for a multifaceted analysis of the disease's impact on the community and health systems, highlighting areas for targeted health policy improvements.

The methodology employed in this study further strengthens its findings. Utilizing a decade-long dataset improves the reliability of trend analysis, supporting the observation of long-term patterns crucial for strategic resource allocation. Advanced spatial analysis techniques identify critical hotspots and cold spots, providing valuable insights that inform targeted interventions and efficient resource deployment. Moreover, the study's examination of perceived and realized healthcare access deepens the understanding of the complex barriers patients face. At the same time, the inclusion of economic analyses underscores the financial challenges associated with managing cervical cancer. Together, these elements offer critical data that can aid in designing health insurance schemes and financial support programs.

Applying robust statistical methods, including multivariable logistic regression and factor analysis, allows for a nuanced understanding of the relationships between various factors and

cervical cancer outcomes. Integrating established theoretical frameworks adds depth to the analysis, facilitating a structured examination of factors influencing health service utilization and patient outcomes. The generalizability of findings is enhanced by the broad range of participants, covering different socioeconomic backgrounds and healthcare settings. This comprehensive approach not only informs effective public health strategies and interventions aimed at reducing the burden of cervical cancer in urban settings like Addis Ababa but also serves as a model for similar studies in other regions.

6.3 Limitations of the study

The study on spatiotemporal dynamics, access to healthcare, and economic impacts of cervical cancer in Addis Ababa has several limitations.

Data reliability and availability: The decade-long dataset relies on the accuracy of record-keeping and data collection from various healthcare facilities and cancer registries. Inconsistencies, missing data, and reporting biases may influence the analysis and conclusions regarding cervical cancer incidence trends.

Generalizability and methodological constraints: Findings are specific to Addis Ababa's urban environment and may not apply to other regions with different healthcare systems or cultural contexts. The cross-sectional nature of the analyses captures correlations at a single point in time without establishing causation, limiting the ability to determine relationships or observe changes over time.

Data collection and spatial analysis challenges: Much of the data, particularly regarding healthcare access and economic impacts, relies on self-reports, which can introduce biases like recall or social desirability bias, potentially skewing reported access or economic burdens. Additionally, spatial analysis techniques depend on the quality of geographical data, which might obscure variations within small areas or lead to overgeneralized findings. The absence of individual-level data on patients' socioeconomic status further complicates identifying direct associations with disparities.

CHAPTER SEVEN: CONCLUSION AND RECOMMENDATIONS

7.1 Conclusions

The thorough investigation into the spatiotemporal dynamics of cervical cancer, healthcare accessibility, and economic ramifications in Addis Ababa, Ethiopia, yielded numerous significant findings. The resulting conclusions corresponded directly with the primary objectives of the study.

Spatiotemporal dynamics: The study revealed significant spatial and temporal disparities in cervical cancer incidence across various Addis Ababa sub-cities. Clustering cases in specific areas highlights regions with elevated risks, suggesting the need for targeted public health interventions and resource allocation to these hotspots. Over the decade, certain sub-cities exhibited consistently higher rates of cervical cancer, influenced by socioeconomic, demographic, and possibly genetic factors.

Access to healthcare services: Both perceived and realized access were assessed, uncovering a complex landscape where many patients still face substantial barriers to accessing essential healthcare services. Despite some improvements, the findings indicate that significant portions of the population have limited access to critical services such as medical consultations, drug availability, and advanced diagnostic tools. Economic barriers, lack of adequate healthcare infrastructure, and uneven distribution of healthcare providers exacerbate these challenges.

Economic burden: The economic analysis highlighted the substantial costs associated with managing cervical cancer, which are often catastrophic for many families. The high treatment costs, including medication, hospital stays, and diagnostic services, exacerbate the financial burden. The study also pointed out the economic disparities between patients with different socioeconomic backgrounds, where those from lower socioeconomic statuses suffer a more pronounced financial strain.

Theoretical implications: This study confirmed one indirect observation: Applying established theoretical frameworks provided a structured approach to analyzing factors influencing health service utilization and patient outcomes. This integration helped us understand the broader context of healthcare access and the socioeconomic dynamics, offering a nuanced perspective on the systemic issues that need addressing to improve health outcomes.

7.2 Recommendations

Based on the outcomes and insights from the study on the spatiotemporal dynamics of cervical cancer, healthcare access, and economic impacts in Addis Ababa, Ethiopia, recommendations can be organized into the following main categories:

7.2.1 Healthcare strategies and disease prevention

A coordinated effort by the government, the Federal Ministry of Health, the Addis Ababa Health Bureau, healthcare providers, and other partners is vital for advancing several key initiatives:

Targeted public health interventions

Develop and implement public health campaigns that focus on areas identified as hotspots to heighten awareness and encourage early screening for cervical cancer.

Enhanced healthcare accessibility

Expand access to medical services by increasing the availability of healthcare facilities equipped with adequate infrastructure to manage cervical cancer.

Affordability programs

Create financial support mechanisms or subsidize care to make treatment more affordable for low-income patients, thereby reducing the economic burden of cervical cancer treatment and improving adherence to treatment protocols.

Education and training

Intensify educational efforts about human papillomavirus (HPV) and cervical cancer prevention, emphasizing the benefits of early vaccination and regular screenings.

7.2.2 Healthcare infrastructure and partnership development

A unified effort by the government, the Ministry of Health, educational institutions, and collaborative organizations is crucial in tackling cervical cancer through the following strategic actions:

Strengthening healthcare infrastructure

Investments should be channeled towards enhancing the infrastructure of existing healthcare facilities, particularly in sub cities identified as hotspots for cervical cancer. This will ensure they are well-equipped to manage screenings, diagnostics, and treatments efficiently.

Partnerships and collaboration

Foster partnerships between government health agencies, non-governmental organizations, and international health bodies to combine resources, share knowledge, and standardize care protocols for cervical cancer treatment across the city. This collaborative approach will help leverage global expertise and resources for local benefit.

7.2.3 Implementation of policy and practice

Practice implications

The study on cervical cancer in Addis Ababa suggests that healthcare providers should expand outreach efforts, especially in underserved areas, to enhance early screenings and education. The economic burden findings highlight the need for medical and financial assistance programs to improve access to treatment. Additionally, the spatiotemporal trends indicate that resources should be strategically allocated in high-incidence areas to increase diagnostic support and service availability.

Policy Implications

To improve cervical cancer treatment access, subsidized programs like voucher systems and sliding fee scales should be implemented to reduce costs, especially in high-incidence areas. Public-private partnerships can expand diagnostic and treatment capacities by bringing in advanced technologies and specialized care. Community-based health education tailored to local cultures can reduce stigma and promote early detection. Additionally, integrating cervical cancer prevention into broader health policies and establishing a national cancer registry will ensure a coordinated, sustainable response.

7.2.4 Strengthen community engagement and education

Leveraging the existing health extension program in primary healthcare, efforts to bolster support should engage community-based initiatives that include local leaders and health workers to enhance awareness of cervical cancer, emphasizing prevention and the crucial role of regular screening.

7.2.5 Technological and data-driven solutions

An effective strategy would be to establish a centralized authority sanctioned by the Ministry of Health and connected with eligible health facilities. This center would focus on enhancing and strengthening data collection systems, enabling the registration of new cases, monitoring the effectiveness of interventions, and tracking progress in the fight against cervical cancer.

Such a centralized approach would facilitate timely adjustments to strategies, ensuring that responses are adaptive and adequately address the evolving landscape of healthcare needs related to cervical cancer prevention and treatment.

7.2.6 Future research directions

The recommendations outlined below can be directed toward educational and research institutions and the Federal Ministry of Health (FMOH), primarily involved in applied research and implementation efforts.

Longitudinal studies

Conduct longitudinal studies to investigate further the long-term trends and outcomes of cervical cancer treatments, focusing on survivorship and quality of life. In addition, such studies should consider individual-level risk factors and longitudinal analyses to better understand the complex interactions between place of residence and cervical cancer risk in urban settings like Addis Ababa.

Healthcare utilization research

Explore the factors affecting healthcare utilization and access among different socioeconomic groups within the city to tailor more effective intervention strategies.

Comparative effectiveness research

These may include cost-effectiveness and other analytical studies that examine the effectiveness of different cervical cancer screening methods and treatment modalities within the Ethiopian healthcare context to optimize resource allocation.

Impact of socioeconomic factors

It would be essential to explore the role of varying socioeconomic factors, including beliefs, culture, religion, and individual characteristics, that influence the incidence and outcomes of cervical cancer, particularly in the current study setting. Qualitative designs would help better understand the disparities observed in different sub-cities.

Integration of Geographic Information Systems (GIS) in health planning

Health authorities, including ministries and universities, could also leverage GIS tools in future studies to enhance the precision of public health interventions and resource distribution

based on spatial analysis findings. This approach would be particularly effective in improving the care continuum for cervical cancer.

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PAPER I

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SYSTEMATIC REVIEW

European Journal of Gynaecological Oncology

Association between delayed initiation of treatment indications and survival in patients with cervical cancer: a systematic review and meta-analysis

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Abstract

This review evaluated the association between delayed time to initiate any treatment with survival in patients with cervical cancer. An internet-based literature search was performed in PubMed/Medline, Cochrane CENTRAL, EMBASE, Web of Science and Scopus databases. All articles published until December 2021 were included. Studies were pooled for meta-analysis in a random-effects model. Microsoft-Excel and the R programing software were employed in the analysis. Between-study heterogeneity was assessed using Q^2, I^2 and tau^2. Results were reported as a function of 4-week delay in treatment initiation and hazard ratio using forest plots at 95% confidence interval. A $p < 0.05$ was considered statistically significant. Eleven studies were included in this review, comprising 50,590 patients. Overall survival was evaluated based on the pooled effect of 11 comparison groups. The subgroup on five-years follow-up following radiotherapy revealed that a 4-week delay in treatment was associated with a 1.27 times higher rate of mortality (Hazard Ratio: 1.27; 95% Confidence Interval: 1.12–1.45). However, a 4-week delay in initiation of combined chemoradiotherapy (HR: 1.31; 95% CI: 0.76–2.23) or surgery (HR: 0.96: 95% CI: 0.60–1.54) did not predict a statistically significant rate of mortality. The same length of waiting time did not predict the rate of mortality in a 3-years follow-up period (HR: 0.76; 95% CI: 0.44–1.32). A 4-week delay in radiotherapy showed a 1.72 times higher rate of disease relapse in the delayed group (HR: 1.72; 95% CI: 1.25–2.35) but not in patients for whom surgery was performed (HR: 0.89; 95% CI: 0.75–1.04). A four-week delay in initiating radiotherapy was associated with a higher rate of mortality. On the other hand, a 4-week delay in initiation of either surgery (hysterectomy) or chemoradiotherapy does not appear to be associated with overall survival, probably accounted, partially, for the waiting time paradox.

Keywords

Cervical cancer; Delayed time to treatment initiation; Survival; Systematic review and meta-analysis

1. Background

Carcinoma of the cervix, also known as cervical cancer, is one of the public health concerns affecting women globally. Depending on its histological characterization, there are two main types of this condition. These are squamous cell carcinoma (SCC) with sets of differentiation occurring in 70% to 80% of the diagnoses, and adenocarcinoma, is common in about 10% to 15% of the cases [1]. The human papillomavirus (HPV), notably its 16 and 18 genotypes, is the predominant cause in the majority of patients with cervical cancer [2]. Even though incidence cases in the age group below 50 had been on the rise until 2018 [3], HPV-based screening [4] and vaccination [3, 5] campaigns have shown greater improvement in prevention efforts.

Though the distribution of cervical cancer differs by geographic regions and the sociodemographic index of populations, there have been an estimated 604,127 cases and 341,831 deaths worldwide in the period 1988 through 2017, according to a report in 2020 [6]. With this, cervical cancer stands as the fourth most common type of cancer in women [7]. It was also the first cause of cancer-related deaths among women in the sub-Saharan African region [7].

Treatment modalities for patients with cervical cancer largely depend on the stage of diagnosis and include surgery, chemotherapy, radiotherapy, or combination therapy [5]. Detection at early FIGO (International Federation of Gynecology and Obstetrics) stages (IA, IB and IIA) of the disease has the advantages of several management options, generally offered with radical hysterectomy with lymphadenectomy, radiotherapy, or chemotherapy depending on age, size of the tumor, comorbid status, stage of the

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disease, or patient preference [8]. For patients with stages IIB to IVA, definitive chemoradiotherapy (CRT), involving weekly or triweekly cisplatin and external beam radiotherapy, is regarded as the standard of care [9]. According to a recent systematic review, immunologic agents, such as bevacizumab and pembrolizumab, administered with chemotherapy, showed acceptable safety and promise in treating patients with recurrent or metastatic cervical cancer [10].

Delay in treatment initiation has been described as a known contributor that determines the rate of remission or survival in cervical cancer [11, 12]. Yet, there is no clearly defined and agreed-upon evidence on the magnitude of the risk of experiencing mortality following a determined delay of treatment initiation, usually one month. Some studies also argued that the effect of shorter [13] or even longer [14] waiting times on survival might be minimal or not significant. A cautious understanding of delays, especially when the gap from diagnosis to treatment initiation becomes huge, is highly important. Given the existing challenges to carrying out high-quality studies and the fact that many national health programs are facing limitations in practicing strong empirical guidelines, evidence from systematically pooled primary studies might provide an up-to-date insight. And, despite the interplay of additional factors, there needs to be a concise understanding of the degree and direction of effect segmented by patient as well as treatment protocols.

This systematic review and meta-analysis is, therefore, aimed to producing evidence on the effect of delay from diagnosis to the initiation of appropriate treatments on overall survival or recurrence among patients with cervical cancer.

2. Methods

2.1 Search strategy

The search strategy employed the use of keywords, index/mesh terms, truncated words, and references from other studies (snowballing) to ensure a maximum possibility of including all eligible articles. Searching was facilitated using the Boolean operators (AND/OR) in the respective sources. Bibliographic searches in PubMed, EMBASE, Cochrane Central, Scopus, Web of science were performed. Similarly, gray literature sources, such as Google Scholar, Networked Digital Library of Theses and Dissertations (NDLTD), and Dissertations and Theses Global, including those unpublished, were searched. There was no limit on the start date, and both English and non-English articles published earlier until December 2021 were considered. Furthermore, both forward and backward reference searching methods were used to locate all potential references (see **Supplementary Table 1**).

2.2 Eligibility and exclusion criteria of included studies

All available observational studies and interventional designs (if the latter may be available in exceptional circumstances, such as planned delays during pregnancy), were considered. The eligibility of studies and populations in the review was based on a consideration of the following criteria: (1) All patients diagnosed and histologically confirmed with primary cervical cancer of any stage, and were treated with chemotherapy, surgery, radiotherapy and/or any combination of these, either as concurrent or sequential deliveries. (2) The time frame between diagnosis and treatment initiation was clearly known, and survival outcomes of any form (disease-specific or overall) were reported. (3) Studies rated as "good quality" based on the Newcastle-Ottawa Scale and those fulfilling all the following criteria were included; (a) studies analyzed with clear comparator groups, and (b) studies that reported the effect of delayed treatment initiation adjusted for other prognostic factors. (4) Studies published until December 2021 were included. To reduce publication bias, all observational studies, either in full-text, abstract, correspondence or letters to editors, dissertations, or meeting abstracts, were eligible. There was no language restriction, but studies other than English should have at least included abstracts published in English. When accessing full text was impossible, authors were requested *via* email. On the contrary, studies that assessed the effect of delay in other forms of treatments, such as immunotherapy, palliative care, and behavioral treatment (psychotherapy, cognitive behavioral therapy) options, hyperthermia (in patients receiving radiotherapy), or findings reported in other measures of effect size (relative risk or risk ratio, odds ratio or correlation), were excluded if sufficient data was not available to calculate hazard ratios or results ignored the importance of time in the outcome.

2.3 Quality assessment of the included studies

Commonly referred to as the risk of bias assessment [15], this approach was utilized to scrutinize and ensure the internal validity of the potential studies. Initially, essential procedures such as protocol registration [16], development, and publication [17] were carried out in accordance with a suitable guideline [18]. Subsequently, all studies meeting the initial inclusion criteria were systematically assessed for their methodological quality. The "Newcastle-Ottawa risk of bias assessment scale" [19] for nonrandomized studies was employed for this purpose. There are commonly recommended steps to be followed in reporting systematic review and meta-analysis results. The "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)" [20] checklist has well been known for reporting randomized controlled trials (RCT) and observational study-based reviews (see **Supplementary Table 2**). In addition, the steps stipulated in the "meta-analysis of observational studies in epidemiology (MOOSE)" [21] (see **Supplementary Table 3**) were followed for the reasons of suitability to assess publication bias, a characteristic common in observational studies [18]. It also allows for inclusive searching considerations, such as the inclusion of non-English-language articles.

2.4 Screening and data extraction procedures

Collated studies and abstracts were screened at a title, abstract and full text level using the Rayyan web-based application [22] before data extraction commences. Keywords of inclusion used in the package were: time to treatment, delayed treatment initiation, overall survival, diagnosis to treatment, survival in

cervical cancer, and cervical cancer. Three reviewers were involved to accomplish the screening, quality assessment, and data extraction processes. While two of the reviewers (TS and BG) were involved independently, the third reviewer (TG) was consulted at times when disputing results arose between the other reviewers. Data on study designs, treatment type, time delayed alternatively used as waiting time, summarized age of patients (as mean, median or/and range), stage of cancer, quality assessment, authors and year of publication, follow-up period, outcome either as HRs or percentage and their 95% confidence interval, and number of patients per waiting time group were extracted.

2.5 Exposure and outcome measures

Exposure was the delayed time to initiate any recommended treatment (chemotherapy, radiotherapy, surgery or any combination of these, such as chemo-radiotherapy). It is counted as any unit of time from a histologically (biopsy) confirmed diagnosis. In cases where waiting time was reported at different patient contacts, such as biopsy confirmation and physician consultation, only the biopsy confirmed dates were considered. The delayed time of interest considered as "exposure" in this review was a 4-week delay computed from diagnosis to receiving treatment. The reference was a less than 4-week timeline from diagnosis to receiving treatment. In addition, more weeks of delay (8-week and 12-week) were also considered for comparison purposes. Evaluating the effect of a 4-week waiting time on survival has become increasingly common in systematic reviews of cancer research [23, 24] considering it the minimum appropriate time to detect clinically significant changes. This time frame also helps to scale the reported waiting times as an array of continuous measures that do not throw away information. The treatment effect of a 4-week or greater delay on overall survival (OS), is reflected using a hazard ratio from time-to-event analyses. OS events were captured using either a three- or five-year follow-up period. The terms "disease-free survival, disease-specific survival, recurrence-free survival, or relapse-free survival" were treated as disease free survival (DFS) which counts from the date of starting a treatment to the date of an event (relapse) or censoring (including death). As all included studies did not report the effect of treatment delay on survival uniformly, a method to convert study-specific HRs measured against diverse timelines into less or greater than 4-week delay, has been necessary. The upper and lower boundaries of the 95% confidence intervals of reported HRs were used to back-calculate standard errors for the log-HRs used in our analyses. The adjusted log-HRs were divided by the number of weeks in the reported waiting time of each study to estimate weekly study-specific log-HRs which were then included in the meta-analysis. Finally, the pooled log-HRs were converted to HRs as a function of a 4-week delay in treatment initiation. Study-specific HRs, either OS or DFS, along with their 95% confidence intervals, were computed and reported (see **Supplementary material 1**).

2.6 Meta-analysis

A quantitative data synthesis was performed in Microsoft Excel and a set of R packages. Initially, extracted data tabulations were entered into MS-Excel, manually cleaned, formatted and sorted. Next, the collated data was transferred into the R programming software version 4.3.1 (R Core Team, Vienna, Austria) [25]. Study-specific log-HRs representing the effect of a greater as opposed to a less than 4-week delay in treatment was pooled across studies and the pooled log-HRs were converted to HRs. The pooled log-HRs were obtained using random effects meta-analysis, taking into account each study's standard error of the effect estimate. A graphical presentation of study-specific waiting times against HRs was visualized using the "ggplot2" package in the "tidyverse" collection. The "meta" and "dmetar" packages were used in the estimation of pooled log-HRs (using the "metabin" function) and corresponding HRs in forest plots as well as the identification of influential studies. To test the presence of influencing factors with the observed pooled estimate, a univariable and multivariable meta-regression was performed using the "mvmeta" package. Alternatively, a multi-model inference analysis was undertaken to identify the most influential moderators in the list. A log linear relationship with waiting times was assumed in a random-effects model, and the dependent variable was the study-specific log-HR weighted by its variance. Results were presented in tables, figures and forest plots with 95% confidence intervals. A prediction interval was also added in the model to estimate the possible interval that future observations may account for.

Different tests, including Cochran's Q squared, I squared and tau squared were employed to estimate the degree of variation across the included studies. While there are limitations in the estimates of between-study heterogeneity applying each metric [26], reporting all is deemed substantial to ease interpretation as well as speculate over the possible source of variation not accounted for by a sampling error alone. A subgroup analysis was carried out depending on heterogeneity of studies, and the type of treatment indication, such as chemotherapy, chemoradiation, surgery and radiotherapy, patients received. Potentially influencing factors, namely treatment type received, follow-up period, proportion of patients with adenocarcinoma, proportion of patients with stage III or higher, and sample size of individual studies were tested in the meta-regression. A sensitivity analysis was carried out by omitting individual studies at a time using a leave-one-out method. Publication bias was assessed using funnel plots generated in Review Manger (RevMan 5.3, The Cochrane Collaboration, Copenhagen, The Nordic Cochrane Center, Denmark) [27] and the degree of asymmetry was determined using Egger's test in R. A $p < 0.05$ was considered statistically significant in all analyses. To precisely operationalize the concepts "exposure" and "outcome" defined earlier, the reviewers used the terms "treated" and "delayed" in figures and texts to referring the relative rate of mortality or recurrence among lesser waiting time (reference) and greater waiting time (exposed) groups respectively.

3. Results

3.1 Study screening and selection

As shown in the figure below, study identification was performed using database searching and other methods. A total of 630,904 articles were located using the database search, such as PubMed, Cochrane Central, and EMBASE. After checking and removing duplicates (n = 158) in a reference manager (EndNote.7), 629,247 items were removed for other reasons, such as an automatic keyword search assisted with manual inspection in Rayyan software (The Rayyan Systems Inc., Cambridge, MA, USA) [22]. Further, we eliminated 1476 articles after checking their titles and abstracts, which finally retained 5 articles for inclusion. On the other hand, gray literature and citation or reference searching were carried out, producing an additional six items. Overall, 11 studies [11–14, 28–34] were identified for our analyses among which we were able to identify18 comparisons for the analysis of treatment delay for either OS or DFS. There were 14 OS comparisons and 4 DFS comparisons. There were more than 11 OS comparisons because two studies reported outcomes evaluated on more than one treatment waiting time. The following three studies, comprising one comparison group each, were excluded from the meta-analysis. The study by Dereje *et al.* [31] was only a 3-year follow-up evaluation of patients receiving radiotherapy given that other studies in the meta-analysis were based on a 5-year follow-up. On the other hand, the type of treatment patients received was not vividly defined in the study by Chen *et al.* [11]. Lastly, in the report by Shen *et al.* [28], it was stated that the patients received all conventional cancer treatments, namely radiotherapy, surgery, and chemoradiotherapy, which poses difficulty in grouping the treatment (Fig. 1).

3.2 Characteristics of included studies

Ten of the 11 articles included in this review were based on a retrospective (historical) cohort design, except one study, which was a prospective cohort [31]. The studies comprised 50,590 patients in total, ranging from a sample size of 183 [31] to 12,603 [33]. All studies were rated as "good quality" based on the Newcastle-Ottawa scale [19] for risk of bias assessment. However, the proportional hazard assumption test was documented only in a few [12, 31, 32] of the studies. Geographically, 4 of the studies were done in Asia [11, 13, 29, 33], 4 in North America [12, 30, 33, 34], 1 in Africa [31], 1 in the Middle East [14], and 1 in South America [29]. Seven studies reported a median age between 44 and 55 years, while the remaining 4 studies reported the mean age of participants ranging from 45.9 to 65.38 years. The stage of cancer evaluated in 9 of the included studies was I to IV [11–14, 28–31, 34], and stages I to II in the remaining two [32, 33]. The types of treatment patients received were radiotherapy in 3 studies [29, 31, 34], surgery in 2 studies [32, 33], and CCRT in 5 studies [11–14, 29]. There was no information on what specific treatment patients received in one study [11]. Meanwhile, eight studies [12, 13, 28–30, 32–34] were documented to evaluate OS with a follow-up of 5 years across all treatments. Of these, the study by Nanthamongkolkul *et al.* [32] included a comparison group that extended the assessment of survival after five years. Three studies [11, 14, 31] evaluated OS in three-year follow-up under CCRT only. Similarly, DFS was reported in two studies [32, 34]. There was inconsistency in considering waiting time for treatment initiation across the studies, ranging from a median of two weeks to 30 months (**Supplementary Table 4**).

The study-specific hazard ratios (HRs) and the corresponding waiting times (weeks) of 11 studies are shown in Fig. 2A. The range is based on waiting time intervals in the respective studies. The comparison groups in one study included differing effect measures, whereby the groups in the 5-year or less follow-up revealed an indifferent rate of mortality between the treated and delayed groups. On the contrary, the second comparison group that was followed for more than 5 years experienced an increase in risk of mortalities. As shown in Fig. 2B, the sketch for studies with two waiting time groups remains the same between the two graphs. However, the log-HRs for studies with more than two categories of waiting time were estimated using the weighted least squares in meta-regression. Further, studies that reported on more than one comparison group, such as based on different waiting times or outcomes of interest (OS *vs.* DFS), were suffixed independently with Roman numerals (Fig. 2).

3.3 Overall survival

There is a significant level of between-study heterogenity presented with purely negative and positive effect sizes among the included studies. Due to the fact that interpreting the higher tau^2 would be difficult from a practical point of view, a prediction interval was added to the model in order to suggest a possible directional change for the true 4-week wait time effect. This was generated only for the pooled estimate of the random effects, as the number of studies in the subgroups was very low.

Overall survival was evaluated based on the pooled effect of 11 comparison groups using a random-effects model. Though many potentially influential moderators (*i.e.*, treatment type received, follow-up period, proportion of patients with adenocarcinoma, proportion of patients with stage III or higher, and sample size of individual studies) were tested in meta-regression, most did not reveal a statistically significatnt contribution to the model. The second moderator (follow-up period) explained the variability in the effect size by 28.3%, substantially higher compared to the first moderator (RT or CCRT *vs.* Surgery) which was very low at 2.8%. Adding all factors to the last model resulted in only a slight improvement (R squared = 32%), with the unaccounted level of hetrogenity still being substantial (I squared = 98%). The multimodel inference analysis also placed the follow-up period at the top. A detailed description of the multivariable meta-regression report has been presented in (**Supplementary Table 5**) attached under the supplementary files. Because merging groups on radiotherapy and combined chemoradiotherapy could not be assumed to be the same from a practical point of view, we separated these options and evaluated them based on a follow-up period. Accordingly, the subgroup on five-year follow-up following radiotharpy revealed that a 4-week delay in treatment was associated with a 1.27 times higher rate of death from

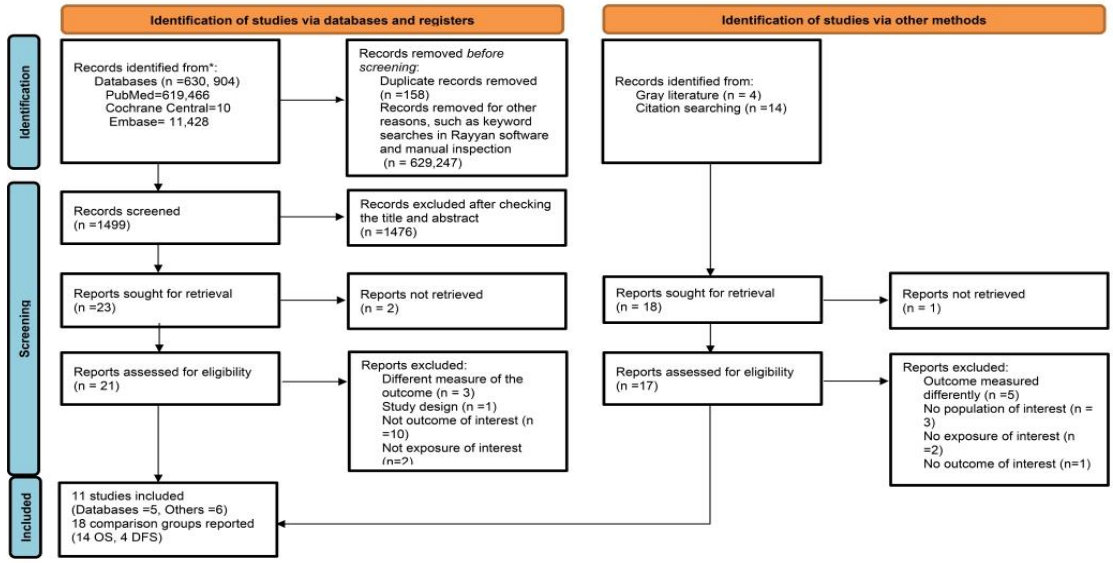


FIGURE 1. PRISMA 2020 flow diagram for included studies.

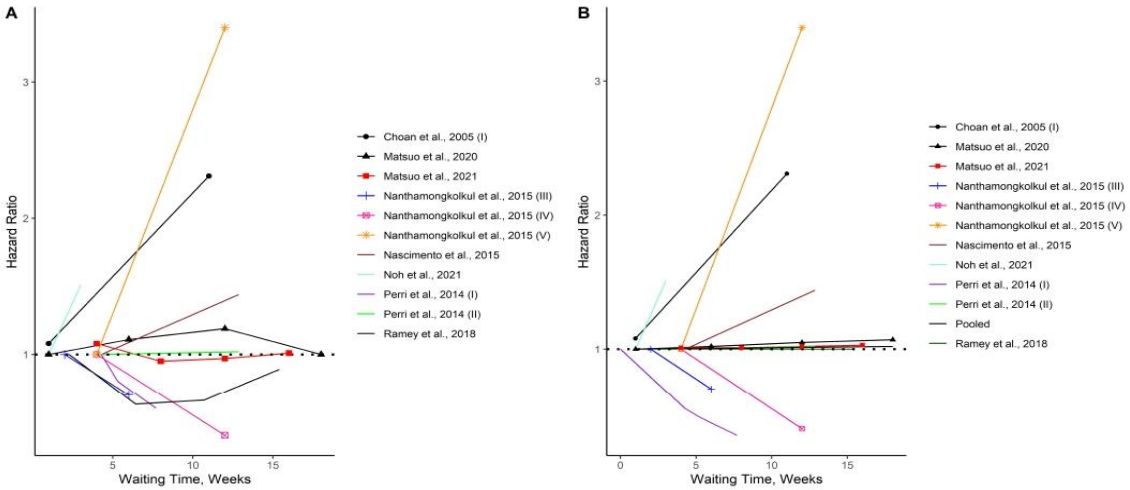


FIGURE 2. Study specific hazard ratios of overall survival plotted against waiting time in weeks. The plot shown in A represents the individual hazard ratios versus waiting time in weeks. The end of lines reflect effect estimate at the reported exposure time compared to the first waiting time category. Plot in B shows, computed hazard ratio per weekly delay of waiting time. The slope of each line indicates a change in logHR per a week of delay. For studies with more than two categories, weekly beta was estimated using a weighted least squared regression.

any cause (HR: 1.27; 95% CI: 1.12–1.45). Similary, evaluation of 8-week and 12-week delay in initiation of radiotherapy showed a 1.61 (95% CI: 1.24–2.09) and 2.04 (95% CI: 1.39–3.01) times higher rate of mortality, respectively, as compared with the non-delayed groups (**Supplementary Fig. 1A,B**). Nontheless, a 4-week delay in initiation of CCRT (HR: 1.31; 95% CI: 0.76–2.23) and surgery (HR: 0.96: 95% CI: 0.60–1.54) was not associated with a statistically significant increase in the hazard of death as compared with the group treated before 4 weeks after diagnosis. In parallel, the same length of waiting time did not predict the rate of death in a 3-year follow-up period (HR: 0.76; 95% CI: 0.44–1.32) (Fig. 3). Neither the 8-week or 12-week delay in treatment initiation among the remaining subgroups nor the overall pooled effect revealed any increased rate of mortality as compared with the respective non-delayed groups. As also depicted in the drapery plot, the effect of a 4-week waiting time on overall survival was assessed at different p-values. As the confidence level decreases and the p-value increases, we note that the confidence interval for the pooled effect gets narrower. The graph also shows study-specific confidence intervals for each 4-week delay in treatment (Fig. 4).

3.4 Disease free survival

As depicted in Fig. 5, the five-year follow-up report revealed that a 4-week delay in radiotherapy may also result in a 1.72 times higher rate of disease relapse (HR: 1.72; 95% CI: 1.25–2.35). However, the stated waiting time for surgery did not show any significant difference between the delayed and treated groups in the five-year period (HR: 0.89; 95% CI: 0.75–1.04) (Fig. 5). In the same way, the effects of either an 8-week or 12-week delays have been measured. The result showed that 8-week and 12-week delays in initiation of radiotherapy were associated with a mortality rate of 3.07 (95% CI: 1.64–5.74) and 5.37 (95% CI: 2.09–13.75), respectively, as compared with the non-delayed groups. Meanwhile, there was no effect difference noted either in the pooled estimate or surgery-received group for the assessed wait times (**Supplementary Fig. 1C,D**).

3.5 Publication bias

Apart from the graphical presentation to depict the plot of the hazard ratio against its standard error (se of logHR) shown below, a statistical method of detecting publication bias using Eggers' test was performed for the overall survival. The test does not indicate the presence of funnel plot asymmetry (intercept: −3.38; 95% CI: −19.55 to −12.80; t: −0.41; p = 0.69) (Fig. 6).

3.6 Influence analysis

As shown in Fig. 7, an influence analysis was carried out using the leave-one-out method to detect potential studies with a significant impact on the pooled effect size. Accordingly, removing two studies, namely Nanthamongkolkul *et al.* [32] (V) and Noh *et al.* [13], independently showed that the pooled effect size would change in the negative direction but was not statistically significant. The former compared the 8-week delay of surgery to post-5-year survival, while the latter assessed presumably 5-year survival following a 2-week delay. The total estimate at the base of the influence array indicates the overall pooled estimate when retaining all items (Fig. 7).

4. Discussion

In this review, we evaluated the effect of a greater as opposed to a less than 4-week wait from diagnosis to treatment initiation on overall survival in patients with cervical cancer. Due to the complexity and interaction in treatment type, stage of cancer, and follow-up period across the included studies, considerable heterogeneity was noted in this review. Indeed, the issue of heterogeneity is always inevitable in meta-analysis, as studies bring diversity clinically and methodologically [35]. From the results across all subgroups, it would be anticipated that statistically significant heterogeneity occurred, partly accounted for by sampling errors. This is likely because, in addition to the small number of studies included in each subgroup, there were studies with very small sample sizes [14, 32, 34]. Alternatively, an additional metric (I squared statistics) has been considered to assess the amount of variation that might not have been accounted for by sampling errors. This test still suggested a substantial degree of variation. With this, a number of reasons in individual studies would be mentioned as having a contribution. The characteristics assessed were: follow-up period, age distribution, treatment type received, stage of cancer, type of carcinoma, and sample size (**Supplementary Table 5**).

One of the comparison groups in the study by Choan *et al.* [34] and the study by Nascimento *et al.* [29] who received radiotherapy were evaluated. It was found that the proportion of stage III or higher cases was lower in the former (23% *vs.* 39%), whereas the percentage of 5-year OS was higher (53% *vs.* 23%). On the contrary, the rate of mortality in the former was higher than what was reported in the latter. Apart from the disparity in sample sizes, there could be a variation in terms of confounding events, possibly non-cancer-related mortality, among the delayed group in the first and the non-delayed group in the latter. Hence, relying merely on the aggregated proportion of stages of cancer or OS might be misleading. A similar variability persists in the subgroup assessed for CCRT as 5-year OS [12, 13, 30]. Despite similarities in mean age and treatment type received, the studies exhibited considerable heterogeneity. This would be owed, possibly, to the proportion of cases with stage III or higher cancer (53% in the study by Matsuo *et al.* [30], 2021 *vs.* 23% or 39.3% in the rest) and the proportion of cases with adenocarcinoma (0% in the study by Ramey *et al.* [12], 2018 *vs.* 11% or 12% in the rest). Meanwhile, the level of precision among the studies would still account for a significant part of the variation (chi squared = 88.5, $df = 2$, $p < 0.01$), as the study by Noh *et al.* [13] had the smallest sample size (389 *vs.* 5105 or 12,237 in others). In the same study, we also assumed that cases were followed for at least five years as it was not reported vividly (since enrolment was between 2001 and 2017 and the report was published in 2021), which could account for the unexplained possible variation.

Similarly, in the studies that considered patients for whom

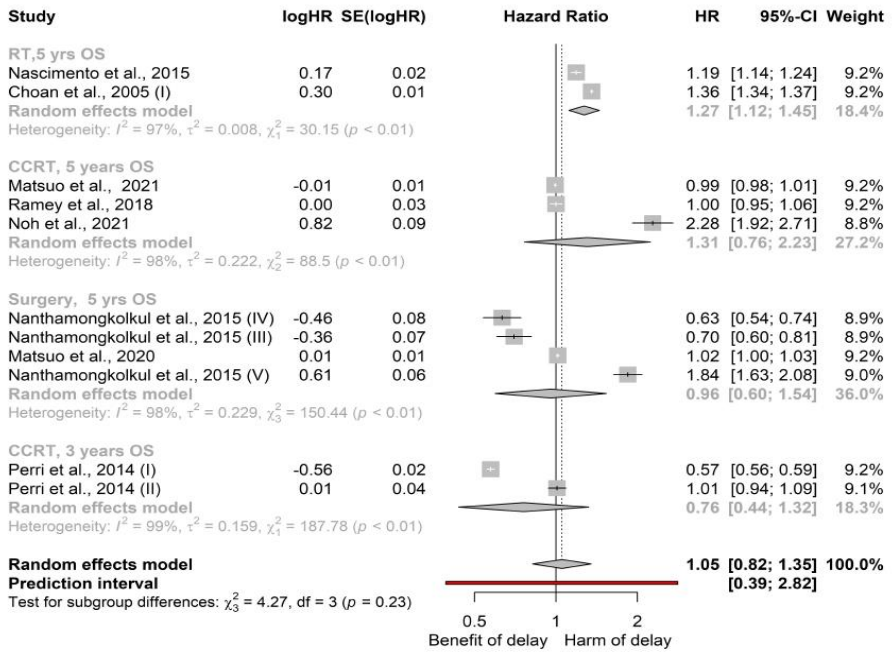


FIGURE 3. Subgroup meta-analysis of overall survival with a 4-week waiting time in patients with cervical cancer. SE: Standard Error; HR: Hazard Ratio; CI: Confidence Interval.

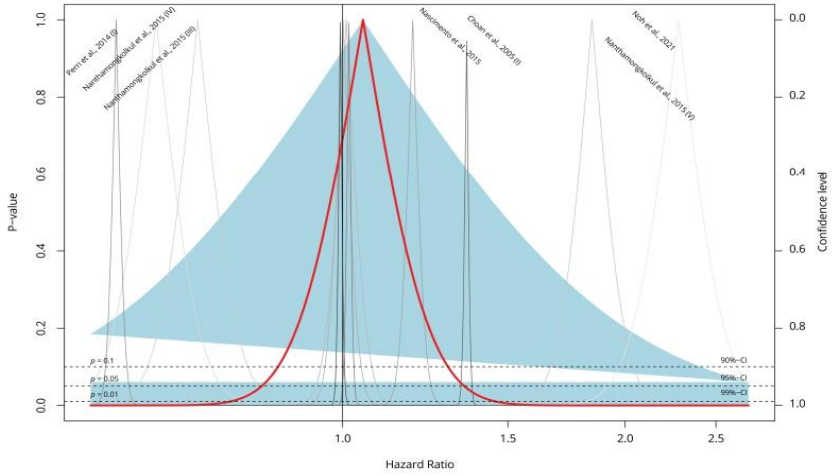


FIGURE 4. Drapery plot showing the association between 4-week waiting time and OS in cervical cancer at different *p*-values.

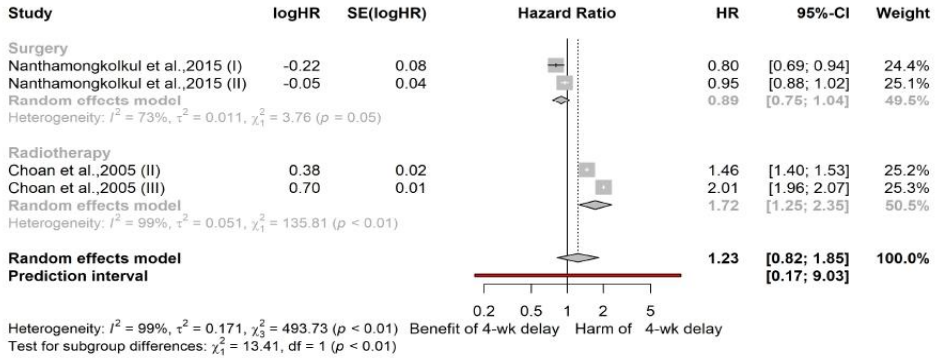


FIGURE 5. Subgroup meta-analysis of disease-free survival with a 4-week waiting time in patients with cervical cancer. SE: Standard Error; HR: Hazard Ratio; CI: Confidence Interval.

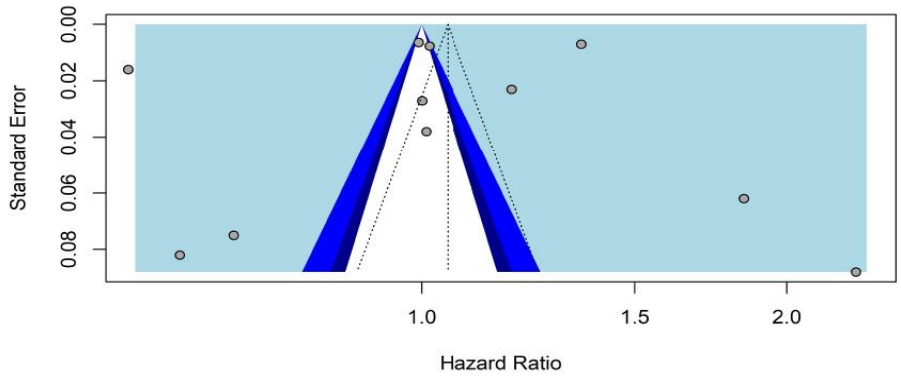


FIGURE 6. Distribution of HR with SE (logHR) in included studies.

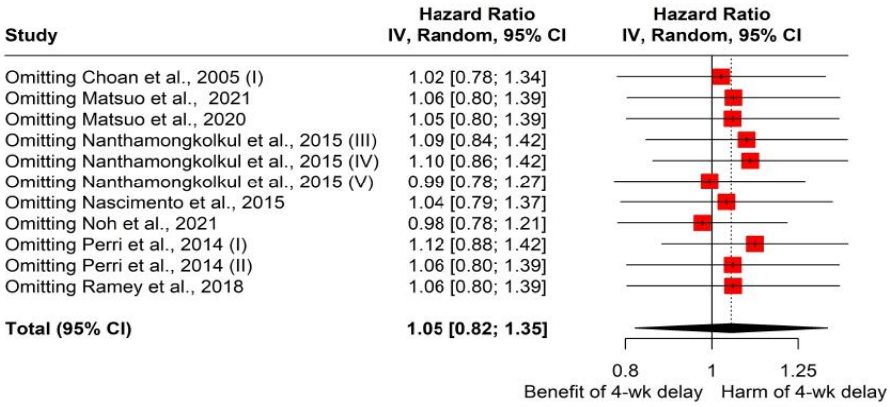


FIGURE 7. Influence analysis of included studies using a leave-one-out method. CI: Confidence Interval.

surgery was performed [32, 33], it can be observed that both the number and size of studies played a substantial role in the between-study heterogeneity (Chi squared = 150.44, $df = 3$, $p < 0.01$). This could not be the only source of variation, as the test statistic (chi squared) still fails to be powerful enough in a small number of studies [36]. There is very high between-study heterogeneity (I squared = 98%), suggesting unaccounted sources of variation across effects considered. Quite distinct from others, one of the comparison groups by Nanthamongkolkul (Nanthamongkolkul *et al.* [32], 2015 (V) evaluated the 8-weeks waiting time against the OS of post-five years. This, then, might overestimate the effect size compared to the other comparison groups in the subgroup. Nonetheless, there is evidence in this line that a few weeks of delay in treatment in early-stage cervical cancer has an inconclusive association with 5-year OS [37] or even 3-year OS as illustrated by two comparison groups in the last subgroup [14]. This could, possibly, be due to an improved cure rate or the very slow prognosis of the disease following management at this stage [8]. Finally, the methods employed in data analysis, assumptions, and robustness of models could be implicated in these differences. For instance, the studies by Matsuo *et al.* [30, 33] employed a cubic spline transformation with a non-linear assumption of waiting times. In some studies, methods were reported to test the proportionality of hazard assumptions, while others lacked them.

While the sources of variability described above could be regarded as potential areas for statistical heterogeneity, it still remains hard to reach a conclusion. Ideally, the tests used (though I squared might be less sensitive to the number of studies compared with the Q squared statistics) might yet fail to detect the precise level of variability between the true and observed effects [26]. There could also be challenges in uncovering other causes of variance ascribed to the design-level or baseline biases in individual studies. These may include the particular intervention types and dosages patients received, the possible method-driven diversities, such as the risk of bias during the recruitment process, outcome measurement, degree of loss to follow-up, or a combination of any of them. For instance, results from studies that consider a cubic spline transformation could exhibit distinct directionality compared to others'. This, in turn, poses a cumulative influence that challenges the easier interpretation of the pooled effect measure in this review.

The random effects meta-analysis strategy used in this paper is intended to handle heterogeneity in effect sizes across studies that is due to sampling error within each study. The pooled effect from a subgroup of two studies showed that a 4-week delay in radiotherapy initiation was associated with a 1.27 times higher rate of death. Extending the waiting time to 8-week or 12-week, we found that the rate of mortality increased by 1.61 (95% CI: 1.24–2.09) or 2.01 (95% CI: 1.39–3.01) respectively, compared to the non-delayed groups. The study by Dereje *et al.* [32] in a cohort of patients with similar stages of cancer and treatment types but with a 3-year follow-up period. It reported that each two-month delay of treatment can increase the rate of mortality twice as much as the group who received the treatment within the same period. The reported level of o mortality among the latter is seemingly higher because ours was based on the weighted averages of two studies over a relatively longer period of follow-up. This is in agreement with guideline recommendations that treatment options requiring radiotherapy should be started within a month [38, 39]. It is reasonable to consider that patient groups under this indication come from an advanced stage of the disease, as was also noted in the included studies. The rate of worse prognosis has been reported to be fast following the delay of treatment in patients with advanced-stage breast cancer [40] though opposing evidence exists in a report among patients with lung cancer [41]. An additional possible reason could be that the samples considered in the pooled studies were slightly younger (median: 51–52 *vs.* 55 years). Patients with advanced age may have an increased rate of mortality owing to the associated comorbidities [42].

On the contrary, no statistically significant rate of mortality was noted between the delayed and non-delayed groups under combined chemo-radiotherapy. Neither did the relatively shorter follow-up period for the same treatment reveal a significant difference. In fact, more than 86% of the patients in the studies by Noh *et al.* [13] and Matsuo *et al.* [30] were diagnosed with squamous cell carcinoma (SCC) at similar stages. Yet, the exclusion of patients with waiting times beyond 1 year in the latter study might underscore the effect of delayed treatment on survival. Longer than optimal lag times were generally reported to increase the risk of mortality in cancer cases [43]. This may contribute to the non-differential rate of mortality among these groups, given that other exposures are alike. A study also reported that patients with squamous cell carcinoma (SCC) have better OS and DFS compared to those with adenocarcinoma following chemoradiation [44]. In the study by Ramey *et al.* [12], even though most of the patients (85%) received chemoradiation therapy, the effect of delay from the expected date of initiation was reported to be lower in this group compared to those who received radiotherapy. Furthermore, the addition of chemotherapy to radiation has been reported to be effective in improving survival outcomes [45] possibly masking the effect of the disparity in waiting times in this population. Waiting time could be a main reason for disease progression. Further to this, factors, such as comorbid conditions, could contribute to the indifference in the risk of mortality, such that the group with non-delayed treatment might have been at increased risk or were experiencing more clinical symptoms. This variation, however, was not assessed, as all studies did not report on such measures. Such a paradox has been widely documented in the literature, where patients with shorter intervals between diagnosis and treatment initiation were reported to experience worse outcomes [43, 46]. Even though assessing potential confounders, such as tumor aggressiveness or cancer cell proliferation, was not possible, it is also likely that patients with symptomatic presentations were referred and treated earlier but had a poor prognosis.

In the same vein, the rate of mortality from any cause in five years among treated and delayed patients of surgery was found to be not statistically significant. One of the studies in this group showed that a waiting time of either a 4-week, 8-week, or 12-week interval had no effect on the difference in overall survival [32]. This might be plausible as the patients in this group were at an early stage of cancer (stages IA–IIB) and had

undergone radical or primary hysterectomy. Studies suggest that early-stage cervical cancer can be treated using either simple or radical hysterectomy with minimal complications [47, 48]. The five-year overall survival following radical hysterectomy was reported to reach up to 90% [48]. The interval between subsequent treatments, including neoadjuvant or adjuvant chemotherapy, has also been implicated as an additional source of bias. For example, the initiation of the next treatment before the complete recovery of patients from the first could lead to a higher risk of mortality [49]. Nonetheless, delays in cancer treatment may be differentially linked with an excess risk of cancer-related mortality [50].

A comprehensive search strategy was followed, following all necessary steps as recommended for meta-analysis of observational studies in epidemiology (MOOSE) [21], in addition to the PRISMA checklist [24] for reporting the outcomes. The result of the publication bias test in this review proved that there was no asymmetry in the included studies, detected either individually or subgroup-wise. In addition, meta-regression and subgroup analyses were considered to minimize biases originating from the waiting time paradox. These may be considered as strengths devised to avoid biases during the selection of studies. Furthermore, sensitivity analysis did not show any significant direction changes in the confidence interval of the effect measure; hence no removal of influential studies was considered in the last model. The review, however, is not without limitations. Firstly, a considerable level of heterogeneity was apparent in the meta-analysis, which might have posed a challenge in the interpretation of the findings. Secondly, despite the fact that subgrouping has been a recommendation when justified variability exists based on predefined attributes, its use in studies like the one we employed for the DFS is discouraged. Third, this review did not present an evaluation of the certainty of the evidence generated. Fourth, the exclusion of articles with no English abstract in the review might have introduced an English-language bias. Finally, the included studies lacked essential and clearly stratified patient-level data. This may include clinical symptoms, a real-time observation period, the specific type and sequence of treatment patients received, and the proportionality of hazards' assumption.

5. Conclusions

Four-week delays in initiation of radiotherapy in patients with cervical cancer resulted in an increased rate of mortality from any cause. However, there is inconclusive evidence on the association between a 4-week delay in the initiation of either surgery (hysterectomy) or chemoradiotherapy and overall survival. This might be confounded, partially, by the waiting time paradox bias. Similarly, a 4-week or more delay in surgery may not change the hazard of DFS events relative to a less than 4-week delay in surgery. It is recommended that future reviews utilize individual patient data (IPD), concentrate on researches with prospective designs when appropriate, and utilize techniques to evaluate the fundamental assumptions of the studies that are included. Additionally, based on clinically relevant stratification—such as stage, pathologic type, geographic region, age, and particular therapy types—present the dangers associated with prolonged waiting times.

AVAILABILITY OF DATA AND MATERIALS

All relevant data are within the manuscript and its supplementary files.

AUTHOR CONTRIBUTIONS

TS—was involved in conceptualization, design, data extraction, quality assurance and draft and final manuscript writing. BG—was involved in data extraction, validation and final manuscript write-up. TGF—was involved in conceptualization, supervision, validation, and editing of the draft manuscript. All authors have read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This systematic review is recorded in the International Register of Systematic Review Protocols (PROSPERO) under the registration number CRD42022299689. A review protocol has been formulated and published. The review adheres to the Meta-analyses of Observational Studies in Epidemiology (MOOSE) format in its conduct and reporting. Ethical approval was not obtained since this study involves a systematic review and meta-analysis of previously published literature.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.ejgo.net/files/article/1801482595405316096/attachment/Supplementary%20material.zip.

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Access to advanced healthcare services and its associated factors among patients with cervical cancer in Addis Ababa, Ethiopia

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Objective: This study aimed to assess the extent of access to healthcare services, perception and associated factors among patients with cervical cancer in Addis Ababa, Ethiopia.

Methods: A facility-based cross-sectional study was conducted from 01 July through 30 August 2023 at two tertiary hospitals. Cases with histopathologic and clinical confirmation of cervical cancer were enrolled using a consecutive sampling technique. Data was collected through a validated questionnaire administered by interviewers using the KoboCollect application. Subsequently, the collected data underwent analysis using Statistical Sciences for Social Sciences (SPSS) version 26.0. Bivariable and multivariable regression models were performed at $p \leq 0.2$ and $p<0.05$ statistical significance, respectively.

Results: A total of 391 patients were enrolled in the study. Health facilities were accessible for obtaining general medical services (56.5%), drugs (57.3%), laboratory diagnosis services (57.0%), imaging diagnosis services (56.8%), and radiotherapy services (55.8%) of the patients. Cost of services was affordable only in 11.5% of the cases. Essential anticancer medicines were out of stock for 229 (58.6%) of the patients during the past three months. About two-thirds of the patients have a good perception of access to healthcare services. In multivariable binary logistic regression, admission to the inpatient (AOR: 0.20, 95% CI: 0.06-0.67), joblessness (AOR: 0.19, 95% CI: 0.08-0.46), lower level of income to the extreme poverty line (3567ETB)(64.9 USD) (AOR: 0.19, 95% CI: 0.10-0.35), no CBHI coverage (AOR: 4.16, 95% CI: 1.76-9.85), having social support (AOR: 3.80; 95% CI: 1.96-7.41), and poor dietary practice (AOR: 2.36, 95% CI: 1.28-4.35) were found to have a statistically significant association with perceived good access to healthcare services.

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Conclusion: Only close to a half of the patients with cervical cancer, in Addis Ababa, have adequate access to healthcare services. Nearly two-thirds of the patients reported perceived good access to the services. Many factors were found to show a statistically significant association with patients' perceived access to healthcare services.

KEYWORDS

access, Addis Ababa, cervical cancer, Ethiopia, healthcare services, perceived access, realized access

1 Background

Cervical cancer causes a devastating health outcome in women of all age groups, potentially leading to morbidity and premature mortality. Although the disease can be prevented and treated effectively, most notably when detected at an early stage (stages I and II), there is a growing disparity in women's access to essential healthcare services (1, 2). The problem worsens when more than eight in ten women diagnosed with and nine in ten women who die from cervical cancer live in low-middle-income countries (3). Compared with women in high-income nations, those in low-and middle-income countries have a 35% higher average life risk of cervical cancer globally (4). The average age at diagnosis was reported to be 53 years, ranging from 44 years (Vanuatu) to 68 years (Singapore), and the average age at death from cervical cancer was 59 years, ranging from 45 years (Vanuatu) to 76 years (Martinique) both reported globally (5).

The prevalence of cervical cancer in Ethiopia ranged from 18% to 23% (6, 7). The age standardized incidence and mortality rates in 2020 were about 21.5 and 16.0 per 100000 population respectively (7). Nearly 6,300 new cases are reported to be diagnosed annually, while about 4,884 women die from the same disease each year, making it the second most common and most deadly cancer in this group in the country (8).

Within health service delivery, access is measured in terms of supply of services, affordability, physical accessibility, and acceptability (9, 10). A more comprehensive perspective to encompass the broader aspects of access can also include elements about the structural features of the healthcare system, such as availability; features of individuals, such as preferences, taste, and information (11, 12); and financial, organizational, and professional factors (13). Nonetheless, as healthcare service delivery is not a homogenous product characterized as a single service, the exact meaning of having access remains vague (14). More precisely, it was also depicted as describing the link between specific patient and organizational dimensions (15). This conception labels access in 5As: availability, accessibility, accommodation, affordability, and acceptability. Further to this, supply-side features of health systems, as well as features of populations, along with the processes describing how access is realized, are mentioned as necessary (16, 17).

A multitude of factors may interact with the access of patients to healthcare, including poor cervical cancer screening, lack of awareness and knowledge of cervical cancer, biological factors such as poor nutrition; infections with the human immunodeficiency virus (HIV), tuberculosis (TB), and malaria; and socioeconomic and sociocultural factors with political inequities (18). Further, challenges related to the health system, psychological (fear of recurrence, negative social attitude, and distress associated with the side effects of treatments), and economic factors were identified as the barriers to women's access to healthcare per a study in Addis Ababa (19). According to recent sources, all such factors could be grouped under three primary types of barriers: structural, financial, and cognitive (20, 21). For example, personal and cultural barriers can inhibit the access or utilization of patients who need medical attention from seeking it or how they act once they obtain the care (22).

To the best of the principal investigator's knowledge, there is an insufficient understanding of the comprehensive aspects of access to advanced healthcare services for patients with cancer, specifically those with cervical cancer in Addis Ababa. This knowledge gap is noteworthy, especially given the growing incidence of cases and the fact that the city hosts the country's oldest and referral oncology service settings. Moreover, the perception of patients regarding the current health service delivery and its associated factors has not been determined, despite its considerable potential to impact patients' utilization of healthcare services and their satisfaction with the care they receive. In other words, the way patients perceive healthcare access is critical, impacting their engagement with the healthcare system, adherence to treatment plans, and overall health outcomes. Through identifying barriers and facilitators at the study settings, these perceptions enable precise interventions and improvements in healthcare delivery.

In the present study, different social, economic, clinical, and health system-related factors were modeled and assessed against their potential contribution to influencing the extent of access to healthcare of patients with cervical cancer in Addis Ababa, Ethiopia. A conceptual model of this theoretical construct has been depicted in Figure 1.

2 Methods

2.1 Study setting, design, and period

The study was conducted at two leading public oncology centers in Addis Ababa, Saint Paul's Hospital Millennium Medical College

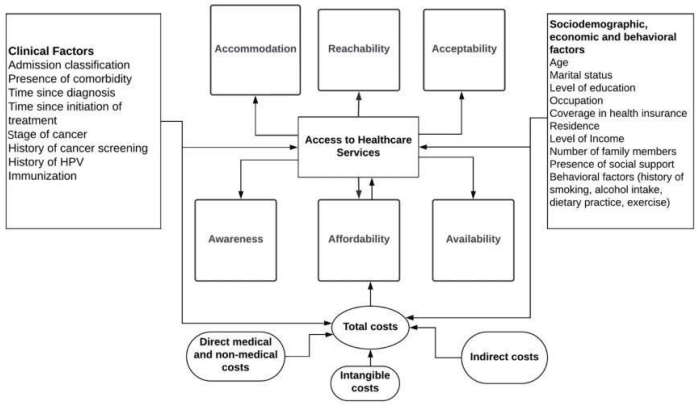


FIGURE 1
Conceptual model of access to healthcare services among patients with cervical cancer in Addis Ababa, Ethiopia.

(SPHMMC) and Tikur Anbessa Specialized Hospital (TASH) at Addis Ababa University. The two public hospitals rank as the country's top referral units, concomitantly delivering all specialized and comprehensive oncology treatment services and medical training in the city. An analytical cross-sectional design was carried out from 01 July through 30 August 2023.

2.2 Populations and eligibility criteria

The source population was all women diagnosed with cervical cancer and visiting the selected public and private hospitals in Addis Ababa, Ethiopia. The study population was all patients with a pathologically and clinically confirmed cervical cancer diagnosis who either started or continued a previous treatment in the selected oncology settings during the study period. All adult cases aged 18 or older, residing in Addis Ababa city, started any treatment and were on follow-up at least for a month, could provide information either themselves or through their caregivers, and those who offered verbal informed consent to participate in the study were eligible.

2.3 Sample size and sampling method

Taking into consideration the fact that earlier reports were not available on the topic, as well as the intent to increase the required sample size, the single population proportion formula with the following assumptions were used (23). These were i) assuming the probability of perceived adequate healthcare service in 50% of the cases (P=0.5), ii) a 95% level of confidence (α=5%), and iii) a 5% tolerable margin of error. This finally results in a total of at least 385 study participants to be included. As the number of cases visiting the hospitals was limited, a consecutive sampling method was employed. All cases that fulfilled the inclusion criteria and visited the centers during the specified period were assessed.

2.4 Data collection instrument and process

Structured psychometric instruments, validated and augmented with a set of objective queries, were utilized for the collection of quantitative data. Both tools were developed as interviewer-administered questionnaires, aiming to comprehensively assess various aspects of access to healthcare services. The design and scope of these instruments were shaped by a thorough literature review. The instrument comprised a total of 68 items, of which nine were on objective measures of access to healthcare services, 19 were on measures of patients' perception of healthcare services, and the rest were on patients' socioeconomic, behavioral, and clinical characteristics. The psychometric measures were based on a five-level Likert questionnaire ranging from 1(strongly disagree) to 5 (strongly agree). All questions were designed and loaded in the KoboToolbox open data source server. Exit interviews were conducted using the mobile phone-based KoboCollect or ODK collect application.

2.5 Data quality assurance

The following steps were taken into account during the process of this study in order to ensure the quality of data and reports. Firstly, a validated instrument for the psychometric measure was used to ensure that the tool addresses both validity and reliability issues. Further, objective measures were designed and added, translated to Amharic, and then back-translated to English to ensure consistency. Secondly, experienced health professionals, namely three nurses and two general practitioners, were employed for data collection. One-day training on research ethics principles, patient privacy, and data confidentiality was delivered to the data collectors. Thirdly, continuous supervision was maintained across all fieldwork processes to minimize potential errors.

2.6 Variables

2.6.1 Dependent variables

The dependent variable in the present study was extent of access to healthcare services, measured using objective also used as 'realized access' and subjective methods—the objective methods covered accessibility, affordability, and availability. Accessibility was measured based on the WHO's definition, in which a health facility was deemed accessible if it is either within 5 kilometers or an hour's distance from a patient's home (24). Affordability, on the other hand, was estimated based on the reported current-month patient expenses for treatments in the current illness and income level for the country's lowest-paid government workers (LPGW). The number of wage days required was computed from the ratio of daily expenses and LPGW rates. A ratio below 1 was assumed affordable and unaffordable otherwise. Availability was calculated based on the observation of data collectors or patient reports on the availability of each service or product during their visit. For palliative care and surgical services, the assumption was whether the facility offered those services or not. The psychometric measure included patients' perception of healthcare services in terms of five dimensions: acceptability (cultural, social and religious factors of seeking or receiving treatment), availability, accommodability (suitability of the facility's infrastructure or health-system for patients seeking treatment), affordability (costs assessed against individuals' ability or willingness to pay), and awareness (patients' feeling of available treatment options, client-provider interactions and the quality of services provided). The subjective assessment encompassed patients' perceptions of obtaining follow-up medical care, such as medications, radiotherapy, surgery, consultations, or any combination of these or other treatments to which a patient with a confirmed diagnosis of cervical cancer is entitled. Hence, the scope was limited to those where medical care needs had already been established and did not include those lacking access to cervical cancer screening, precancerous diagnosis, or education services in the community. Perception level was measured on a five-scale Likert questionnaire that ranged between 1 (absolutely disagree) and 5 (absolutely agree), and the aggregate score over the mean was considered "good access" and "poor access" otherwise.

2.6.2 Independent variables

Socio-demographic and economic characteristics: these included marital status, literacy status, education level, occupation, religion, average monthly income, residence, number of families, presence of supporting people around, current status of community-based health insurance (CBHI) coverage, and age.

Clinical characteristics: these included the presence of comorbidity, the name of comorbidity, time since cervical cancer was first diagnosed, time since treatment began, cancer stage, history of cervical cancer screening, and history of HPV vaccination.

Lifestyle and substance use-related variables: included current dietary practice, current physical exercise (adequate vs. inadequate), current history of alcohol intake, current history of smoking cigarettes or using tobacco products, and current history of khat consumption.

2.7 Operational definitions

Physical exercise: also known as physical activity, was measured based on the recommendations set by the US physical exercise advisory committee (25) and the American Cancer Society (ACS) (26) as well as the World Health Organization (WHO) (27) that patients with chronic illness, particularly those with cancer patients could accommodate engaging in moderate exercise. Accordingly, a patient needs to engage in 150-300 minutes of moderate exercise, or 75-100 minutes of vigorous physical activity per week. Considering these recommendations, a patient was classified to engage in either moderate or vigorous physical activity or not at all, based on the self-reported assessments during the study period.

Current history of dietary practice: as defined in the guideline by the American cancer society (26), the dietary recommendation for cancer patients entails taking foods that are high in nutrients in amounts that help them get to and stay at a healthy body weight, a variety of vegetables (dark green, red, and orange, fiber-rich legumes (beans and peas), and others), and fruits, especially whole fruits in a variety of colors, as well as whole grains. In the meantime, it is advised that patients reduce or limit red and processed meats, sugar-sweetened beverages, highly processed foods and refined grain products. This study used these criteria to classify patients' current dietary practices as "good" (when they report practicing any combination of the recommended diets during the study period) or "poor" (when they report practicing any of the high-risk diets or do not have access to make an adequate diet at all during the study period).

Current use of excess alcohol: was defined based on the response of a participant to the question 'do you currently drink excess alcohol? (i.e >1 bottle a day) that has been set by the American Cancer Society (26).

Current use of cigarettes: as per the definition by WHO (27), it refers to the use of cigarettes (smoked or non-smoked) reported by the respondents during the study period.

Current use of khat or other stimulant substances: was defined depending on whether a patient reports of using khat or other stimulant substances (i.e Hashish, Ganja or other controlled substances) during the study period.

Extent of access to healthcare services: refers to the degree of availability of crucial advanced healthcare services for cervical cancer patients, assessed through either objective or subjective measures as outlined in the 'dependent variables' subheading.

2.8 Data analysis

Data entered into KoboToolbox was exported to MS Excel, cleaned for completeness, trimmed for unwanted or confidential elements, and coded manually to numerical forms. Quantitative data was then entered into IBM Statistical Packages for Social Sciences (SPSS) for Windows, version 26.0 (IBM Corp., Armonk, N.Y., USA) (28) for further analysis. Apart from presenting univariate and bivariate descriptions of participant attributes, perceived good access to healthcare and associated factors were modeled in binary logistic regression. The bivariate and multivariable logistic regression

models were performed at $p \leq 0.2$ and $p<0.05$ levels of significance, respectively, and 95% confidence interval. Model assumption tests, including multicollinearity diagnosis, were performed using variance inflation factor (VIF). While model significance was measured using the Omnibus test, global model goodness of fit was assessed using the Hosmer and Lemeshow test. Similarly, non-parametric tests and chi-squared statistics were used to identify a relationship between realized and perceived access to healthcare services.

2.9 Ethical consideration

The study was approved by the institutional review board (IRB) of the School of Pharmacy, College of Health Sciences, Addis Ababa University (Ref.no: ERB/SOP/543/15/2023), and Saint Paul's Hospital Millennium Medical College (SPHMMC) (Ref.no: PM23/284) before commencing actual data collection. A support letter was written to the selected oncology centers. A verbal informed consent was obtained from every study participant. Participation in the study was voluntary. Data was analyzed in aggregate, and the study did not use personal identifiers. The confidentiality of data collected and the privacy of patients was protected.

3 Results

3.1 Socioeconomic profile of patients

A total of 391 patients were enrolled in the present study. Six of the extra patients added to the minimum sample size were included following a paper-based completion by one of the enumerators. The mean (± SD) age of participants was 50.3(12.2) years ranging from 22 to 89. Similarly, the mean (± SD) of participants' average monthly income was 4960.8(4046.3) Ethiopian birr which ranges from 0 to 50000 ETB. With this, the majority were in the age group of 50 or less (n=238, 60.9%), above the extreme poverty line (n=229, 58.6%), married (n=225, 57.5%), able to read and write (n=243,62.1%), had no formal education (n=166, 42.4%), housewives (n=128, 32.7%), had a community-based health insurance (CBHI) coverage (n=304, 77.7%), had no any form of social support (n=224, 57.3%) and had five or less number of families in the household (328, 83.9%) (Table 1).

TABLE 1 Socioeconomic profile of patients with cervical cancer in Addis Ababa, Ethiopia (n=391).

Variable	Label	Frequency	Percentage
Age (Yrs.)	50 or less	238	60.9
	>50	153	39.1
Average monthly income of the household	3567 ETB or less	162	41.4
	>3567 ETB	229	58.6
Marital status	Single	20	5.2
	Married	225	57.5
	Widowed	76	19.4
	Separated or separated	70	17.9
Able to read and write	Yes	243	62.1
	No	148	37.9
Education level	No formal education	166	42.4
	Primary education (grade1-8)	109	27.9
	Secondary education (grades 9-12)	75	19.2
	Tertiary education (University or college)	41	10.5
Occupation	Housewife	128	32.7
	Private employee	121	30.9
	Government employee	29	7.4
	Jobless	74	18.9
	Others*	39	9.9
Community-based health insurance coverage	Yes	304	77.7
	No	87	22.3
Presence of social support	Yes	167	42.7
	No	224	57.3
Household size	5 or less	328	83.9
	>5	63	16.1

*Includes merchants, students, housemaid, farmer.

3.2 Behavioral characteristics of patients

Assessment of behavioral characteristics of the participants revealed that none were currently utilizing any form of the addictive substance (ganja), whereas only a few consumed cigarettes (n=4), Khat (Khata edulis) (n=4), or an excess level of alcohol (more than one bottle a day) (n=10). Considering dietary habits, the majority (n=205, 52.4%) had poor practices, while the remaining 47.6% had good dietary habits. Meanwhile, over two-thirds of the patients reported that they were currently engaged in either moderate (n=273, 69.8%) or vigorous (n=7, 1.8%) exercise (Figure 2).

3.3 Clinical profile of patients

Over half (222, 56.8%) of the patients were accessed from Tikur Anbessa Specialized Hospital (TASH). The mean (± SD) years since confirmed diagnosis was 1.45(1.25), ranging from 1 month to 10 years, while the mean (± SD) of years since any treatment was initiated was 1.36(1.15), which ranges from 1 month to 9 years. Most of the patients were visiting the outpatient department (n=367, 93.9%), nearly half were in stage II of FIGO classification

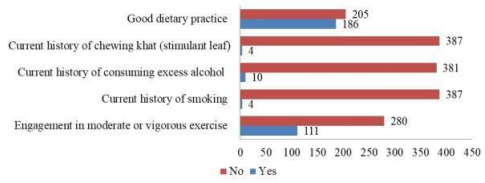


FIGURE 2
Behavioral characteristics of patients with cervical cancer in Addis Ababa, Ethiopia (n=391).

(n=202, 51.7%), three-fourth had no any history of cervical cancer screening (295, 75.4%), nearly one-third received only chemotherapy (n=124, 31.8%) and over a half (n=232, 59.3%) had no any history of chronic comorbidity (Table 2).

3.4 Common chronic comorbidities

Of those who reported having any history of chronic comorbidities, hypertension was reported as the commonest reported by 74(46.5%), followed by human immune deficiency virus/acquired immune deficiency syndrome (HIV/AIDS) (n=48, 30.0%) and type 2 diabetes mellitus (n=35, 22.5%) (Figure 3).

3.5 Realized access to healthcare services

The realized access to healthcare services was assessed in three dimensions, namely, accessibility, availability, and affordability. The geographic access was measured using the number of minutes it would take for patients to reach the nearest health facilities to obtain different healthcare services related to their current illness. Accordingly, health facilities are accessible in obtaining general medical services in 221 (56.5%), drugs in 224 (57.3%), laboratory diagnosis services in 223 (57.0%), imaging diagnosis services in 222 (56.8%), and radiotherapy services in 218 (55.8%) patients. Among the patients with no CBHI coverage (n=87), the health services offered in the facilities were affordable only for 10 (11.5%). On the other hand, evaluating the availability of any of the selected essential anticancer medicines during the past three or fewer months revealed that most were out of stock for 229 (58.6%) of the patients at least once. On the contrary, any basic diagnostic services required for the current illness were available most of the time (n=372, 95.1%) (Table 3). In this line, surgical and palliative care services were also available at the health facilities.

3.6 Perceived access to healthcare and factors associated with perceived good access to healthcare services

In two-thirds of the patients assessed (n=266, 68.0%), the perceived access to healthcare services was rated good. A binary logistic regression was performed between the dependent variables

TABLE 2 Clinical profile of patients with cervical cancer in Addis Ababa, Ethiopia (n=391).

Variable	Label	Frequency	Percent
Hospital	TASH	222	56.8
	SPHMMC	169	43.2
Admission classification	Outpatient	367	93.9
	Inpatient	24	6.1
Stage of disease	Stage I	70	17.9
	Stage II	202	51.7
	Stage III	100	25.6
	Stage IV	19	4.9
History of cervical cancer screening	Yes	96	24.6
	No	295	75.4
Treatments received/being received	Surgery only	45	11.5
	Chemotherapy only	124	31.8
	Radiotherapy only	9	2.3
	Chemotherapy and radiation	24	6.2
	Surgery and radiation	47	12.1
	Chemotherapy and surgery	33	8.4
	Chemotherapy, radiation, and surgery	78	20.0
	Traditional medicine and others*	31	7.9
Presence of any chronic comorbidity	Yes	159	40.7
	No	232	59.3

*includes any combinations of chemotherapy, surgery, or radiotherapy.

and independent variables. Variable which fulfilled the bivariable analysis (p≤0.2), namely service classification, ability to read and write, occupation status, household health insurance coverage, average monthly income of the household, the household size, presence of social support, dietary practice, age category, and lifestyle were included in the multivariable model.

The Omnibus test coefficient revealed that the final (fit) model was statistically significant compared to the null model with $\chi^2(16)$ = 194.47, p< 0.001. Global model fitness test of Hosmer and Lemeshow statistics showed a good fit with $X^2(8)$=10.40, p=0.24. The model explained 55.0% (NagelkerkeR^2) of the variance in perceived access to healthcare and correctly classified 85.7% of cases. There was no multicollinearity noted between the independent variables (VIFs ranged between 1.1 and 1.4). Neither was there an interaction identified between suspected factors and covariates.

The multivariable binary logistic regression analysis demonstrated that the perceived good access to healthcare services among inpatients was about 80% lower (AOR: 0.20, 95% CI: 0.06-0.67) than the outpatients. Similarly, as compared with housewives, patients who had no job and others, including

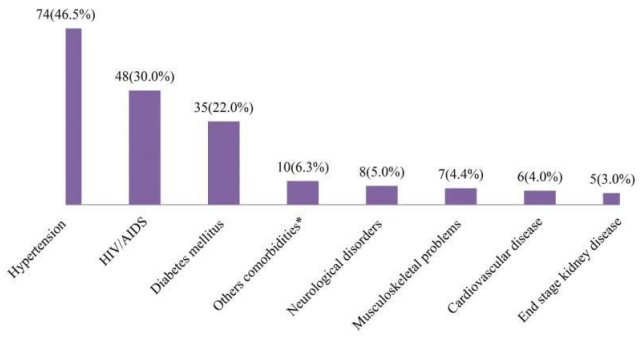


FIGURE 3
Common comorbidities among patients with patients with cervical cancer in Addis Ababa, Ethiopia (n=159). *eye cataracts, thyroid disease, anemia, lupus or asthma.

merchants, farmers, students as well as housemaids, were about 81% (AOR: 0.19, 95% CI: 0.08-0.46) and 70% (AOR: 0.30, 95% CI: 0.11-0.84) less likely to have perceived good access to healthcare services, respectively. Finally, in this category, patients with lower levels of income to the extreme poverty line (3567ETB) (64.9USD) were 81% (AOR: 0.19, 95% CI: 0.10-0.35) less likely to have perceived good access to healthcare services.

On the other hand, patients with no CBHI coverage were 4.2 times more likely to have perceived good access (AOR: 4.16, 95% CI: 1.76-9.85) than those with CBHI coverage. Patients who reported to have any form of social support were 3.81 times (AOR: 3.81; 95% CI: 1.96-7.41) more likely to have perceived good access than those without social support. Finally, patients with poor dietary practice were 2.36 times (AOR: 2.36, 95% CI: 1.28-4.35) more likely to have perceived good access to healthcare services (Table 4).

4 Discussion

This study attempted to assess the extent of access to healthcare that patients with cervical cancer have had and the associated factors within an urban context in Ethiopia. Utilized were both actual and perceived measures of access, which, in turn, were guided by a theoretically grounded conceptual model. Even though the cancer care continuum is complex, encompassing all services from screening to palliative care, this study focused on interim cancer care when patients demand accessibility to treatment options after a confirmed diagnosis.

The measure on realized availability of the essential services uncovered that slightly over half (range: 55%–57%) of the patients had access to such healthcare services as medical consultation, drugs, laboratory diagnosis, imaging, and radiotherapy. This suggests that many patients still lacked access to essential healthcare services in the city. There was a concordance between the reports of those with a relatively higher level of realized access and those who perceived good access to healthcare services (Supplementary Material). A recent qualitative study that engaged senior providers in one of the study settings remarked that the lack of an adequate number of oncologists, oncology nurses, radiotherapy technologists, and medical physicists was a challenge while the number of cancer cases was growing (31). The obtained figure on accessibility of most of the services, in the current study, is much lower than a report from cancer survivors in the United States, which outlined that only 6% of the patients had reported not to receiving general medical care services required in this group of patients (32).

Evaluating the cost of healthcare services received at the health facilities, it was found that only a small proportion (11.5%) of the patients could afford them, indicating that the services were unaffordable for nearly the entire population. The affordability of the services in the present settings was still lower compared to the figure reported in the latest study conducted in Rwanda, where 20% of the anticancer medicines were affordable (33). One potential difference between the results could be that the current study considered all estimated patient expenses for services received in the month, while the latter evaluated only medicines. We considered the wage days to calculate affordability; the method used in the latter was not clearly stated.

The availability of essential diagnostic services in the study settings was reported to be maintained during most of the time patients visited the facilities (95%), while essential anticancer drugs were available at a lower percentage (41%). The figure is the same as the one reported at public hospitals in Rwanda (33). A study in Mexico reported that the availability of anticancer drugs at public hospitals was 61.2% (34).Though the difference in the latter could be assumed to happen as a result of a better health system in a middle-income country, the finding revealed that the availability of anticancer medicines was far behind the recommended 80% target of the WHO (35).

Nearly two-thirds of the patients with cervical cancer in Addis Ababa have perceived good access to healthcare services. The low perception in a third of the cases could reflect the lack of sufficiency in the physical, financial, and system-level factors that patients face across the continuum of medical care, which, in turn, is close to the figure in the realized access. The report by Haileselassie et al. (31)

TABLE 3 Objective measures of access to healthcare services among patients with cervical cancer in Addis Ababa, Ethiopia (n=391).

Variable	Category	Frequency	Percent
Nearest health facility from home to seek general medical consultation services for the current health problem	Accessible	221	56.5
	Inaccessible	170	43.5
Nearest health facility from home to get drugs for the current health problem	Accessible	224	57.3
	Inaccessible	167	42.7
Nearest health facility from home to get laboratory diagnosis services for the current health problem	Accessible	223	57.0
	Inaccessible	168	43.0
Nearest health facility from home to get imaging diagnostic services for the current health problem	Accessible	222	56.8
	Inaccessible	169	43.2
Nearest health facility from home to get radiotherapy for the current health problem	Accessible	218	55.8
	Inaccessible	173	44.2
Affordability of cost of healthcare services received (n=87)*	Affordable (<1 day's wage)	10	11.5
	Unaffordable	77	88.5
Availability of any of the essential generic drugs (cisplatin, carboplatin, bleomycin, paclitaxel/ docetaxel, rituximab, bevacizumab, gemcitabine) or their brand counterparts at the health facility during the study period (n=259)	Yes	107	41.4
	No	252	58.6
Availability of basic diagnostic services (laboratory, ultrasound, histopathology) required for the current illness	Yes	372	95.1
	No	19	4.9

*Estimation made for non-insured patients and an LPGW daily wage of 50 ETB per minimum wage reported in 2015 (29) and method used elsewhere (30).

demonstrated that the perception of patients with cancer about themselves and their trust in the health system remains challenging, along with external factors such as providers, administration, and technology. According to Bourque and Loiselle (2022) (36), how healthcare services are structured, including setting, schedule, and location, are critical in cancer treatment that patients would raise concerns about and influence their perception. From the findings, one could note that realized poor experience during the uptake of a health service can prompt patients to perceive it negatively, influencing their poor utilization of health services provided. One study highlighted that the lack of high-technology equipment, poor coordination, and unskilled professionals would be barriers to quality oncology services (37).

Assessment of factors associated with perceived good access to healthcare services revealed that inpatients, average monthly income below the extreme poverty line, occupation groups, namely jobless and others (merchants, students, farmers and housemaids) were less likely to have perceived good access to healthcare. The lower rate of perception of adequate access among inpatients could be derived from the fact that hospitalization is associated with high costs and the availability of adequate health infrastructure compared with ambulatory services. On the contrary, the hospitals lack sufficient resources. Recent studies indicated that lack of supplies, trained professionals, and service costs were among the common challenges to delivering quality healthcare services at Tikur Anbessa Specialized Hospital (TASH) (31, 38). Patients' income level, either independently (jobless) or indirectly through the aggregate variable 'others ', can also be a significant driver of perceived poor access to healthcare services in the current setting. This is likely because, patients with a relatively higher income level can afford direct and indirect medical or nonmedical expenses compared to those with lower monthly earnings or no job. Generally, lower income is associated with negative utilization of cancer care (39). On a further diagnosis, it was noted that there was a significant difference in average monthly income level of the households between housewives and those reporting as 'jobless' (mean difference: 2267.8; 95% C.I: 678.7-3856.8, p=0.001). On the other hand, the group coded as 'others' was comprised of 79.5% identified as merchants among whom 71% were members of the CBHI scheme. A possible account on the inverse relationship between CBHI coverage and perceived good access to healthcare has been elucidated in the next paragraph.

On the contrary, patients with no CBHI coverage, those with poor dietary habits, and those with good social support were more likely to have perceived good access to healthcare services. The observed negative relationship between CBHI scheme coverage and good perceived access to healthcare might not be direct, which, in turn, is against the usual understanding. Acting as an intermediary, the extent of patient satisfaction could predominantly affect patients' perceptions of quality in healthcare services rendered (40). Patients enrolled in a CBHI scheme have been reported to have poor or moderate satisfaction with the services they received (41). This, in turn, could be attributed to patients' increased demand and expectation to consume quality health services following their investment in the scheme compared to those not enrolled in it. This also has a link with the perceived acceptability, accommodation and awareness domains of access. On a related note, the positive association between poor dietary habits and perceived good access to healthcare services might be indirect, as the observed relationship between the two variables appears to be quite unapparent. From the chi-square analysis, it was noted that a higher proportion of patients with poor dietary habits were on outpatient visits (54.0%) as compared with those attending the centers as inpatients (29.2%) (p=0.021). Social support is integral to cancer care as it combines and optimizes patient factors, psychosocial and economic issues, and health system-related dimensions. A recent study in one of the current settings revealed that family caregivers had an immense role in patients' treatment uptake, enhancing patient-provider communication and providing psychosocial support (42).

This study has employed both objective and subjective measures of access to assess the current extent of health service accessibility

TABLE 4 Factors associated with perceived good access to healthcare services among patients with cervical cancer in Addis Ababa, Ethiopia (n=391).

Variable	Category	Perceived access to healthcare services		COR	95%CI for COR		AOR	95% CI for AOR	
		Poor (n)	Good (n)		Lower	Upper		Lower	Upper
Service classification	Outpatient	103	264	Ref			Ref		
	Inpatient	19	5	0.10	0.04	0.28	0.20*	0.06	0.67
Marital status	Single	4	16	Ref			Ref		
	Married	64	161	0.63	0.20	1.95	1.35	0.28	6.58
	Widowed	24	52	0.54	0.16	1.79	3.40	0.60	19.25
	Separated or divorced	30	40	0.33	0.10	1.10	1.33	0.25	7.14
Able to read and write	Yes	56	187	Ref			Ref		
	No	66	82	0.37	0.24	0.58	0.93	0.46	1.86
Occupation	Housewife	29	99	Ref			Ref		
	Private employee	25	96	1.13	0.62	2.06	0.50	0.20	1.27
	Government employee	4	25	1.83	0.59	5.69	0.66	0.15	2.89
	Jobless	46	28	0.18	0.10	0.33	0.19*	0.08	0.46
	Others**	18	21	0.34	0.16	0.73	0.30*	0.11	0.84
CBHI coverage***	Yes	111	193	Ref			Ref		
	No	11	76	3.97	2.03	7.80	4.16*	1.76	9.85
Household's average monthly income	≤3567 ETB	92	70	0.12	0.07	0.19	0.19*	0.10	0.35
	>3567 ETB	30	199	Ref			Ref		
Number of family members	Five or less	96	232	1.70	0.98	2.96	1.43	0.66	3.07
	>5	26	37	Ref			Ref		
Presence of social support	Yes	33	134	2.68	1.68	4.26	3.81*	1.96	7.41
	No	89	135	Ref			Ref		
Dietary habit	Poor	41	164	3.09	1.97	4.83	2.36*	1.28	4.35
	Good	81	105	Ref			Ref		
Age category (Yrs.)	50 or less	52	186	3.02	1.94	4.70	1.91	0.89	4.14
	>50	70	83	Ref			Ref		
Physical exercise	Poor	76	197	1.66	1.05	2.61	1.01	0.52	1.94
	Good	46	72	Ref			Ref		

*Indicates statistically significant association; **Includes merchants, students, housemaids, and farmers; ***Community-based health insurance; COR, Crude Odds Ratio; AOR, Adjusted Odds Ratio.
Model fitness results: Omnibus test of fit model: $X^2(16)=194.67$; $p<0.001$; Hosmer & Lemeshow test:$X^2(8)=10.40$; $p=0.24$; Nagelkerke R^2:55.0%; Test of multicollinearity: VIF of 1.1 to 1.4.

for patients with cervical cancer. Strong adherence to statistical model assumptions has also been followed to ensure the validity of the findings to be generalized across Ethiopian settings. Efforts were made to minimize potential bias introduced during data collection. With this, assessing access to healthcare services among patients with cervical cancer in Addis Ababa provides a comprehensive understanding of the challenges they face and informs targeted interventions to improve healthcare delivery, reduce disparities, and enhance overall health outcomes. Nonetheless, there were limitations to this assessment. Firstly, the study was limited only to the population in Addis Ababa City, and the findings generated may not reflect the actual extent of the situation in other contexts of the country. Secondly, the scope of healthcare services considered in the work entailed mainly treating confirmed cases; hence, it did not embrace all packages of essential health services, such as screening and diagnosis.

5 Conclusion

The present study revealed that nearly half of the patients with cervical cancer in Addis Ababa have optimal access to most of the

healthcare services required for their treatment. Lower income levels to the extreme poverty line, occupation groups with no job or farmers, and admission to the inpatient were negatively associated with perceived good access to healthcare services. In contrast, absence of CBHI coverage, social support, and poor dietary adherence were positively associated with perceived good access to healthcare services. The Ministry of Health should take steps to map and facilitate the expansion of cancer care centers equipped with complete infrastructure to low-access areas. Specifically, health leaders should map drug availability, allocate resources strategically, strengthen the supply chain, explore partnerships, enforce regulations, invest in capacity building, establish monitoring systems, conduct patient education, collaborate internationally, and offer incentives to the pharmaceutical industry. Efforts by health facilities to improve the quality of services offered irrespective of CBHI coverage status could impact patients' satisfaction positively. Existing facilities should equip themselves regarding the availability of drugs, health technologies, and trained providers. Finally, patient education and public awareness addressing illiteracy related to cancer prevention, detection, and management should be actively implemented across health facilities and schools. Future research should also involve patients with other types of cancer and employ various methodologies, such as concentration indicators and the Gini coefficient, to evaluate healthcare access comprehensively across all regions in the country.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Saint Paul Hospital Millennium Medical College IRB and Addis Ababa University, School of Pharmacy IRB. The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because of no greater than minimal risk due to the research.

Author contributions

TS: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing. BG: Supervision, Validation, Writing – review & editing. TG: Conceptualization, Methodology, Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

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PAPER III

PLOS ONE

RESEARCH ARTICLE

Validation of the Amharic version of perceived access to healthcare services for patients with cervical cancer in Ethiopia: A second-order confirmatory factor analysis

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Abstract

Background

Accessing healthcare services is a multifaceted phenomenon involving various elements, encompassing the demand, identification, reach, and utilization of healthcare needs. The literature offers methods for capturing patients' perceptions of healthcare access. However, to accurately measure patient perceptions, it is imperative to ensure the validity and reliability of such instruments by designing and implementing localized language versions.

Aim

The primary aim of this study was to validate the Amharic version of the perceived access to health-care services among patients diagnosed with cervical cancer in Ethiopia.

Method

A cross-sectional study was conducted among cervical cancer patients at oncology centers in Addis Ababa, Ethiopia. A consecutive sampling approach was used and data collection took place from January 1 to March 30, 2023. Following initial validation and pretesting, a KoboCollect mobile phone application was employed for data collection. Subsequently, the collected data underwent cleaning in Microsoft Excel and analysis through Amos software v.26 and R programming. Various validity and reliability tests, such as content validity, convergent validity, face validity, divergent validity, known-group validity, and reliability tests, were executed. A second-order confirmatory factor analysis was developed to calculate incremental model fit indices, including CFI and TLI, along with absolute measures, namely SRMR and RMSEA.

Results

A total of 308 participants were involved in the study, with 202 (65.6%) being patients referred from outside Addis Ababa. The initial evaluation of content validity by expert panels

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indicated that all criteria were met, with a CVR range of 0.5 to 1, I-CVI values ranging from 0.75 to 1, an S-CVI value of 0.91, and face validity values ranging from 2.4 to 4.8. The internal consistency of items within the final constructs varied from 0.76 to 0.93. Convergent, known-group, and most divergent validity tests fell within acceptable fit ranges. Common incremental fit measures for CFI and TLI were achieved with corresponding values of 0.95 and 0.94, respectively. The absolute fit measures of SRMR and RMSEA were 0.04 and 0.07, indicating good and moderate fit, respectively.

Conclusion

The study indicated a high internal consistency and validity of items with good fit to the data, suggesting potential accuracy of the domains. A five-domain structure was developed which enables adequate assessment of perceived access to health-care services of patients with cervical cancer in Ethiopia. We suggest that the tool can be utilized in other patient populations with a consideration of additional constructs, such as geographic accessibility.

Background

Access to healthcare services is a multifaceted phenomenon encompassing broader concepts, involving the demand, identification, reach, and utilization of healthcare needs within the context of the ability to provide these services [1]. Frequently, access in the healthcare context has been viewed as the capacity of patients to reach services, healthcare providers, or institutions without encountering geographic, economic, or social barriers [2]. Gulliford et al. [3]. has argued that defining access in healthcare involves considering both vertical and horizontal equity factors across at least four dimensions: supply, utilization, acceptability, and affordability of services. Certain authors have presented clear and separate definitions of healthcare access. According to the theory by Penchansky and Thomas [4], access is achieved when the dimensions of affordability, availability, accessibility, accommodation, and acceptability, pertaining to both client and provider characteristics, are satisfied. Latter, an additional dimension, awareness, has been added by Saurman [5] as an integral component to access that should be considered along with the earlier dimensions.

Researchers have devised and suggested methods to capture patients' perceptions regarding access to healthcare services. Levesque et al. [1] introduced a more intricate assessment of access that took into account the capabilities of both recipients and providers. According to the authors, a comprehensive understanding of access involves measuring five dimensions of ability for accessibility (Approachability, Acceptability, Availability and accommodation, Affordability, Appropriateness) and the abilities of populations (Ability to perceive, Ability to seek, Ability to reach, Ability to pay, Ability to engage). On the other hand, a literature review by Quinn et al.(2017), highlighted that eleven main domains which six were related to access (access to primary care, specialty care, urgent care, spatial access, communication and cultural access) and five were related to care coordination(longitudinal, relational, informational, cross-boundary and follow-up) were reported [6]. An adaptation of previous theories has been utilized by Zandam et al. (2017) in Nigeria to develop a six-domain construct of access from users perspective [7]. In a more recent development, a Persian version of a questionnaire assessing perceived access to healthcare based on six domains was created, tested, and

validated in patients attending health centers [8]. A summary of the main definitions or dimensions proposed in the literature is presented in the table below (Table 1).

Given the descriptions and concepts provided thus far, individuals may perceive access to healthcare services differently in various contexts. Currently, perceptions of the primary domains, namely geographic accessibility, availability, affordability, acceptability, accommodation, and awareness, serve as crucial indicators influencing healthcare utilization, especially in Ethiopia. These domains are elucidated by various theories present in the literature, applicable in the developing context [9, 15]. Although there has been growing progress in various domains facilitating the measurement of access to healthcare resources, a gap exists in the validation of these tools for different contexts, where each component may be psychometrically understood inconsistently. The widespread adoption of validating a localized version of psychometric measures is particularly evident, especially in the case of cancer patients [16–18]. The approach ensures that the instrument is suitable, culturally sensitive, and reliable within the distinct context of the target population. Addressing this knowledge gap is a key objective of the study, especially in the Ethiopian context where the utilization of health services is considerably shaped by patients' perceptions [19, 20].

While ensuring the access of populations to health-care services still remains as a big challenge globally [21, 22], the problem faces a double-burden in Ethiopia augmented with

Table 1. Summary of definitions or dimensions of access commonly reported in the literature.

Study ID. and reference	Summary of Definitions, Models, or Dimensions
Cabieses and Bird, 2014 [9]	The article outlined a glossary of terms and clarified the concept of access, underscoring its relevance to low and middle-income countries.
Buss et al., 2009 [10]	It delineates a managerial approach for healthcare access and emphasizes the administrative responsibilities essential for ensuring accessibility to health coverage, providing a detailed account of the execution of these tasks.
Gulliford et al., 2002 [3]	Highlighted the dependence of access on the affordability, physical accessibility, and acceptability of services.
Aday and Andersen, 1974 [11]	The article explored indicators related to access to healthcare services. In this framework, the dimensions of system and population were classified as process indicators, while utilization and satisfaction components were recognized as outcome indicators within a theoretical model of access.
Penchansky and Thomas,1981 [4]	Originally introduced, a definition stipulating that access is demarcated by five distinct dimensions: availability, accessibility, accommodation, affordability, and acceptability.
Levesque et al.,2013 [1]	Formulated the five dimensions of accessibility as follows: 1) Approachability; 2) Acceptability; 3) Availability and accommodation; 4) Affordability; 5) Appropriateness. Simultaneously, the Levesque framework established five corresponding abilities of populations to facilitate access: 1) Ability to perceive; 2) Ability to seek; 3) Ability to reach; 4) Ability to pay; and 5) Ability to engage.
Beth E Quill, 2008 [12]	Defined access to healthcare as the achievement of individual utilization of healthcare services and the factors that either enable or impede one's health.
IOM,1993 [13]	Outlined access to medical care as the timely utilization of individual health services aimed at achieving optimal health outcomes. Emphasized that such access should be marked by safety, effectiveness, timeliness, patient-centeredness, efficiency, and equity.
Anderson, 1968 [14]	Proposed the initial three-stage behavioral model of healthcare access, utilizing predisposing, enabling, and need components to explain the varied utilization of medical care services by families.
Saurman, 2016 [5]	Modified Penchansky's access model by integrating the component of awareness.
Quinn et al., 2017 [6]	Expressed that metrics like 1) acceptability of the distance to the care site, 2) the burden on patients to access and coordinate care and billing, and 3) provider familiarity with veteran culture and processes are limited in standard assessment instruments.

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inequitable accessibility of inputs [23, 24] and poor uptake of services on the other end [25]. This may be attributed to differences in the level of health facilities, economic status of patients, provider-related issues, and causes rooted in local contexts. While the healthcare system in Ethiopia primarily emphasizes a preventive approach, initiatives to enhance tertiary care services, especially for individuals with cancer, are in their early stages. The country introduced its initial national cancer control plan, aligning with the national priorities of the Health Sector Transformation Plan (HSTP) 2015/16-2019/20. The goal was to reduce the incidence and mortality of cancer through comprehensive preventive and treatment strategies [26]. As yet, the incidence of cervical cancer and its associated risk factors is increasing, establishing it as the second most prevalent and the second most fatal cancer in the country according to a 2018 report [27]. A recent qualitative study highlighted that lack of awareness, misconceptions, and negative perceptions were common reasons for the low uptake of cervical cancer screening [20]. Another study reported that patients had low perceptions of risk to cervical cancer while availability of equipment, space and training for providers [28]. Due to the abstract and comprehensive nature of the concept, the existing reports in Ethiopia may not provide a full picture of the issue under consideration. This could be due to reports focusing on only certain domains, employing solely qualitative methodologies, or using non-validated tools. Consequently, comprehending the extent of the problem and its contributing factors may pose a challenge, given the lack of standardized and validated tools, especially for patient reported outcomes that involve a psychometric component. Psychometric measures facilitate the modeling and establishment of how psychological constructs, like human intelligence or psychological abilities, can be quantitatively estimated based on a set of observable scores [29]. Their function in illustrating individual cognitive variations and attitudes toward a behavior can assist researchers in making informed decisions when crafting a study, including determining the optimal number of trials for a task [30]. Additionally, measuring patients' perceptions of the care provided at tertiary centers is highly significant for identifying their expectations and designing appropriate interventions [31, 32].

The objective of this study was to validate the psychometric assessment of the Amharic-version regarding patients' perceived access to healthcare services in the Ethiopian context. Access to healthcare services was treated as a second-order latent factor, incorporating additional latent domains reported in the literature as first-order factors.

Methods

Study context, design, and population

This research was conducted at the oncology centers of two tertiary public hospitals, Tikur Anbessa Specialized Hospital (TASH) and Saint Paul's Hospital Millennium Medical College (SPHMMC) in Addis Ababa, Ethiopia. These hospitals are among the top referral units in the country, providing specialized and comprehensive healthcare services along with medical training. Established in 1969 by the German Evangelicals, SPHMMC is currently under the administration of the federal Ministry of Health of Ethiopia (FMOH). In addition to its academic functions, it offers a diverse range of healthcare services with 392 beds, serving an annual average of 200,000 patients and a catchment population of over 5 million [33]. The hospital, currently, provides all chemotherapy services except radiotherapy to patients diagnosed with cervical cancer. TASH is likely the oldest and largest referral hospital in the country, boasting 700 beds and being owned by Addis Ababa University. In addition to providing training across various health disciplines, the hospital offers healthcare services to patients referred from all parts of the country. The hospital's dedicated oncology unit, situated in the 5th police station, provides both inpatient and outpatient oncology services, covering radiotherapy,

chemotherapy, surgery, and chemoradiotherapy [34]. A cross-sectional design was implemented between 1st January and 30th March 2023 to validate the 30-item Amharic version of perceived access to health-care services in patients with cervical cancer. Efficient and swift, this design was deemed suitable for our study, aiming to gauge the validity of constructs related to access to healthcare services. The assessment occurs at a specific point in time, capturing a snapshot of the data from patients. All patients with a confirmed diagnosis of cervical carcinoma, undergoing follow-up during the study period, and consenting to participate, were consecutively enrolled. Although not a strictly random selection technique, consecutive sampling was chosen in this study because the participants shared homogeneity in terms of diagnosis, the patient population's number and flow were limited and stable, ensuring temporal representation during the three-month data collection period. This technique also reduces selection bias, provided that the primary referral settings were simultaneously included. As studies suggested that a participant to item ratio of 5:1 or that a sample size of at least 200 would be adequate for factorial validity [35, 36], a total sample of 308 patients was recruited and assessed.

Validity and reliability of the instrument

Ensuring the validity and reliability of any quantitative research tool is a crucial step to assure the internal and external validity of findings. This is especially pertinent in cases like ours, where the tool predominantly incorporates a hierarchical and abstract psychometric component. This, in turn, plays a significant role in generating robust and accurate results that can be replicated [37]. The validity and reliability of the instrument used in data collection have been emphasized, employing a variety of approaches sequentially to ensure its accuracy and consistency. Presently, the concept of access to healthcare remains intricate, and the proposed domains and items may not comprehensively capture its complexities. Various additional factors may still influence, potentially resulting in insufficient scoring or factor loading. In some cases, an item might show reliability without indicating validity, posing a challenge when trying to generalize results. Despite this, the steps highlighted in the guidelines by Tsang et al. [38], and Yusoff and colleagues [36] were adhered to during the adaptation and validation process of the questionnaire. In general, the entire process of instrument development has undergone a sequence of five key steps, which include instrument design and adaptation, translation, validity testing of the draft instrument, piloting, and psychometric evaluation of the construct. The specific method, whether qualitative or quantitative, to be employed, along with the detailed steps and necessary inputs during each stage, are described below.

Instrument design and adaptation

The psychometric domains and constructs for assessing patients' perceived access to healthcare services have been adapted from a recently developed and validated questionnaire by Hoseini and colleagues [8]. The tool has demonstrated satisfactory fit in the Persian context, where the health system and economic conditions are quite similar to ours. In fact, some sections of the tool were designed and recommended by previous researchers for assessing access to healthcare [1, 4]. The earlier instrument, which focused on primary healthcare services, has been modified to suit the current study settings, particularly secondary healthcare services for patients with cancer. Consequently, the constructs were adjusted to be applicable to any health facility, not restricted to health centers. The items assessing availability were entirely revised to inquire about the availability of medicines, an adequate number of staff, and the skills of health personnel at the settings. The first domain, originally named 'accessibility,' has been changed to 'reachability' to better reflect geographic access to services. Additionally, the first item, 'the services I request are given at the health center,' was removed as it was considered redundant

with specific inquiries under the 'availability' domain. Furthermore, an item in the 'acceptability' domain has been revised to account for religious diversity in the current setting, in addition to the cultural differences mentioned in the earlier version. As details on the contents of sections 1 and 2 of the instrument have been provided in previous sections, the focus of validation and subsequent descriptions will be on the adapted psychometric instrument. To navigate cultural nuances during the translation and validation processes, various measures were implemented. These included engaging experts in public health and research with a background in tool translation, consulting with senior experts familiar with the local health system, ensuring that all experts involved in the tool content validation were informed about the study objectives, incorporating back-translation, and conducting pilot testing of the instrument.

Forward translation to Amharic version

Two translators took part in the translation process of the initially adapted psychometric instrument into Amharic. In an effort to minimize disparities in content interpretation, the principal investigator (PI), possessing a master's degree in pharmacoepidemiology and considerable experience in translating research instruments, undertook the initial translation of the original content. Subsequently, a public health specialist, well-versed in tool translation and qualitative research, and without prior knowledge of the study's objective, conducted the second translation. Any discrepancies arising between the two translations were addressed through discussion or by seeking the input of a third translator.

Backward translation

In this phase, the Amharic version of the instrument underwent back-translation into English to ensure the consistency of items with the adapted version and to identify any unforeseen deviations. Two public health specialists, well-versed in research methodology and unfamiliar with the study objectives and the intended message of the entire instrument, participated in the back-translation process.

Content validity

Validity, by definition, refers to the extent to which collected data accurately represents the phenomenon under investigation or "measures what is intended to be measured" [39]. Both qualitative and quantitative methods of content validity have been implemented, as they were employed by a panel of experts in the primary psychometric evaluation of the original tool [8]. The purpose of this assessment was to evaluate the instrument, in a multidisciplinary approach, for potential use in the Ethiopian context. It is recommended that the content validation process includes four essential steps: domain definition, domain representation, domain relevance, and appropriateness of the test construction procedure [40]. As a qualitative method for ensuring validity, a purposively selected group of health professionals, including physicians, nurses, pharmacists, researchers, and public health experts, were invited to assess the domain content, wording, appropriate placement of items, and relevance for measuring perceived access to healthcare services, specifically in patients with cervical cancer. The selection of the expert panel was specifically guided by the contents of the tool from the perspectives of the mentioned professions, some of whom had experience in cancer care and research. Subsequently, individual information was collected and incorporated into the tool before proceeding to quantitative evaluation. The feedback received from the panel played a crucial role in refining and enhancing the final instrument. A systematic process was followed to incorporate the feedback, which included thorough reviews of each input, prioritization based on relevance and potential impact, discussions with panel experts, iterative revisions, and validation.

The quantitative process of content validation in this study has undergone the necessary steps outlined elsewhere, including domain definition and representation. The approach was carried out using both a face-to-face (by panel of experts) and a non-face-to face approach (using an electronic assessment form) [36] and was centered on assessing the essence, relevance, and appropriateness of the scale.

The evaluation criterion for item relevance was structured using a 3-level Likert scale: "item is essential," "item is useful but not essential," and "item is not essential." Subsequently, content validity ratio (CVR) and content validity index (CVI) values were calculated. The formula for content validity ratio was CVR = (Ne—N/2) / (N/2), where Ne is the number of panelists indicating that the item is "essential," and N is the total number of panelists, as documented earlier by Lawshe [41]. The decision of whether to include an item in the scale depended on the number of experts and the corresponding minimum ratio recommended in Lawshe's table. Panelists or experts were furnished with an evaluation format to assess the level of agreement they could report based on the essence of the items in question.

Similarly, we employed a widely recognized method of content validity known as the content validity index (CVI). The CVI assesses the relevance and clarity of items. According to Davis [42], a 4-point ordinal scale (1 [not relevant], 2 [somewhat relevant], 3 [quite relevant], and 4 [highly relevant]) was incorporated to evaluate both dimensions.

Utilizing the scale provided in the table, two measures were computed: the item-level content validity index (I-CVI) and the scale-level content validity index (S-CVI). The I-CVI indicates the proportion of agreement on the relevance of each item, ranging between 0 and 1, while the S-CVI is defined as "the proportion of total items judged content valid." An I-CVI of 80 percent or higher is generally considered "appropriate" [43]. Some studies suggest that 78% (0.78) is an acceptable lower threshold for I-CVI, while S-CVI is considered excellent when it achieves a score of at least 80% [44].

Face-validity

Face validity was assessed to determine if the instrument ultimately gains acceptability based on its face value by the respondents. This aspect of validity addresses whether an instrument appears valid to subjects, patients, and/or other participants [38]. One can address this question from the participants' perspective by assessing their agreement with the items and their wording in the instrument to fulfill the research objectives. Another definition of face validity is the extent to which a test seems to measure what it asserts to measure. It provides a broad evaluation as a quick assessment of what the test aims to measure [45]. Face validity can be assessed using a 5-point Likert questionnaire with options such as 'very important,' 'important,' 'relatively important,' 'slightly important,' and 'unimportant.' An item impact score is calculated by multiplying the frequency and importance. Frequency is determined by the percentage of participants with a score of 4 or 5, while importance is assessed by averaging the sum of scores for each item. Ultimately, the item impact score is obtained by multiplying these two results. The general guideline is that if the item impact of an item is equal to or greater than 1.5 (mean frequency of 50% and an importance mean of 3 on the 5-point Likert scale), it is advisable to retain it in the instrument; otherwise, it may be eliminated [46].

Piloting the instrument

A sample size of 30 participants was employed in this test, a size deemed suitable for identifying any issues (such as ambiguities or misunderstandings) in the instrument, as per documented acceptability [47]. In this phase, the demographic makeup closely mirrored that of the broader study population with respect to variables like diagnosis, study setting, and source

population. However, it's crucial to emphasize that the pilot sample was separate and not included as part of the official study population. The primary objective of the pilot testing was to verify the face validity and internal consistency of the items and assess the duration required for an interviewer to complete the questionnaire. According to Yusoff [36], acquiring a standardized method for distributing the tool and conducting interviews, particularly for interviewer-administered questionnaires, was emphasized. Additionally, improvements were made to the flow, process of items, administration, and logistical aspects of the fieldwork during this phase. Accordingly, altering the sequence some items, determining the estimated time that an interview would take, and the management of the data collection process through the Kobo-Collect application were among the areas revised during this time. The rationales behind the modifications were to ensure logical flow of items, improve responders' trust, and ensuring the quality of the data collected. Finally, at this phase, a preliminary internal consistency test was performed to make sure if items are eligible for further development. This was done so because Cronbach's alpha is not an absolute measure of consistency under all circumstances [48], and variability across different samples is always inevitable-hence the need to test reliability of the measure for both the pilot and the construct validation. While the use of Cronbach's alpha was meant to check and improve the internal consistency of items per each domain, the confirmatory factor analysis was to assess the underlying construct validity of the instrument. In the context of our study, the goal was to measure specific constructs related to access to healthcare, and the CFA allows us to confirm that the observed variables (survey items) align with the hypothesized latent constructs, both at the first and the second order levels.

Initial reliability analysis of factor constructs

Reliability assesses the internal consistency of items within a scale, indicating whether the items in the instrument are conceptually compatible. In this study, the internal consistency of item constructs was evaluated using Cronbach's alpha. While a sample size of 20 to 30 patients is considered sufficient for evaluating the reliability of a survey instrument, as recommended elsewhere [49], we used the entire sample of respondents recruited as part of the factor analysis above, which also enhances the precision of estimates. In doing so, an alpha value of at least 0.7 was deemed acceptable [50].

Confirmatory factor analysis

Construct validity is a crucial concept in assessing a questionnaire designed to measure an unobservable construct, often referred to as latent variables. Evaluating the construct validity of a new instrument involves estimating its association with other measures within the same domain, typically utilizing a different scale. This correlation may manifest as positive, negative, or null [48]. As such, this study assessed four types of construct validity: convergent validity (positive correlation), divergent (discriminant) validity (poor correlation), known-group validity, and factorial validity.

Derived from content analysis, factorial validity was utilized in this study as the suitable method for evaluating the validity of item constructs within the domains of access to healthcare services. This choice was made due to the presence of 30 items distributed across six latent domains associated with the concept of perceived access to healthcare. In the analysis of factorial validity, it is expected that several items intended to measure a specific dimension within a construct of interest would exhibit higher interrelatedness compared to those measuring other dimensions [7, 48]. This implies that factor analysis unveils relationships among items, between items and constructs, and among different constructs [51].

The interpretation of results from the confirmatory factor analysis (CFA) was as follows: Model fit was considered good if the Tucker Lewis Index (TLI), Normed-Fit Index (NFI), non-normed-fit index (NNFI), and goodness of fit (GFI) were ≥ 0.95 or acceptable if ≥ 0.90. Comparative fit index (CFI) and adjusted goodness of fit (AGFI) were considered acceptable if ≥ 0.90. For the root mean square error of approximation (RMSEA), a fit was considered good if ≤ 0.05 and moderately acceptable if between 0.05 and 0.08. The ratio of $\chi 2$ to degrees of freedom ($\chi 2$/df) was deemed the best fit when below 2 and moderate fit when it ranged between 2 and 3 [52, 53]. To distinguish the discriminant validity across included latent variables in the model, Henseler's later heterotrait-monotrait (HTMT2) ratio method [54] was utilized.

Data collection process and quality assurance

After translation and initial content and face validation, data for the study were gathered using an interviewer-administered structured instrument created in the KoboCollect mobile-based application. Subsequently, the data were managed through the KoboToolbox server [34]. Five data collectors, consisting of three individuals with master's degrees and two general practitioners, were engaged in the data collection process. A one-day training session was conducted for both data collectors and supervisors, encompassing a comprehensive orientation to research ethics, study objectives, and familiarity with the instrument. This thorough training aims to equip data collectors and supervisors with the essential skills, understanding, and cultural awareness needed for consistent and accurate data collection, thereby enhancing the overall quality and reliability of the study findings. In addition to pretesting and training, continuous supervision of the data collection process and adherence to the study protocol were implemented to ensure quality.

Data analysis

Data was cleaned and coded in MS-Excel for windows, R programming [55], and Amos software v.26 for analysis [56]. Descriptive statistics were utilized to illustrate participants' profiles, while structural equation modeling (SEM) was employed to present model fitness indices, a standardized correlation matrix, and the structure of the construct. Given the violation of normality assumptions, measurements were compared against bootstrapped estimates with confidence intervals and standard errors of the sample. Known group validity was confirmed using Student's t-test (for two-grouped variables) and one-way analysis of variance (one-way ANOVA) for variables with more than two categories. The estimates in the t-test were based on the second row (assuming unequal variances), while the post-hoc pairwise comparison in ANOVA utilized Dunnett's T3 calculation [57]. The computation of divergent validity was estimated the methods proposed by Henseler et al. [54]. The application of the mentioned models and specified analysis methods was considered suitable for the nature of the collected data, aiming to generate quantitative findings relevant to the research question objectives.

Ethics consideration

The study received ethics approval from Saint Paul's Hospital Millennium Medical College (SPHMMC) (Ref.no: PM23/284), and a support letter was issued to Tikur Anbessa Specialized Hospital (TASH) (Ref.no: PM23/295) as part of the mini-grant offer obtained from Saint Paul Institute for Reproductive Health and Rights (SPIRHR). Verbal informed consent was obtained from all patients participating in this study. The informed consent process entails a comprehensive explanation of the study objectives, procedures, and potential risks and benefits to participants. Verbal consent requests are presented to participants, and any questions

they may have are addressed before securing their voluntary agreement to participate. To uphold confidentiality and privacy, participant identities are anonymized, data is securely stored, and access is restricted to authorized personnel. These measures are implemented to safeguard sensitive information and maintain ethical standards throughout the study.

Results

Characteristics of participants

A total of 308 participants took part in the current survey. Among them, 202 (65.6%) were referred patients from outside of Addis Ababa. The mean (SD) age of the patients was 50 (±11) years, ranging from 24 to 83. Over half (57.8%) were married, and approximately half (51%) had basic literacy skills. Additionally, more than two-thirds (69.5%) reported having a family size larger than 5. The median monthly income for households was reported to be 4000 ETB, with a mean (SD) of 4539 (±3325) ETB. About 55.5% of the respondents surpassed the extreme poverty line according to the World Bank's income classification for low-income countries. Among the respondents, 138 (44.8%) were housewives, and nearly three-quarters (74%) had coverage under community-based health insurance (CBHI). Examining clinical profiles, 128 (41.6%) were in stage II of the disease, followed by 111 (36%) in stage III. The majority (64%) had no history of any chronic comorbidity (see Table 2). In broad terms, the demographic profile of participants indicates that a significant portion of oncology center attendees were referred from various regions of the country, were married, had family sizes exceeding 5, earned monthly incomes above the extreme poverty line, possessed coverage under CBHI, and had a history of comorbidities. Consequently, the validated instrument is expected to be applicable and relevant to patients with similar characteristics throughout the country.

Initial validity and reliability assessment

In this phase, a series of qualitative and quantitative validity assessments were conducted. Seven experts with diverse specializations, including clinical (MD), public health research (MPH), qualitative methods (MPH), pharmacy service (BPharm), Microbiology (MSc), pharmacoepidemiology (MSc), and lab quality assurance (MSc), were invited to evaluate the content and face validity of the 30-item adapted instrument. Two experts were involved in both forward and backward translation processes. After modifying two components (changing the factor name from 'access' to 'reachability' or referring to geographic access and altering 'screening for cervical cancer' to 'breast or colon cancer'), quantitative measures were derived from expert opinions. The first adjustment aimed to prevent confusion. In the earlier version, the term 'access' referred specifically to geographic access, causing confusion with the broader concept of access covering all constructs under investigation. In the second modification, we opted to replace "screening for patient breast or colon cancers" instead of cervix. This change was made to align with the study population, which consists of patients already diagnosed with cervical cancer. The Content Validity Ratio (CVR) calculated ranged from 0.5 to 1, while the Item-Level Content Validity Index (I-CVI) values varied from 0.75 to 1. The Scale-Level Content Validity Ratio (S-CVR) was 0.91. Additionally, face validity scores ranged from 2.4 to 4.8. The obtained content validity ratio (CVR) and item-level content validity index (I-CVI) values suggest strong content validity for the instrument. Higher values indicate a consensus among experts on the necessity and relevance of the items, affirming the quality of the instrument in assessing the intended constructs related to healthcare access in the study context. Following content and face validity assessments, the instrument was distributed to a sample of 30 participants to measure its reliability. The Cronbach's alpha for the entire scale was 0.72. Higher

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Table 2. Characteristics of study participants among patients visiting oncology centers in Addis Ababa, Ethiopia.

Characteristic	Label	Frequency	Percent
Residence			
	Addis Ababa	106	34.4
	Outside Addis Ababa	202	65.6
Age category (Yrs.)			
	50 or less	184	59.7
	>50	124	40.3
Marital status			
	Married	178	57.8
	Single	15	4.9
	Separated	10	3.2
	Divorced	33	10.7
	Widowed	72	23.4
Literacy status			
	Yes	157	51.0
	No	151	49.0
Number of family members			
	5 or less	214	69.5
	> 5	94	30.5
Average monthly income*			
	3567 or less ETB	137	44.5
	>3567 ETB	171	55.5
Presence of social support			
	Yes	167	54.2
	No	141	45.8
Employment status			
	Government employee	18	5.8
	Private employee	53	17.2
	House wife	138	44.8
	Jobless	49	15.9
	Others**	50	16.2
Current status of CBHI coverage			
	Yes	228	74.0
	No	80	26.0
Stage of cancer			
	Stage I	48	15.6
	Stage II	128	41.6
	Stage III	111	36.0
	Stage IV	21	6.8
Presence of any chronic comorbidity			
	Yes	114	37.0
	No	194	63.0

*classification was based on the 2022 update on extreme poverty classification (USD 2.15/person/day) for low income countries [58] and the USD and Birr exchange rate in August 2023.

** indicates merchants or farmers.

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Table 3. Factor-level reliability test assessment of indicators on perceived access to healthcare among patients visiting oncology centers in Addis Ababa, Ethiopia.

Factor	Number of items	Factor-level reliability (std. alpha)	Item label	Reliability if an item is dropped (std. alpha)	Remark
Availability	2	0.76	AV3	0.62	Retained after removal of AV1 and AV2
			AV4	0.62	
Acceptability	7	0.93	AC1	0.92	Retained after removal of items AV6 and AV7
			AC2	0.92	
			AC3	0.91	
			AC4	0.92	
			AC5	0.92	
			AC8	0.92	
			AC9	0.92	
Affordability	3	0.87	AF1	0.75	No item has been dropped
			AF2	0.73	
			AF3	0.95	
Accommodation	3	0.76	ACC1	0.81	Retained after removal of items ACC2, ACC3, and ACC6
			ACC4	0.63	
			ACC5	0.56	
Awareness	4	0.90	AW1	0.86	Retained after removal of AW5
			AW2	0.91	
			AW3	0.85	
			AW4	0.87	

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alpha values, typically greater than 0.7, reflect stronger internal consistency, reinforcing the instrument's reliability in consistently measuring the factors under investigation.

Internal consistency of factors

As illustrated in Table 3 below, an assessment of factor-level reliability was conducted to evaluate the internal consistency of item constructs within each of the six domains. If the removal of an item resulted in an improvement in factor-level consistency, that specific item was excluded. However, all factors were required to exhibit a Cronbach's alpha of at least 0.7 to qualify for subsequent factor analysis. Additionally, a factor loading of at least 50% in the structure matrix was expected. Despite the factor 'reachability' achieving an acceptable Cronbach's alpha value of 0.98 with two items, it was excluded from the final second-order structure matrix due to its very low loading (0.12).

Convergent validity

The assessment of convergence among the items within each factor and the latent variables explaining perceived access to healthcare services involved evaluating composite reliability (CR) and average variance extracted (AVE). Upon examination of these measures, it was observed that all factors met the recommended minimum threshold of 0.6 for CR, signifying a high level of reliability for the scale. This measure aligns with Cronbach's alpha values, suggesting good construct reliability. Similarly, the AVE for each scale was computed, and the findings indicated that the average reliability of each factor exceeded the recommended threshold of 0.5, affirming model fit. In conclusion, both CR and AVE measures support the notion that the construct fits the data well. Additionally, the higher CR compared to AVE suggests strong reliability. The latent variables of the first-order scale were treated as inputs for the second-order model (Table 4).

Table 4. Convergent validity of latent factors in perceived access to health-care services in patients with cervical cancer visiting oncology centers in Addis Ababa, Ethiopia.

Factor	Composite reliability (CR)	Average variance extracted (AVE)
Availability	0.67	0.67
Acceptability	0.93	0.67
Affordability	0.88	0.72
Accommodation	0.77	0.54
Awareness	0.90	0.69
Perceived access to health care	0.95	0.80

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Divergent validity

The instrument's divergent validity was assessed using the updated criterion of the hetero-trait to mono-trait (HTMT2) ratio, as proposed by Henseler et al. (48). This method involves calculating the ratio of the sum of intra-factor level correlations to inter-factor level correlations to gauge the discriminant ability of a latent variable in comparison to other latent variables. Among the ten pairs of factors examined, eight demonstrated an acceptable level of discriminant validity (below 0.90), while two pairs, specifically acceptability vs. awareness and acceptability vs. availability, exhibited a slightly higher value (0.91) compared to the recommended threshold mentioned earlier (Table 5). While this ratio helps determine the extent to which different latent variables discriminate from each other, the implications of the two factor pairs, acceptability vs. awareness and acceptability vs. availability, showing higher values (0.91), suggest a potential overlap or shared variance between these constructs. This may indicate some degree of interrelatedness or conceptual similarity between acceptability and awareness, as well as acceptability and availability.

Known-group validity

The instrument's validity was assessed by examining its ability to discriminate between various groups within the same sample, anticipating differences in their perceptions of access to healthcare services. These groups included income category, health insurance coverage, social support presence, and occupation. The construct effectively differentiated between groups based on average monthly income, with those above the extreme poverty line scoring significantly higher than those below the line ($t = -5.95$; $df = 187.8$; $p<0.001$). Similarly, individuals with current community-based health insurance (CBHI) coverage exhibited a relatively low mean aggregate score, indicating a poorer perception of access to healthcare services ($t = -5.65$ $df = 200.7$; $p<0.001$). Moreover, respondents reporting any form of social support had a significantly higher mean aggregate score for perceived access to healthcare services ($t = 3.39$; $df = 186.4$; $p = 0.001$). Furthermore, a post-hoc analysis using one-way ANOVA with

Table 5. Divergent validity of latent factors in perceived access to health-care services in patients with cervical cancer visiting oncology centers in Addis Ababa, Ethiopia.

Awareness					
Accommodation	0.76				
Acceptability	0.91	0.81			
Affordability	0.74	0.66	0.79		
Availability	0.85	0.76	0.91	0.74	
	Awareness	Accommodation	Acceptability	Affordability	Availability

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Dunnett's T3 comparison method revealed variations in perceived access to healthcare services among different occupation groups. Specifically, government employees had a significantly higher mean aggregate score compared to housewives (mean difference = 7.10; 95% CI = 1.85–12.27; p = 0.003) or those with no job at all (mean difference = 12.72; 95% CI = 5.16–20.18; p<0.001). The findings from the known group validity analysis indicate that the instrument effectively distinguishes between groups based on income, health insurance status, social support, and occupation. Higher mean scores among individuals with income above the extreme poverty line, those without current community-based health insurance (CBHI) coverage, and those reporting any form of social support suggest a more favorable perception of access to healthcare services in these groups. Additionally, the instrument highlights significant variations in perceived access to healthcare services among different occupation groups, with government employees scoring notably higher compared to housewives or those without employment. Overall, these results demonstrate the instrument's ability to discriminate between diverse groups based on their characteristics and perceptions of healthcare access.

Model fitness indices

The overall fit of the construct was evaluated using various parameters, as outlined in Table 6. Despite the chi-square statistics for goodness of fit not rejecting the null hypothesis of good fit (pCMIN<0.001), the ratio of minimum discrepancy to the degree of freedom fell within the range of 2<CMIN/df<3, indicating a well-fitting model. The normed fit index (NFI), a size-insensitive measure of fitness, yielded a favorable value of 0.93, suggesting that the present model was a good fit. An alternative adjustment to the NFI using the incremental fit index (IFI) and comparative fit index (CFI), both considering sample size and degrees of freedom, resulted in higher values (0.95), indicating a well-fitted model. Additionally, the Tucker-Lewis Index (TLI), accounting for degrees of freedom, indicated a better fit. The standardized root mean square of residuals (SRMR), measuring the difference between observed and implied correlation matrices, was notably lower at 0.04, well below the recommended ceiling of 0.08. Lastly, the standardized root mean square error of approximation (RMSEA) value was quite low at 0.07, suggesting a moderate to acceptable fit of the data to the model (see Table 6).

Observing these results, the model fitness indices collectively indicate a good fit of the data. While the chi-square statistic did not reject the null hypothesis of a good fit, other indices such as NFI, IFI, CFI, TLI, SRMR, and RMSEA consistently support the conclusion of a well-fitted model. These indices consider factors such as size, sample characteristics, and degrees of freedom, providing a comprehensive evaluation of the overall fit of the model.

Table 6. Measures of fit indices of latent constructs in perceived access to health-care services among patients with cervical cancer visiting oncology centers in Addis Ababa, Ethiopia.

Fit measures	Fit indices of the default model
CMIN	386
CMIN/df	2.82
IFI	0.95
NFI	0.93
CFI	0.95
RFI	0.91
TLI	0.94
SRMR	0.04
RMSEA	0.07

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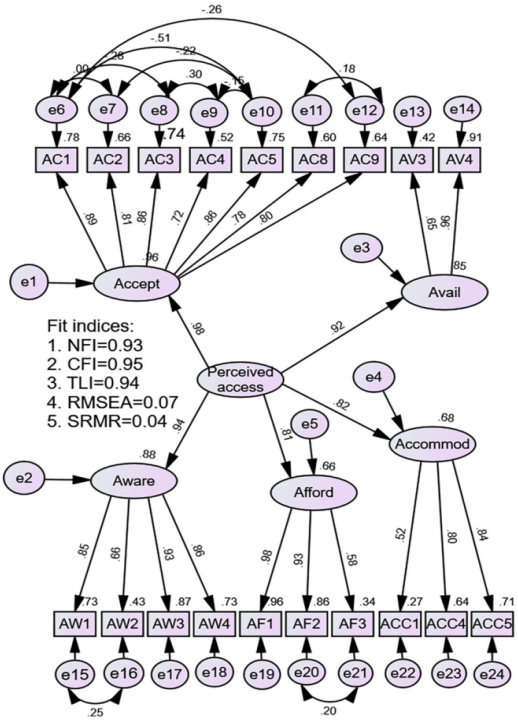


Fig 1. Structural equation modeling of the construct structure in perceived access to healthcare services among patients with cervical cancer visiting oncology centers in Addis Ababa, Ethiopia.

https://doi.org/10.1371/journal.pone.0300815.g001

The second-order structure of the instrument, comprising 19 items and 5 latent domains, along with selected model fit indices, is illustrated in the figure below (Fig 1).

Discussion

The objective of this study was to validate the Amharic version of a psychometric measure assessing the perceived access to health-care services among patients with cervical cancer in Ethiopia. The research adhered to the necessary epistemic procedures essential for a psychometric test. Significantly, it addressed a crucial aspect of the validation process by not only focusing on the measures of interest but also ensuring the validity of the employed procedures [59]. Validating the measure in the Ethiopian context is crucial as it ensures that the instrument is culturally and linguistically appropriate, contributing to the accurate assessment of perceived access to healthcare services among the target population in Ethiopia. This validation enhances the reliability and applicability of the measure in the local context, facilitating more meaningful and culturally sensitive research in the field of cervical cancer care in Ethiopia. Furthermore, preparing and validating a local-language version of an instrument is deemed beneficial to ensure stability of measures it stands for and eases comparison of

findings across similar settings. The requirement for a valid tool in such researches stems from the need in a theoretically founded and precise comprehension of abstract concepts commonly encountered in health sciences [60].

The initial activity (phase I) involved the design and adaptation of the original instrument, encompassing both qualitative and quantitative tasks. This was succeeded by piloting the instrument (phase II) and conducting factorial analysis (phase III), with the latter two phases discussed in subsequent paragraphs. During the qualitative evaluation, domain-specific items were revised so that the scope and relevance of an item would be examined to fit in the present context. As such, consideration from the earlier sources [1, 4, 8] were taken into account with an effort to fit the population of interest, treatment setting and relevance of a variable. This is an important element in cross-cultural adaptation of an instrument since failure to consider current settings may result in deviated outputs [61]. Almanasreh et al., (2019) too regarded content validation a necessary step as an item is identified than quantitatively scored [40]. In other words, the expert panels were to evaluate and decide which items to be included in the new instrument, how the wording should be put in the Amharic version and if some words should be replaced with synonyms (for example, screening for colon or breast cancer instead of cancer). In the quantitative component, numeric ratings were assigned to the items within each domain. These scores were then aggregated and compared against established thresholds. As a result, the outcomes from the subsequent calculations fell within the acceptable range, indicating a consensus among expert ratings. The minimum value in the CVR, I-CVI, and S-CVI were 0.5, 0.75, and 0.91 respectively. Out of a total of 30 items, only two items scored an I-CVI of 0.75 whereas, in the remaining, it was 0.88 or higher. Hence, most of the scores are in agreement with suggested ranges in the literature [8, 62]. More specifically, quite conservative reports in the literature have been reported for an excellent I-CVI score falling at 0.78 or higher [36, 44, 63].

After the successful assessment of the initial phase and the reliability evaluation of the piloted instrument on a limited sample size (Phase II), it was subsequently employed on a larger sample of cases for the assessment of factorial validity. The internal consistency of items in the factor analysis was found to satisfy the model excellently for most of the constructs. Sequential improvement was sought for some of the dimensions by dropping items from the construct. In fact, this was carried out only for those unidimensionality was severely disturbed and not in cases where the minimum level of at least 0.7 was attained. There is evidence in the literature claiming that a very high alpha value is not always trustable as it may offer limited reliability, especially, when testing a scientific knowledge [64]. In addition, we restricted item inclusion with a factor loading 0.4 or higher both for the first and second order model structures. This follows the recommendation proposed by Stevens (2012) as the minimum cut-off criteria for factor loading in structural equation modeling [65]. On the other hand, Hair et al., (2011) argued that a standardized factor loadings of at least 0.5 for an item or a construct (for higher orders) to explain 25% of the variance of a construct of interest [66]. Accordingly, the final model, in the present study, contained five domains with 19 observed items. One of the first order constructs 'reachability' was not included in the matrix structure of the second order CFA as its loading value was extremely low (0.12). Alternatively, the six-domain model could also be structured with acceptable fit assuming independent identification of factors. However, perceived access to healthcare services should better be conceptualized as second order construct from the other first order constructs (accessibility, acceptability, availability, accommodability, and awareness) as it offers a reasonable theoretical basis of the usual healthcare care practice. The observed high internal consistency indicates strong coherence among items within constructs. The decision to selectively drop certain items, guided by factor loading criteria, enhances the instrument's applicability and reliability. By retaining only items

with substantial contributions, the refined instrument becomes more precise, aligned with theoretical foundations, and offers improved reliability and validity in assessing perceived access to healthcare services.

Other measures of validity namely, convergent validity, divergent validity and known-group validity were performed. The result of convergent validity of items per each construct was such that both composite reliability (CR) and average variance extracted (AVE) met the acceptable value of at least 0.6 and 0.5 respectively as suggested elsewhere [67, 68]. Divergent validity assessment using the improved HTMT2 methods [54] revealed a good fit to the threshold except a couple of the constructs suggesting presence of multicollinearity, i.e the factors acceptability and availability and acceptability and awareness showed a concern of discriminant validity. As opposed to items meant for measuring poorly related concepts in which case the value of discriminant validity would expected to be low [69], this result could be viewed as to the fact that the constructs considered are substantially correlated. The observed multicollinearity between certain constructs suggests potential overlap or correlation between them. This could arise due to shared conceptual elements or interconnected aspects of the constructs being measured. The presence of multicollinearity may impact the interpretation of results by making it challenging to isolate the unique contributions of each construct. In other words, the high correlation between certain factors may lead to challenges in attributing variations in the outcome specifically to one construct, potentially complicating the understanding of the individual effects of those correlated constructs. The significant multicollinearity observed between these pairs of constructs may suggest their interconnected nature rather than indicating a flaw that needs further refinement, particularly in the case of acceptability vs. awareness. However, a thoughtful examination and exploration are warranted to better understand the interconnectedness of acceptability vs. availability in the healthcare context. Likewise, the instrument was able to discriminate between independent groups of the sample with considerable discrepancy of the outcome measure. It is presumably sound to accept that people at least with different income level [70], status of community-based health insurance coverage [71], presence of social support [72] and employment status [6] do act or react to access of healthcare services quite differently. The convergent validity findings assure that the instrument accurately measures intended constructs, enhancing its quality. Divergent validity identifies potential correlations, providing nuanced insights. Known-group validity signifies the instrument's ability to discriminate among diverse demographic groups, enhancing its utility across populations. Collectively, these findings affirm the instrument's quality, reliability, and applicability in assessing perceptions of healthcare access.

The model also demonstrated that the commonly utilized incremental fitness indices, namely CFI and TLI were achieved with the corresponding values of 0.95, and 0.94. This suggests that the sample data was able to fit the model adequately compared to the baseline (worst case) model. On the other hand, absolute fit measures, namely RMSEA and SRMAR were still in the acceptable range with corresponding values of 0.07 and 0.04 respectively. These indices measure how the hypothesized data fits the model compared to the perfect model. Even though it has been reported that RMSEA should be 0.05 or lower in order for a model achieves excellent fit [73], Chen et al. also argued that this classification does not have an empirical support to identify an absolutely good fit [74]. They proposed that other factors, such as degrees of freedom and sample size should also be taken into account. A level at or below 0.08 has also been suggested acceptable fit [36]. The SRMR is a measure of badness of model fit measured from the residuals covariance and the implied sample with values closer to zero indicating a characteristic of good fit [75]. The incremental fitness indices, CFI and TLI, indicate that the sample data fits the model adequately compared to the baseline model, enhancing confidence in the instrument's validation. The acceptable range of absolute fit measures, RMSEA (0.07)

and SRMR (0.04), suggests reasonable model fit. While the commonly cited threshold for excellent fit is an RMSEA of 0.05 or lower, it's important to consider additional factors like degrees of freedom and sample size. The SRMR, with values closer to zero, further supports the instrument's good fit. Overall, these nuanced interpretations collectively contribute to the comprehensive validation of the instrument.

The current study aimed to refine and validate the Amharic version of perceived access to healthcare services in the Ethiopian context, where no similar method was available. The model utilized a hierarchical second-order analysis, aligning with the theoretical conception of the phenomenon under investigation. Results obtained from the sample were compared with bootstrapped output, incorporating 95% confidence intervals to mitigate the impact of skewed distribution. Additionally, the study adhered to a series of recommended steps during the reliability and validity testing processes. However, limitations included an inadequate sample size impacting generalizability, a lack of discrimination between constructs affecting precision. In addition, relying on constructs from previous literature may introduce bias and limit adaptability to the specific Ethiopian context, potentially influencing outcomes by overlooking crucial factors.

Conclusion

The Amharic version of perceived access to health-care services revealed a good fit to be utilized by Ethiopian patients with chronic illness, particularly of cancer diagnosis. The developed scale embraces multidimensional psychometric domains which comprising of acceptability, availability, accommodability, affordability and awareness from patients perspective. The introduction into practice of this instrument will be useful for researchers, health service providers and policy makers to easily capture the perception of patients on their behavior towards demanding and consuming health. This will then guide their practice of service delivery and set for appropriate intervention plans. While the outcomes obtained through the method will be prone to reports of subjective nature, we recommend that researches and quality improvement initiatives that assess access to health-care utilization of patients also accompany with objective methods of measurement. We also suggest that the tool can be utilized in other patient populations with a consideration of additional constructs, such as geographic accessibility. Finally, future studies should prioritize larger samples, refine measurement items, and adopt a more context-specific approach to construct definition.

Supporting information

S1 File.
(DOCX)

S2 File.
(DOCX)

S3 File.
(DOCX)

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PAPER IV

BMJ Open

Spatiotemporal dynamics and prevention strategies of cervical cancer incidence in Addis Ababa, Ethiopia: an ecological study

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ABSTRACT

Objective This study analysed the spatial and temporal patterns of cervical cancer incidence in Addis Ababa from 2012 to 2021.

Design An ecological study was conducted from 1 September to 30 November 2023 to examine the spatiotemporal trends of cervical cancer incidence.

Setting The research was conducted in Addis Ababa, the capital city of Ethiopia.

Participants Included were all patients with clinically and/or histopathologically confirmed diagnoses of cervical cancer.

Data analysis The study employed advanced analytical tools including R programming, Quantum Geographic Information System V.3.36.0, GeoDa V.1.2.2 and System for Automated Geoscientific Analyses GIS V.9.3.2. Techniques such as Bayesian empirical testing with a block weighting matrix for hotspot identification, Global Moran's I for spatial autocorrelation, nearest neighbour imputation and universal Kriging interpolation were used to manage data gaps. Joinpoint trend analysis and direct age-standardised incidence rate (ASIR) using the Segi's World standard population was applied to compare trends across subcities. A statistical significance threshold was set at $p<0.05$.

Results Between 2012 and 2021, a total of 2435 new cervical cancer cases were recorded in the Addis Ababa City Population-based Cancer Registry, with significant spatial clustering observed in Nifas Silk Lafto, Bole, Kirkos as well as parts of Gulele and Yeka sub cities (z score>1.96) in 2018. The citywide age-standardised incidence rate varied from 19 to 26 cases per 100 000 women-years during 2013 and 2016, respectively. Subcity trends varied significantly, with increases and decreases noted in Akaki Kality and Kolfe Keraniyo over different periods while Bole subcity showed modest increase at 4.2% APC (95% CI: 0.6% to 7.9%; p=0.026).

Conclusion The study highlights substantial fluctuations in ASIR and significant geographic disparities in cervical cancer throughout Addis Ababa. To address these challenges, the implementation of school-based human papillomavirus vaccination programmes, alongside targeted interventions, active campaigns and sustained surveillance, is critical. These strategies are essential to effectively reduce the cervical cancer burden and improve health outcomes in the community.

STRENGTHS AND LIMITATIONS OF THE STUDY

⇒ This study's analysis spans a decade (2012–2021) using data from the Addis Ababa cancer registry, offering extensive insights into the spatial and temporal trends of cervical cancer.
⇒ The utilisation of sophisticated spatial and temporal analytical techniques, including Bayesian empirical testing and spatial autocorrelation, enhances the robustness of the findings.
⇒ Dependence on registry data that may suffer from under-reporting or incomplete records could potentially affect the accuracy of incidence rates.
⇒ The absence of detailed individual-level information, such as human papillomavirus status and socioeconomic factors, might limit the exploration of specific determinants of cervical cancer incidence.

INTRODUCTION

Cervical cancer continues to be a significant global health challenge, ranking as the fourth most common cancer among women, with nearly 660 000 new cases and 350 000 deaths reported in 2022, according to the WHO.[1] This burden is especially severe in low-income and middle-income countries, where access to prevention and early detection resources is critically limited.[2] Cervical cancer is primarily caused by persistent infection with high-risk human papillomavirus (HPV) types, particularly HPV 16 and 18, which are commonly transmitted sexually.[3] Preventative and clinical practices focus on reducing the incidence and enhancing early diagnosis through HPV vaccination,[4] regular screening[5 6] and timely treatment.[6] HPV vaccines, especially recommended for young adolescents before virus exposure, have proven highly effective in reducing HPV infection rates. Screening

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methods, such as Pap smears and HPV testing, are vital for the early detection of precancerous lesions, allowing for intervention before cancer develops. Collectively, these preventive strategies could significantly reduce cervical cancer incidence and improve patient outcomes, underscoring the need for accessible prevention programmes in high-risk populations. Prevention efforts and targeted interventions could be further optimised by using up-to-date evidence generated through rigorous methodologies, including spatial and temporal analyses.

Spatial analysis, a branch of geographic analysis employing mathematical techniques and geometry, elucidates the topological patterns of phenomena. While geographic information systems (GIS) facilitate the study and comprehension of real-world processes through manipulation, analysis criteria and modelling, spatial analysis, an integral aspect of GIS, allows modelling of both vector-based and raster data using sophisticated tools.[7] Its application in health programme monitoring and performance indicator display is well documented.[8 9] Temporal analysis, on the other hand, observes chronological event occurrences to reveal trends over time. Combining spatial and temporal metrics forms a spatiotemporal framework, an emerging field known as spatiotemporal data mining (STDM), which encompasses analysing event-based data, trajectories, time series, spatial maps and raster data. Key tasks within STDM include clustering, anomaly detection, frequent pattern mining, relationship mining, change detection and predictive learning.[10]

Globally, a variety of studies have depicted either the spatial or spatiotemporal pattern of cervical cancer, highlighting the significant role of GIS in its detection and mapping, along with other cancers.[11] According to a report on the application of spatial analysis in China, GIS can effectively display the distribution of cancer cases and employ spatial analysis methods and scanning statistical techniques to identify key areas of cancer incidence, thereby informing the development of regional public health policies and recommendations for cancer screening and resource allocation.[11] Many of these studies rely on national-level or district-level cancer registry centres, ensuring stable population data and high-quality epidemiological recording. Moreover, a spatial study in Uganda conducted by Beyer *et al* demonstrated the usefulness of population-based cancer registry data and geospatial mapping in low-resource settings, supporting cancer prevention and control efforts and enabling research into geographic factors influencing cancer outcomes.[12]

Many findings reported in the literature show an improvement in combining spatial and temporal analyses. Furthermore, several studies have incorporated multiple covariate models to assist in identifying potential factors exhibiting spatial autocorrelation.[13–15] Taking into account the specifics, Zhao *et al* demonstrated that cervical cancer incidence trends over time vary by religion, indicating disparities in sexual practices, lifestyle and culturally associated beliefs between Muslims and Buddhists. This suggests distinct risk factor profiles for these groups. For example, the elevated incidence rates (IRs) in Sadao and Hat Yai were reported to be attributed to the major road leading to Malaysia passing through these areas, facilitating frequent commercial sex trade. As such, targeting female sex workers as a vulnerable population for screening efforts is imperative to mitigate the persistent burden of cervical cancer.[13]

The incidence of cervical cancer in Ethiopia has been recorded at approximately 22.3 cases per 100 000 women per year, while the age-standardised mortality rates are estimated at 16.8 per 100 000 women-years.[16] These statistics highlight the considerable burden of the disease, positioning cervical cancer as the second most prevalent and fatal cancer among women.[17] Presently, there is a dearth of evidence concerning the spatial and temporal trends of cervical cancer, emphasising the crucial need for targeted resource allocation toward its prevention and management. This study endeavours to bridge this gap by offering a comprehensive and current understanding of the disease's IR, as well as its spatial and temporal dynamics in Addis Ababa, Ethiopia.

METHODS

Study area, design and period

The study took place in Addis Ababa, Ethiopia's capital city, strategically situated at the heart of the country with geographic coordinates of 9°2′N latitude and 38°45′E longitude. Encompassing a total area of 540 km^2 and boasting an average altitude of 2400 MASL,[18] the city is divided administratively into 10 subcities: Arada, Kirkos, Yeka, Addis Ketema, Gulele, Kolfe Keraniyo, Nifas Silk Lafto, Akaki Kality, Lideta and Bole. An additional subcity, named 'Lemi Kura', was established in 2021, which now shares a significant portion of the Bole subcity. Currently, there are 116 woredas (lower administrative units) in Addis Ababa. According to the 2007 national population and housing census,[19] Addis Ababa's population totalled 2 739 551, growing at an annual rate of 3.8%. Subsequent data from 2021 reported a population increase to 3 773 999, with Kolfe Keranyo, Yeka, Nifas Silk Lafto and Bole subcities recording the highest figures.[20] Addis Ababa serves as the economic hub of the nation, contributing approximately 29% of the urban gross domestic product (GDP) and 20% of the national urban employment.[21] Its economy is predominantly service oriented, accounting for about 75% of its GDP, followed by the industrial sector at 24.3% (Central Statistical Agency, 2021).[18] From 1 September to 30 November 2023, an ecological study design was conducted to assess the spatial and temporal trends and IRs of cervical cancer throughout Addis Ababa (online supplemental figure 1).

Populations, data sources and eligibility criteria

The source population consisted of all females residing in Addis Ababa during the specified review period. The study population encompassed all newly diagnosed cases from 1 January 2012 to 31 December 2021. Data regarding these

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cases were sourced from the Addis Ababa cancer registry, while estimates of age-grouped and woreda-level female populations for the same period were obtained from the Ethiopian Statistical Service. Exclusions from the incident cases comprised individuals for whom subcity-level or district-level data were unavailable, those with source codes indicating locations outside Addis Ababa and cases involving cancer sites other than the cervix.

Data extraction and processing

Spatial and temporal data, encompassing patient age, date of confirmed diagnosis, test method, cancer stage, treatment history, subcity, woreda/kebele and report date, were extracted from the cancer registry using a structured format. To facilitate external comparison, age data was segmented into 5-year age groups (that is, 0–4, 5–9, …, ≥80+) for the period spanning from 1 January 2012 to 30 December 2021 and standardised to the world standard population proposed by Segi.[22] Initially, age-group-specific crude rates were computed for each subcity. Subsequently, specific crude IRs calculated for each subcity were weighted by standardised proportions. Ultimately, age-adjusted cumulative IRs were estimated by aggregating the weighted rates for each subcity and for the entirety of Addis Ababa. Microsoft Excel V.10 was used for all calculations.

Data analysis

Following data processing in MS Excel, additional manipulation and analysis were conducted using a combination of R programming packages and the Quantum Geographic Information System (QGIS) V.3.36.0 software.[23] Descriptive statistics were performed to describe the cohort. Direct age standardisation was performed using the Segi's World standard population.[22] Age groups were estimated using a 5-year group age classification. Reverse geocoding of locations at woreda level was executed in QGIS using the OpenStreetMap provider.[24] For instances of missing geographic coordinates (n=11), nearest neighbour imputation was performed using R. Subsequently, GeoDa software V.1.2.2[25] was used to visualise the spatial distribution of cervical cancer hotspots and cold spots across 99 geographic locations. The Local Indicator of Spatial Autocorrelation was applied, employing the Bayesian Empirical Test with a significance threshold of $p<0.05$. Weight matrix estimation was conducted using the block method. To address locations with minimal or absent values, spatial interpolation was performed using the System for Automated Geoscientific Analyses GIS V.9.3.2 software.[26] The best fitting model, whether spherical, cubic or Gaussian, was determined based on the results of semivariogram analysis conducted for each year's data. Subsequently, the universal Kriging method was employed to interpolate and map values at unknown locations. The spatial dependence of cervical cancer across the study area was estimated using the Global Moran's I statistic and z score. Finally, temporal trends of incident cases and rates across subcities and age groups were analysed using the Joinpoint trend analysis software from the National Cancer Institute.[27] The appropriate number of joinpoints, which best describes the underlying structure of the data, was determined using the Bayesian information criterion (BIC). The results were presented as annual per cent changes (APC) in IR per 100 000 person-years. Statistical significance was considered at $p<0.05$.

RESULTS

Profile of cases and data preparation

From 1 January 2012 to 31 December 2021, a total of 2441 cases of cervical cancer were reported. Among these, six cases were missing information at both the subcity and woreda levels and were consequently excluded, leaving the number of eligible cases at 2435. The lowest number of new cases was reported in 2013 (n=191) while the highest number was recorded in 2021 (n=287). The majority of these cases were diagnosed by histology of primary tumour (n=2248, 92.3%), followed by those diagnosed through cytology (n=88, 3.6%), and clinical investigation or ultrasound (n=53, 2.2%). The mean (±SD) age of the cases was 51.8 (±12.4) years, ranging from 20 to 99. The 25th, 50th and 75th percentiles of age were 42.0, 51.0 and 60.0 years, respectively. The stage of cancer was unknown for the majority of cases (n=1882, 77.3%). Among the reported stages, the majority were stage IIB (n=160, 6.6%), followed by stage IIIB (n=103, 4.2%), and stage IV (n=74, 3.0%). All identified cases were malignant; no preinvasive lesions were registered (online supplemental table 1).

Local spatial clustering of new cases

Assessment of hotspots and cold spots from 2012 to 2021 reveals dynamic spatial patterns in cervical cancer incidence across subcities in the study area. In 2012, 30 high–high cluster woredas were identified primarily in Nifas Silk Lafto, Kirkos, Yeka, Gulele, Lideta, Kality and Addis Ketema subcities, while the majority of woredas (n=61) were classified as cold spots surrounded by other cold spots (low–low) (figure 1A).

The trend continued in 2013 with a similar proportion of woredas (n=26) exhibiting high–high clustering compared with the previous year, while the number of low–low clustering areas remained consistent (figure 1B). By 2014, high clusters of cases expanded to Nifas Silk Lafto, Addis Ketema, Gulele and Akaki subcities, with the majority of locations maintaining coldspot characteristics (figure 1C).

In 2015, the number of high–high spots diminished significantly (n=2), mainly localised in Nifas Silk Lafto and Kirkos subcities. Conversely, certain woredas in Nifas Silk Lafto, Akaki, Yeka and Kolfe Keraniyo subcities emerged as high cluster areas surrounded by low cluster woredas, while others were identified as low–low or non-significant spots (figure 1D). Subsequent years saw fluctuations in clustering patterns. In 2016, an increase

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Figure 1 Clusters of reported cervical cancer cases in Addis Ababa from 2012 to 2016.

in high–high clusters was observed in various subcities, while other areas remained predominantly cold spots or non-significant (figure 1E).

This trend continued with minor variations in 2017, 2018 and 2019 (figure 2A–C). In 2020, a restabilised pattern of spatial dependence emerged, with high–high areas identified in specific subcities, while the majority of woredas exhibited low–low or non-significant spatial dependence (figure 2D). In 2021, there was a further decrease in high–high clustering, with an increase in locations exhibiting high–low clusters. However, the majority of woredas remained either non-significant or low–low clusters (figure 2E).

Global clustering and interpolation with space and time

The universal Kriging interpolation from 2012 to 2021 sheds light on the spatial distribution of new cervical cancer cases across Addis Ababa with statistically significant positive spatial autocorrelation (Moran's I range: 0.947–0.989). In 2012, hotspots with moderate elevation above the mean (z score above 0.80) were clustered in the western part of Kolfe Keraniyo and Nifas Silk Lafto subcities. Similarly, moderate numbers of cases (z score 0.64–0.80) were observed in most parts of Nifas Silk Lafto, Kirkos, Lideta, Gulele, Addis Ketema and Yeka, while the remainder of the city exhibited low clustering near the entire mean (figure 3A).

Subsequent years showed dynamic shifts in hotspot trends. In 2013, hotspots shifted to the southern parts of the city, particularly in Nifas Silk Lafto, Kolfe and Akaki Kality subcities (z score above 0.92), with moderate clusters prevalent in these areas (z score 0.80–0.92) (figure 3B). By 2014, high clusters of cases emerged in woredas of Bole, Yeka, Kolfe Keraniyo, Gulele and Nifas Silk Lafto (z score above 1.0), surrounded by moderate levels of cases (z score 0.60–1.0), while other subcities exhibited cold spots or average clustering (z score 0.0–0.60) (figure 3C).

In 2015, areas with z scores above 1.0 indicated significantly more cases, particularly in southeastern, eastern and northeastern parts of Akaki Kality, Bole and Yeka subcities. Most woredas in these areas reported moderate numbers of cases (z score 0.80–1.0), with other parts of the city showing insignificant variability from the mean (figure 3D). The trend continued in 2016, with high clusters prevalent in multiple woredas of Nifas Silk Lafto, Kolfe, Gulele, Yeka and Bole, along with moderate clustering (z score 0.6–1.0), while the rest of the city demonstrated non-significant variability (figure 3E).

Further years continued to show fluctuations in hotspot distribution. In 2017 and 2018, an increasing trend of clustering was observed in several woredas of various subcities with high clusters prevailing in certain areas, namely Bole, Nifas Silk Lafto, Kolfe Keraniyo, Yeka and Gulele (z score

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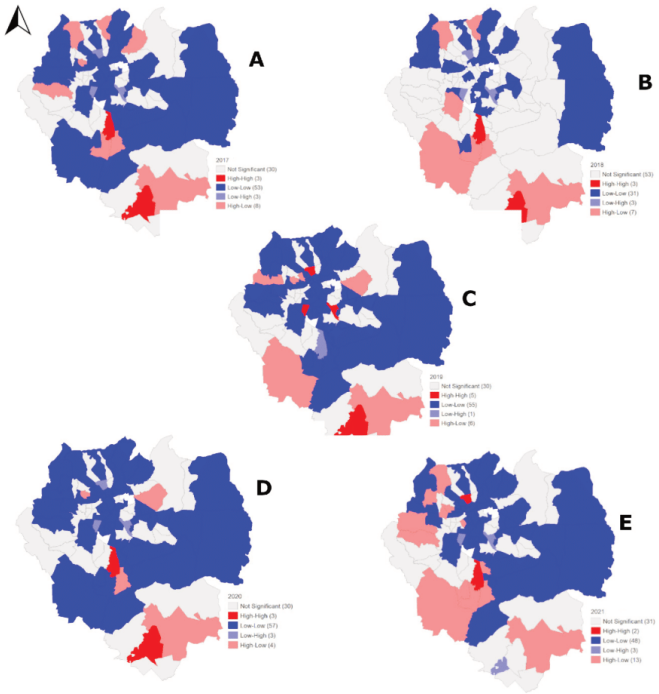


Figure 2 Clusters of reported cervical cancer cases in Addis Ababa from 2017 to 2021.

above 1.0) and moderate clustering in neighbouring woredas (figure 4A,B). Particularly, a statistically significant spatial autocorrelation (z score>1.96) was recorded in 2018 in the subcities, Nifas Silk Lafto, Bole, Kirkos and parts of Gulele and Yeka (Figure 4B). Similarly, in 2019 and 2020, hotspot patterns persisted in specific woredas, with high numbers of cases (z score above 1.0) identified in certain areas across the city (figure 4C,D). The trend continued into 2021, with specific woredas in various subcities exhibiting high numbers of cases as that of 2018/2019 (z score above 1.0), indicating the persistence of hotspot areas (figure 4E). In summary, although many woredas exhibited strong case clustering from 2012 to 2021, as indicated by high and positive Global Moran's I values, statistically significant spatial autocorrelation (i.e $p<0.05$) was observed only in 2018.

IR of cervical cancer in the city

The IR of cervical cancer in Addis Ababa city was assessed for the years 2012 to 2021. Analysis of age-standardised IR per 100 000 women-years revealed no significant changes across the entire city, with rates ranging from a minimum of 19 in 2013 to a maximum of 26 in 2016. When examining subcities individually for each year, Kirkos had an IR of 33 in 2012, followed by Gulele, Nifas Silk Lafto and Bole, each with an IR of 23 in 2013. In 2014, Arada recorded an IR of 26, while Yeka had an IR of 32 in 2015, and again in 2016. Gulele had an IR of 32 in 2017, Bole recorded an IR of 24 in 2018, Kolfe Keraniyo had an IR of 30 in 2019, Bole reached an IR of 33 in 2020 and Akaki Kality had the highest IR of 39 in 2021 (table 1).

Analysis of specific age groups for each year revealed a consistent increase in cervical cancer risk among individuals aged 45–74 years. The age group with the highest IR varied across the years: in 2012, it was 50–54 years (IR=5); in 2013, 60–64 years (IR=4); in 2014, both 50–54 and 60–64 years (IR=4 each); in 2015, both 45–49 and 60–64 years (IR=4 each); in 2016, 60–64 years (IR=5); in 2017, 55–59 years (IR=4); in 2018, 60–64 years (IR=4); in 2019, both 45–49 and 60–64 years (IR=4 each); in 2020, both 45–49 and 60–64 years (IR=4 each); and in 2021, 45–49 years (IR=5) (online supplemental table 2).

Trend analysis of age-specific IRs and count of cases

Figure 5 depicts the trend of age-specific counts (figure 5A) and IRs (figure 5B) of cervical cancer over the years. Consistent with the figures in table 1 and online supplemental table 2, the number of new cases among age groups 45 through 74 exhibited a steady increase, particularly noticeable from 2018 onwards (figure 5A). However, the age-standardised IR per 100 000 women per year remained relatively stable from 2017 onwards, compared with the peak estimate observed in 2016. Additionally, across the plot, age groups 45 through 74 consistently displayed the highest rates of new cases per 100 000 women per year over the years (figure 5B).

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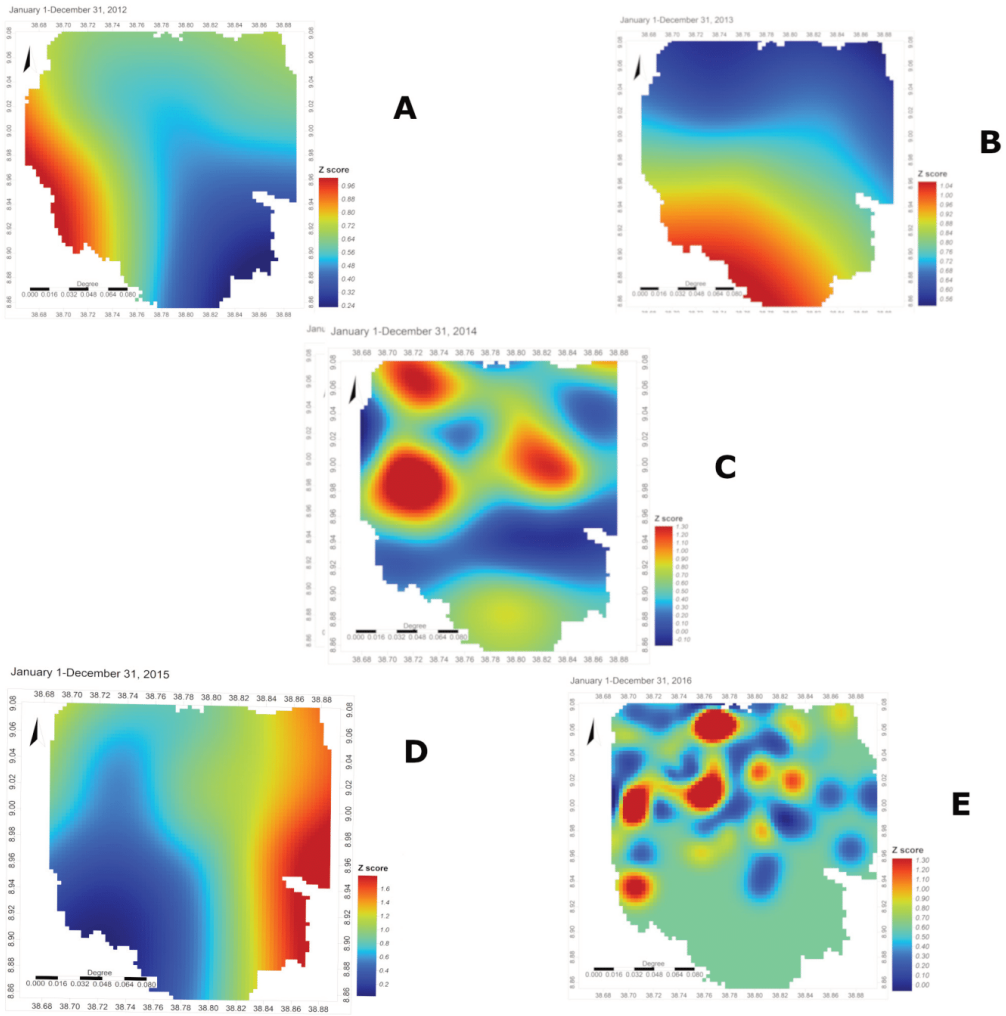


Figure 3 Global clustering of incident cervical cases in Addis Ababa from 2012 to 2016.

Time series analysis of IRs by subcity and year

The comprehensive joinpoint regression analysis revealed distinct trends in cervical cancer IRs across various subcities. Akaki Kality, Nifas Silk Lafto and Kolfe Keraniyo exhibited a single joinpoint, with Akaki Kality and Nifas Silk Lafto experiencing trend turning points in 2014, while Kolfe Keraniyo showed a trend change in 2019. Conversely, the remaining subcities were estimated to have zero joinpoints based on the BIC estimation. In Akaki Kality, there was a notable 10.6% (95% CI: −46.5% to 49.4%) APC decrease in IRs from 2012 to 2014. This, however, was not statistically significant (p=0.598) suggesting a random variation. However, from 2014 to 2021, the trend reversed, with an almost 10.0% (95% CI: 5.2% to 15.1%) significant APC increase observed (p=0.003). Similarly, Kolfe Keraniyo exhibited a statistically significant 13.5% (95% CI: 5.9% to 21.8%) APC increase in IRs from 2012 through 2019 (p=0.006). Subsequently, from 2019 to 2021, there was a decline in the trend, with an APC decrease of 18.1% (95% CI: −69.6% to 120.5%) but not statistically significant (p=0.627). And, in Bole subcity, the trend in cervical cancer IRs showed a statistically significant but modest 4.2% (95% CI: 0.6% to 7.9%; p=0.026) APC increase from 2012 through 2021 (figure 6).

DISCUSSION

This study aimed to explore the spatial and temporal patterns of cervical cancer incidence in Addis Ababa,

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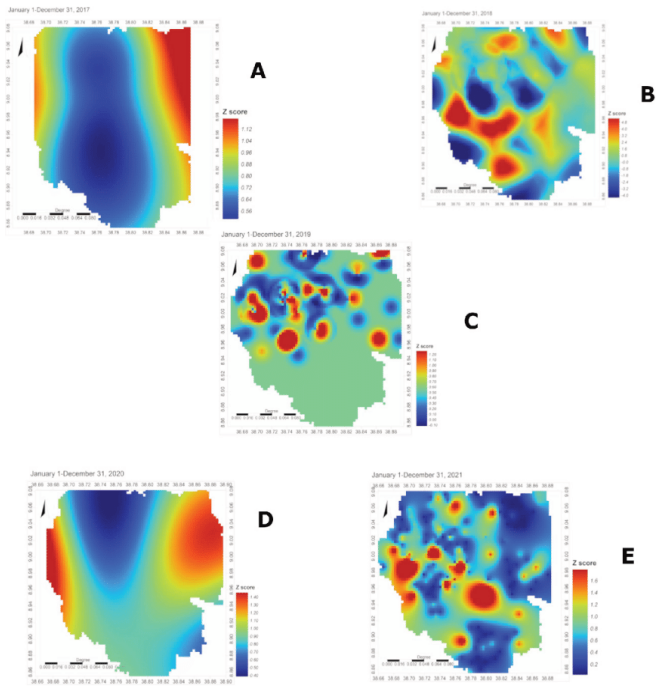


Figure 4 Global clustering of incident cervical cases in Addis Ababa from 2017 to 2021.

Ethiopia, spanning a decade from 2012 to 2021. The research sought to illuminate how cases were distributed across various subcities, age brackets and years, offering crucial insights to inform public health interventions and resource allocation. The number of newly identified cases of cervical cancer in Addis Ababa over the past decade appears to be relatively lower compared with a report for the eastern African region. In our study, the most recent data from 2021 indicates an age-standardised IR of 24 cases per 100 000 in Addis Ababa, whereas the 2022 estimate for Eastern Africa was reported to be 40.3 cases per 100 000.[28] The relatively higher figure in the latter report may be attributed to regional variations in disease burden across countries, potentially inflating the overall rate.

Understanding the spatial autocorrelation of cervical cancer within subcities and woredas was a crucial step in identifying geographic locations with elevated risk and implementing targeted interventions. The findings revealed a notable clustering of cervical cancer cases in specific subcities and woredas within Addis Ababa, with varying trends observed over the years. The spatial autocorrelation analysis for each review year indicated that

Table 1 Age-standardised incidence rate of cervical cancer per 100 000 women-years by year and subcity in Addis Ababa, Ethiopia, 2012–2021

Subcity	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Akaki Kality	26	14	16	21	21	23	22	28	24	39
Nifas Silk Lafto	27	23	21	20	28	25	23	29	24	29
Kolfe Keranyo	14	14	18	11	27	21	27	30	27	18
Gulele	26	23	16	25	19	32	22	21	18	21
Lideta	31	15	22	30	27	26	23	15	11	27
Kirkos	33	22	19	30	29	26	22	15	17	13
Arada	23	17	22	20	18	13	10	19	20	18
Addis Ketema	20	18	22	22	18	17	21	19	20	25
Yeka	29	19	20	32	32	22	21	23	25	29
Bole	17	23	19	30	26	20	24	27	33	25
Addis Ababa	24	19	20	23	26	22	22	24	23	24

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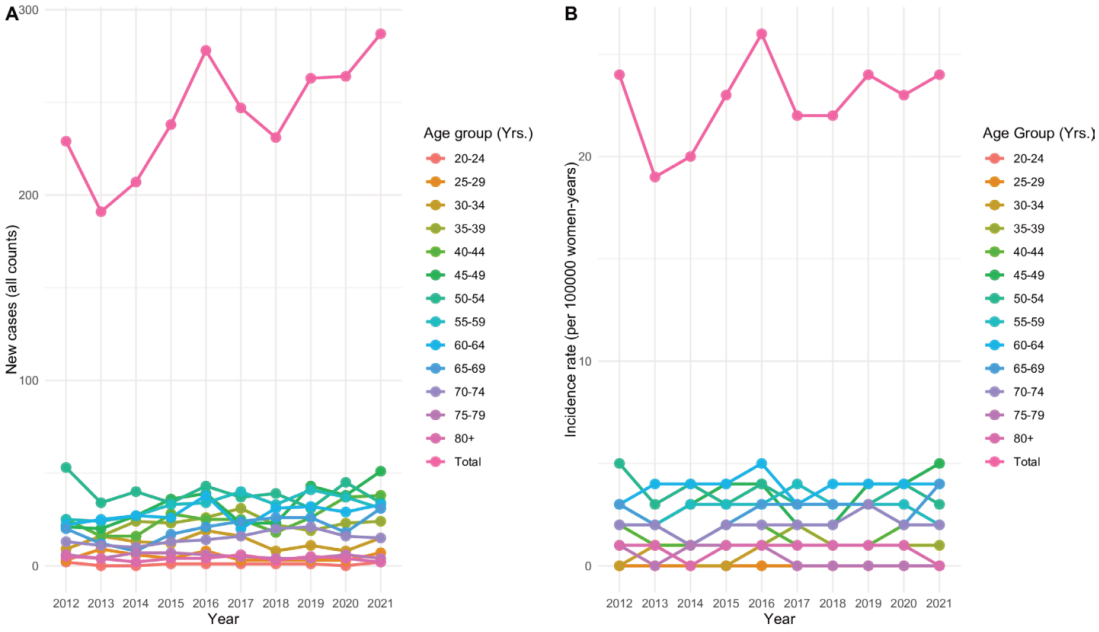


Figure 5 Trend line depicting age-specific count and age-standardised incidence rates of cervical cancer from 2012 to 2021.

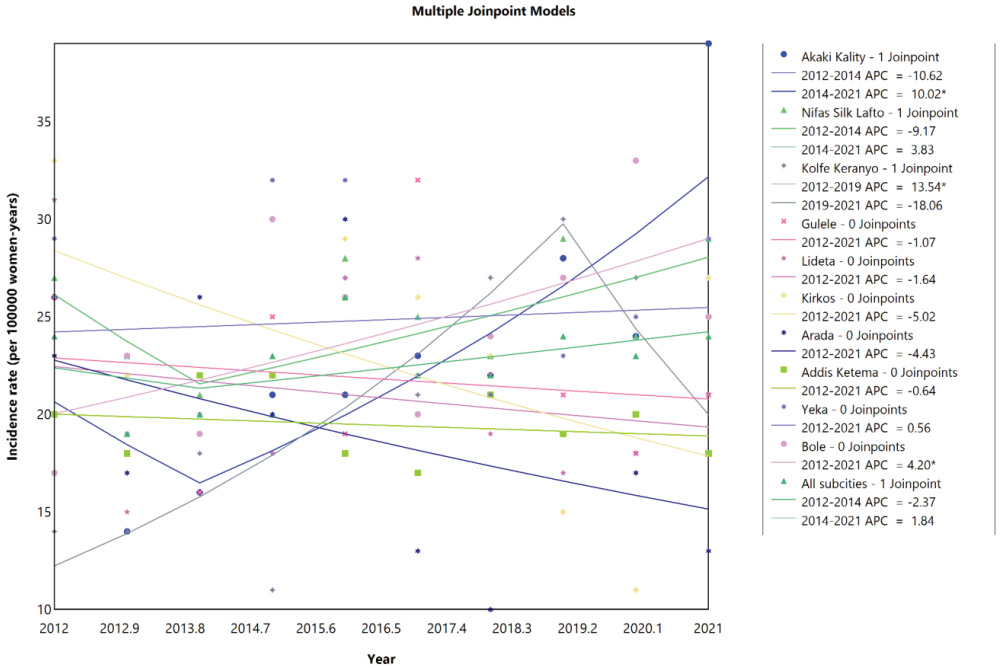


Figure 6 Joinpoint regression analysis of cervical cancer age-standardised incidence rates per 100 000 women-years by subcity in Addis Ababa spanning from 2012 to 2021. APC, annual percent change. *Statistically significant.

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the distribution of cervical cancer cases was non-random and influenced by geographic factors. A similar trend of clustering in the incidence of non-cervical cancer types has been reported in Saudi Arabia.[29] The risk of cervical cancer in Thailand also demonstrated spatial and temporal dependence, revealing higher incidences in certain provinces such as Chiang Rai and Nan, while others remained cold spots. Generally, there was a decreasing trend over time observed in these areas.[30] In a nationwide study conducted in South Africa, the incidence of cervical cancer among people living with human immunodeficiency virus was found to be higher in locations with accessible health facilities compared with areas with low affluence. Specifically, the IRs were reported as 3.18 in areas with accessible health facilities, whereas in areas with lower affluence, the IRs were recorded at 1.52.[31]

The stability observed in the age-standardised IRs of cervical cancer across Addis Ababa city over the study period is notable. However, comparing the age-standardised IRs in the current study to a specific year of 2012 with a figure in Shijiazhuang city in China revealed a significant difference.[32] Specifically, there was a nearly tripled figure in Addis Ababa compared with Shijiazhuang city, with IRs of 24 vs 8.4 persons per 100 000 women, respectively. The same figure, however, was comparable to a finding in Shexian County in rural China, where the IR was reported as 25.2 per 100 000 women.[32] The higher figure in our study compared with those in China is likely linked to factors such as differences in access to screening, prevalence of HPV infection and socioeconomic conditions, all of which may contribute to the disparity in findings. Ethiopia's low-income status may hinder widespread cervical cancer prevention efforts, leading to a higher disease burden compared with more developed regions like Shijiazhuang city in China. While the stable IRs suggest a consistent level of risk, it is important to recognise that cervical cancer remains a significant cause of morbidity and mortality, particularly among women in low-resource settings.[33 34] The estimated age-standardised IRs in our study remain higher compared with a similar report in Kampala, Uganda, which documented relatively low subcounty-level IRs of cervical cancer from 2008 to 2015. However, both studies noted distinct spatial dependence in certain counties, resembling our findings.[12] The observed differences between the two studies could stem from various factors, including differences in population demographics, review years, underlying risk factors, and potential genetic variations, among other factors.

Subcity-level analysis revealed spatial disparities in cervical cancer incidence, with certain areas consistently exhibiting higher rates compared with others. Specifically, the subcities of Akaki, Bole and Kolfe Keraniyo demonstrated an increasing trend, although the latter showed a slight decline in the last 3 years. These disparities may stem from various factors, including changes in population demographics, variations in access to healthcare services, differences in screening and diagnostic practices, and the prevalence of HIV, among others. For instance, community-based screening campaigns conducted by health extension workers have been widely implemented in the city along with the expansion of many health centres and a few hospitals over the past decade, potentially contributing to the number of observed new cases in some of the subcities. The lack of staging information for most reported cases might be due to these campaigns being carried out at lower-level facilities with limited diagnostic capabilities. On the other hand, recent projections for HIV prevalence in 2022–2023 indicated that Bole and Kolfe Keraniyo were among the leading subcities with 3.5% and 3.6% burden of the infection, respectively.[35] This could also lead to the high number of cervical cancer cases in these areas. Furthermore, it is worth noting that a significant portion of Bole represents the highest socioeconomic class, whereas the remaining subcities represent among the low socioeconomic class inhabitants. This socioeconomic disparity could influence the observed rising trends in cervical cancer incidence. Factors such as access to healthcare resources, education levels, lifestyle behaviours and environmental exposures may vary significantly between these socioeconomic classes, potentially contributing to differences in cervical cancer risk and IRs. Studies have revealed that lower socioeconomic status often leads to a disproportionate utilisation of screening services, potentially contributing to disparities in cervical cancer detection and treatment.[36] According to reports, poorly managed dietary practices[37] and a sedentary lifestyle[38] have been associated with an increased risk of cervical cancer burden.

Age group analysis highlighted a consistent increase in cervical cancer risk among individuals aged 45–74 years. This figure is different from what is observed in high or upper-middle-income countries where age-standardised IRs increased up to 35 or 39 years.[39 40] However, the same reports documented that the ASIR exhibited an increasing trend during the late years, which is in agreement with our finding. The higher incidence observed in the upper age group may be attributed to the low screening practices, limited healthcare access and demographic factors specific to Ethiopia. In Ethiopia, the lack of widespread, early screening and preventive services,[41] especially among those of lower age,[42] may delay detection until later ages, while higher fertility rates and prolonged reproductive years could increase cumulative exposure to HPV and related risks. Additionally, HPV infection can persist for years or even decades before developing into cervical cancer, with the risk of progression increasing with age.[43] According to a research, the average duration from HPV infection to the diagnosis of CIN3 or more severe conditions is approximately 9.4 years, with a SD of 4.1 years. The progression from CIN3 to invasive cervical cancer typically spans 10 to 20 years and varies based on the HPV genotype.[44 45] Additionally, a modelling study by Burger *et al* indicated that the median time from HPV acquisition to the detection of cervical cancer ranges between 17.5 and 26.0 years.[46] Therefore, the higher IRs

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observed in older age groups may reflect the cumulative effect of HPV infection over time. Furthermore, studies have reported that cumulative exposure to HPV infection increases with age, while the clearance rate of the virus decreases with increasing age.[47] These findings are consistent with previous research demonstrating an association between increasing age and elevated cervical cancer risk.[48] While the primary aim of the current study was to estimate incidence and trends, the findings also imply the importance of robust prevention strategies. The WHO urges countries to achieve the 90-70-90 targets by 2030: 90% of girls fully vaccinated with HPV vaccine by age 15, 70% of women screened with high-performance tests by ages 35 and 45, and 90% of women with pre-cancer or invasive cancer receiving appropriate treatment, aiming to eliminate cervical cancer within the next century.[1]

Since 2015, the Ethiopian Ministry of Health has developed and expanded a national cervical cancer prevention and control programme.[49] The guidelines include three components of care: primary prevention (eg, condom use, HPV vaccination), secondary prevention (eg, screening and treatment of precancerous lesions) and tertiary care (eg, surgery, radiotherapy and palliative care). Visual inspection with acetic acid (VIA) and more recently primary HPV precision testing followed by VIA is the standard cervical cancer screening method in Ethiopia, though utilisation remains low among younger age groups.[42] While the guidelines recommend HPV vaccination for girls aged 9–14, the country introduced vaccination for 14-year-old girls in December 2018 due to vaccine supply shortage, covering over 6.3 million girls in this age group to date.[50] Additionally, the guidelines outline procedures for managing precancerous lesions, including cryotherapy, along with more advanced techniques like loop electrosurgical excision procedure and conization (cone biopsy). Advanced procedures and tertiary care are primarily accessible in urban centres with teaching hospitals, particularly in Addis Ababa. For instance, functional radiotherapy services are currently available only at Tikur Anbessa Specialized Hospital, making it the sole provider for this treatment in the country. As a result, patients referred from across Ethiopia must travel to a few hospitals in Addis Ababa for follow-up care, which places a heavy burden on these facilities and leads to catastrophic expenditure and significant delays in timely treatment.

In the current study, we employed multiple models and statistical approaches to visualise and obtain reliable estimates, enhancing the robustness of our findings. This novel approach adds significant contributions to the existing literature on cervical cancer epidemiology, particularly in the context of low-resource settings such as Ethiopia. By elucidating the spatial and temporal dynamics of cervical cancer incidence, our study offers essential information for guiding targeted interventions, resource allocation and public health policies aimed at reducing the burden of cervical cancer in the region. The study, however, is not without limitations. One limitation is that there was no detailed information about the time points of screening campaigns or specific health centre efforts to increase screening, which could easily boost the number of newly diagnosed patients during a certain time period. Additionally, the lack of individual-level data limited our ability to explore factors such as HPV infection status, socioeconomic status and lifestyle behaviours, which could have provided further insights into the determinants of cervical cancer incidence. At last, our study focused specifically on Addis Ababa, and the findings may not be generalisable to other regions or countries with different demographic, cultural and healthcare system characteristics.

In conclusion, our study identified significant spatial clustering of cervical cancer cases in specific subcities and woredas of Addis Ababa from 2012 to 2021. Concurrently, the age-standardised IRs varied over the years, with a notable increase in individuals aged 45–74. To address these trends, it is crucial to not only improve access to screening and treatment services, particularly for vulnerable populations, but also to confront socioeconomic disparities that contribute to disparate risk levels. Importantly, implementing a school-based HPV vaccination programme could serve as a foundational preventive measure, targeting young populations before exposure to HPV. Sustained surveillance, strategic prevention and control measures, including widespread HPV vaccination, are essential to reduce the impact of cervical cancer in Addis Ababa and improve health outcomes for its community.

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Contributors Conceptualisation and design of the study were done by TS and TGF. Supervision was performed by TGF, EJK and MA. Data acquisition, cleaning, coding, analysis and interpretation were performed by TS. Draft and final manuscript were prepared by TS. Critical review and provision of feedback on the final manuscript were done by TGF and EJK. TS is responsible for the overall content as the guarantor. All authors have read and approved the manuscript for submission.

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Competing interests None declared.

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Ethics approval The project received approval from the institutional review board (IRB) of the College of Health Sciences, Addis Ababa University before commencing actual data collection (Ref.no: 055/23/SoP). Support letters were written to the Addis Ababa Cancer registry center and the Ethiopian Statistical Service (ESS). No informed consent was sought as the study dealt with archived data from a public repository. Data was analyzed in aggregate, and personal identifiers were not utilized in the study. The confidentiality of collected data and the privacy of patients were maintained throughout and after the completion of the project.

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Data availability statement All data relevant to the study are included in the article or uploaded as online supplemental information. The dataset without identification, which was used during the current study, is available from the corresponding author on reasonable request.

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PAPER V

The Economic Burden of Cervical Cancer in Addis Ababa: A Matched Case-Control Study

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Abstract

Background

Cervical cancer poses a major global health challenge with significant financial burdens, especially in advanced care settings. In developing countries like Ethiopia, limited evidence exists on its economic impact. The objective of this study was to evaluate the economic burden of cervical cancer in Addis Ababa, Ethiopia.

Methods

A matched case-control design was employed at tertiary oncology centers from July 1st to September 30th, 2023. Participants were consecutively recruited. Data was collected using an interviewer-administered questionnaire developed after a literature review, and medical records were abstracted. Data entry was done via Epi Info v.7.2.5, followed by cleaning, transformation, and export to IBM SPSS v.26 for further analysis. Descriptive statistics, Student's t-test, and Tukey's biweight regression were applied using SPSS and R (v4.2.2). Statistical significance was determined at $p < 0.05$ with a 95% confidence interval.

Results

A total of 932 participants were enrolled in the study, comprising 466 cases and 466 controls. The findings indicated that cervical cancer patients (cases) incurred significantly higher total annual costs compared to hypertensive controls. The first-year total cost for cases was 3196.27 INT$, compared to 206.26 INT$ for controls ($p<0.001$). Direct medical costs were the largest component (cases: 2638.05 INT$, controls: 169.18 INT$). Post-first year, costs for cases remained higher at 2235.86 INT$, while controls reported 234.60 INT$. Specifically, diagnosis and treatment represented the largest expenses in both the first year and the post-first year phases. In the first year, diagnosis costs were the highest, averaging INT$1,548.16 (±SD INT$1,946.87), followed by treatment costs at INT$1,004.18 (±SD INT$1,403.45). In the post-first year, diagnosis costs remained significant at INT$1,020.91 (±SD INT$2,344.55), while treatment costs averaged INT$796.26 (±SD INT$1,001.36). Key predictors of total costs included larger household size ($\beta=492.82$, $p<0.05$), presence of comorbidities ($\beta=834.96$, $p<0.001$), lack of social support ($\beta=627.48$, $p<0.001$), poor diet ($\beta=740.27$, $p<0.001$), and advanced cancer stage ($\beta=1,324.12$, $p<0.001$).

Conclusion

Cervical cancer imposes a significant economic burden, with average annual costs of 3196.27 INT$ in the first year and 2235.86 INT$ afterward. This makes the problem to present with a significant incremental cost as compared with hypertensive controls. Direct medical costs dominate expenses, with household size, comorbidities, lack of social support, poor diet, treatment timing, and advanced cancer stage driving costs. Targeted interventions like early diagnosis and financial support are essential to reduce this burden.

Keywords: cervical cancer, cost of illness, economic burden, incremental cost, matched case-control study

Background

The term "cost of illness" (COI), also known as "burden of disease" (BOD) or "economic burden," encompasses a wide range of expenses and financial challenges faced by countries, regions, communities, or individuals [1]. Depending on the methods employed, cost assessments typically utilize either incidence or prevalence-based approaches to capture costs and indicate the impact on longevity, morbidity, and even the health-related quality of life (QoL) for patients [2]. Expanding the measurement of the cost of illness could involve considering financial losses related to both direct and indirect expenditures resulting from premature death, disability, or injury caused by the associated disease and/or its comorbidities [1, 3].

The expenses associated with illness subsequent to cervical cancer constitute a significant share of the overall burden of the disease, both in the general population and specifically within this particular group. As reported in the United States [4], the average annual medical cost of treating cervical cancer shows considerable variability depending on the treatment phase. For instance, the mean cost of care during the last year of life could reach up to $118,000 for patients below 65 years and up to $79,000 for those aged 65 and above. In Ontario, a population-based estimate from 2016 revealed that the average overall care cost for cervical cancer was $39,137 in the first year following diagnosis. By the fifth year after diagnosis, the mean unadjusted cost increased to $63,131 [5].

Regarding the cervical cancer situation in Ethiopia, it is noteworthy that the prevalence of cervical cancer in the country falls within the range of 18% to 23% [6, 7]. The incidence and mortality rates are approximately 17.3% and 16.5%, respectively [7]. Annually, around 6,300 new cases are diagnosed, with approximately 4,884 women succumbing to the disease each year. This posits cervical cancer as the second most common and deadly cancer within this population in Ethiopia. Reflecting the scale of this issue, a previous study revealed that the mean outpatient cost per patient for cervical cancer was $407.2, with the direct outpatient cost constituting the largest portion [8].

The expenses incurred by patients in advanced care settings encompass various components across the care continuum. Currently, there is a lack of evidence regarding the economic impact of the disease in many developing contexts, including Ethiopia. Notably, there is no documented report to date that compares the incremental costs of the disease with other non-communicable diseases in a single study using a matched sample. Similarly, the patient attributes that predominantly influence the total cost in cervical cancer are not clearly understood.

This study endeavors to evaluate the economic repercussions of cervical cancer, specifically aiming to discern direct medical costs, direct non-medical costs, and indirect costs. Moreover, the study explores the incremental costs associated with the disease and identifies predictors of the overall cost within this vulnerable group. To provide context, hypertensive patients were selected as a control group. As a common, manageable chronic condition, hypertension offers a clear baseline for comparing the economic burden of cervical cancer with a less resource-intensive disease. This comparison helps to differentiate cost drivers specific to cervical cancer, such as diagnostic tests, complex treatments, and late-stage care, from the more stable and

predictable costs associated with hypertension. The research is concentrated on patients residing in and visiting oncology units at leading referral and tertiary care hospitals in Addis Ababa, Ethiopia.

Methods

Context and settings

The study was conducted at Saint Paul's Hospital Millennium Medical College (SPHMMC) and Tikur Anbessa Specialized Hospital (TASH), the main public oncology centers in Addis Ababa, Ethiopia. These leading referral hospitals provide comprehensive healthcare and medical education. SPHMMC serves around 200,000 patients annually, with a catchment population of 5 million, while TASH treats nearly 500,000 patients annually through its 700 beds. Both hospitals offer basic and specialized oncology services, making them crucial for cancer treatment in the country.

Study design

The study employed a matched case-control design to compare cervical cancer patients (cases) with hypertensive patients without cancer (controls). Participants were matched based on age and socio-demographic characteristics, ensuring a robust comparison between groups.

Study period

The study was conducted from July 1st to September 30th, 2023 following a predefined cost of illness study plan.

Source population

The source population for the cases consisted of all women diagnosed with cervical cancer who sought care at both public and private health facilities in Addis Ababa, Ethiopia. Likewise, the source population for the controls included all women diagnosed with hypertension who visited both public and private health facilities in the city.

Study population

The study population consisted of all patients with a pathologically and clinically confirmed cervical cancer diagnosis who either had started treatment or were on follow-up care in the

selected hospitals during the study period. Controls were age- (±5 years), sex-, residence-, hospital- and admission classification- and follow-up period-matched known hypertensive patients. The controls were similar in most aspects of their background except that they were free from any form of confirmed cancer.

Inclusion criteria

All adult cases and controls (18 years of age or older) who lived in Addis Ababa city, began treatment and were monitored for a minimum of one month, were able to provide study-related information, had proxies or people with whom medical records and history could be verified, and provided verbal informed consent to take part in the study were eligible.

Exclusion criteria

Patients below the specified age and those with suspected diagnoses were excluded from the study. This includes cases (those with cancers other than cervical cancer), controls (those suspected of having any type of cancer), and proxies (those representing non-consenting patients). .

Sample size estimation

A minimal standardized mean difference (SMD) of costs was estimated to be 0.2, despite the fact that population or sample mean estimates and standard deviations for the proposed research question are not currently available. Cohen [9] proposed three levels of this measure, 0.2, 0.5, and 0.8 or more, as small, medium, and large impact sizes, respectively. The SMD is also known as Cohen's d or effect size, and the value of 0.2 was taken to increase the sample size and precision of estimates. As a result, the minimal sample size needed was computed using the following formula.

$$n=2[\frac{Z\frac{\alpha}{2}+Z\beta}{ES}]^2$$

Which:

$$ES=\frac{\mu 1-\mu 2}{\sigma}$$

And, where:

n=required sample size per group

Zα/2=standard normal z-value for a significance level **α**=0.05 (two-tailed) which is 1.96

Zβ=standard z-value for a power of 80% which is 0.84

	A minimal cost standardized mean total cost difference of 20% is assumed, with **ES**=0.2 Considering a 20 % for non-complete data
Plotting the elements mentioned above would result:	N*final*=2n =942 participants

Sampling technique

The sampling technique was guided by careful consideration of the similarity of the populations being studied, the flow of cases, and the accessibility of healthcare facilities when selecting hospitals. Accordingly, a consecutive sampling method was adopted to include cases in the study. Then, the selection of controls was performed in a similar manner, ensuring that eligibility and matching criteria were met at each individual hospital to effectively achieve the study objectives.

Epidemiologic approach and perspective

A prevalence-based approach was considered to evaluate the economic impact of illness from cervical cancer on society per patient per year. This examination adopted a societal perspective, encompassing all associated expenses. This includes direct medical costs (covering medications, diagnostics, supplies, hospitalization, and physician consultations), direct non-medical costs (encompassing transportation, food, and caregiver expenses), and indirect costs (accounting for lost earnings due to job absenteeism and productivity reductions incurred by caregivers).

Instrument design

Following a review of the literature on cancer [8, 10, 11] and other chronic illnesses [12-14] the data collection format for the cost of illness was designed. The purpose of the instrument was to capture data on patients' direct medical and nonmedical expenses as well as any indirect costs incurred during the previous three months. The tool included various components, such as sociodemographic and economic factors, behavioral aspects, and the clinical profiles of participants. Additionally, it featured a format documenting the history of all medical expenses incurred over the past 90 days. The locally validated MD Anderson symptom inventory (MDSAI) tool was employed to capture the patient-reported inventory of common symptoms among cases [15]. Through face-to-face interviews and observation of medical records, data on patients' profiles and all expenditures was collected retrospectively through a bottom-up approach. The projected costs of illness were based on net salary or wages and market earnings. We assessed indirect costs with the human capital technique [16]. This is the money that would

be lost as a result of morbidity at the hospital, home, or in other healthcare settings for patients or their companions (family members or caregivers). Because of this, the number of days that the patients or their care givers have lost was used to assess the expenses associated with absenteeism and patient productivity loss through interviews. For working participants, the daily average per capita net earnings were used; however, for laborers, housemaids, students, or housewives who were employed elsewhere, the market price of daily wages was taken into consideration [17]. Women over 60 or in retirement had no productivity losses because the human capital method is based, only, on market earnings.

Data collection procedure

Data collection was conducted by six trained data collectors, including two general practitioners and four individuals with master's degrees in public health. The team underwent extensive training on the data collection tool, ethical considerations, and effective communication techniques to ensure accurate responses. Eligible participants were approached at selected healthcare facilities, where interviews were conducted in private settings to ensure confidentiality and comfort. Informed consent was obtained prior to participation. All costs were captured in Ethiopian birr to ensure consistency and avoid errors

Valuation of costs and sensitivity analysis

Following data collection and entry in local currency units (Ethiopian birr), the costs were computed and documented in International Dollars (INT$), taking into account a purchasing power parity (PPP) of 20.0 local currency units (LCUs) per international dollar for Ethiopia. This PPP was derived from the 2022 reported LCU for the country, which stood at 17.8, factoring in an annual growth rate of 12.45% [18]. When real-time comparisons were required (such that studies reported in local currencies) a US$ was used considering the exchange rates that were in effect during the study period (1USD=55ETB) in Ethiopian birr (ETB) and US Dollars (USD). The cost of illness was estimated at market prices and net salary or wages. Indirect costs were estimated using the human capital approach [16]. This is the income that either patients or their companions (relatives or caregivers) would lose due to the morbidity at the hospital, home, or other health settings. Hence, both patient productivity loss and absenteeism costs were estimated via interviewing from the number of days that the patient or the companion has lost. The daily average per capita net earnings was used for working participants whereas, market price of daily

wages was considered for laborers, housekeeping, students, or housewives as was employed elsewhere [17]. Productivity losses for women who are retired or are over the age of 60 will be ignored, as the human capital approach is based on market earnings. There was no discounting applied since it was anticipated that all expenses would be incurred within a year. Finally, we conducted a sensitivity analysis using a ±20% range for the main cost drivers, including diagnosis, treatment, palliative care, as well as direct non-medical and indirect costs. This approach was used to account for variability and potential non-reported factors that could affect the total annual costs. The analysis helped to assess the robustness of our findings and determine which cost components had the greatest influence on overall expenses under different scenarios.

Data quality assurance

Before designing the data collection tool, a comprehensive literature review was conducted to inform the development process and ensure the quality of the data collected. To enhance data quality and accuracy, we implemented a system of supervision, provided thorough training sessions for data collectors, and conducted pretesting of the data collection instrument. Additionally, a three-month timeframe was established for data collection to minimize the potential for recall bias in cost estimation. .

Definitions of terms

Physical exercise was assessed based on the recommendations provided by the US Physical Activity Advisory Committee [19], the American Cancer Society (ACS) [20] and the World Health Organization[21]. These guidelines suggest that patients with chronic illnesses, particularly those with cancer, should engage in either 150-300 minutes of moderate exercise or 75-100 minutes of vigorous physical activity per week. Patients were classified as 'good' if they meet either of these recommendations and 'poor' if they do not.

Dietary Practice: Following the guidelines of the American Cancer Society [20] it is recommended that to consume foods high in nutrients to maintain a healthy body weight. This includes a variety of vegetables (dark green, red, and orange), fiber-rich legumes, fruits (especially whole fruits in different colors), and whole grains. Patients were classified as having 'good' dietary practices if they follow any combination of these recommended diets, and 'poor' dietary practices if they engage in high-risk diets or lack access to an adequate diet.

Current Use of Excess Alcohol: Current use of excess alcohol was defined based on a participant's response to the question of whether they currently consume more than one bottle of alcohol per day, as set by the American Cancer Society[20].

Current Use of Cigarettes: Current use of cigarettes, as per the World Health Organization [21] definition, refers to the use of cigarettes (smoked or non-smoked) reported by respondents during the data collection period.

Current Use of Khat or Other Stimulant Substances: Current use of khat or other stimulant substances is defined based on whether a patient reports using khat or other stimulant substances (such as Hashish, Ganja, etc.) during the data collection period.

Clinical symptoms: The common clinical symptoms namely, pain, fatigue, distress, sadness and numbness were selected from the MDASI questionnaire as they have been reported to be common experiences among cancer patients in the current study settings were used. The Amharic version of the tool has been validated earlier for Ethiopian patients [15].

Data analysis

Data entry was done using Epi-Info v.7.2.5 and exported to computer languages such as MS Excel, Statistical Packages for Social Sciences (SPSS) version 26 [22] and R programming version 4.2.2 for additional cleaning, recoding, transformation, and modeling. The analysis and presentation of data, including percentages, means, and standard deviations, were done using descriptive statistics. The Student's independent t-test was utilized for group comparisons of incremental costs among the distinct cost categories. to handle uncertainties, the incremental cost model was expanded to include a bootstrapping of 1000 samples due to the data's right-skewed non-normal distribution. As the overall expense was likewise typified by positively skewed data that was right-skewed and had outliers, we fitted a Tukey's biweight regression model to evaluate the variables related to the yearly total expenditures of illness from cervical cancer. In addition to conducting diagnostic tests for the model, we have verified if the robust model outperforms the ordinary least square (OLS) method. The results of the analysis were presented in the reports using tables, charts with percentages, and numbers. Statistical significance was established at $p<0.05$ and a 95% confidence interval.

Ethics Approval

Prior to starting the data collection, the study was approved by the institutional review board (IRB) of Saint Paul's Hospital Millennium Medical College (Ref. no: PM23/284) and the School of Pharmacy, Addis Ababa University (Ref. no: ERB/SOP/543/15/2023). A letter of support was sent to the chosen cancer centers. Each study participant provided verbal informed consent. The verbal informed consent was documented by the research team through written records during each interview. A trained witness, typically a healthcare professional, was present to confirm the consent process. This approach was approved by the Institutional Review Board (IRB) of Saint Paul's Hospital Millennium Medical College and Addis Ababa University School of Pharmacy, in accordance with ethical guidelines for research involving human participants. Involvement in the study was entirely voluntary. No personal identifiers were used in the study; instead, data was analyzed in aggregate. Both patient privacy and the confidentiality of the data collected were safeguarded.

Results

Sociodemographic and economic characteristics

A total of 932 participants, comprising 466 cases and 466 controls with a 1:1 case-to-control ratio, were recruited and included in the study. Among the case-control pairs, 53.6% (250 pairs) were from SPHMMC, with the remaining participants from TASH. The mean age for cases was 51.7 (±10.6) years, and for controls, it was 52.8 (±10.9) years, both groups averaging approximately to 52 years. A slightly higher percentage of cases (58.2%, n=271) belonged to the age group 52 years or less compared to controls (48.3%, n=225). In terms of marital status, more than two-thirds of both cases (74.7%, n=348) and controls (69.5%, n=324) were married. Additionally, a similar proportion of cases (69.7%, n=325) and controls (71.5%, n=333) were able to read and write. Similarly, almost equal proportions of cases (37.3%, n=174) and controls (37.8%, n=176) had not attended formal education, representing the predominant category in both samples. Geographically, a significant number of cases were from Addis Ketema sub-city (14.4%, n=67) and Kolfe Keranio sub-city (13.5%, n=63), while controls were primarily from Lideta (15%, n=70) followed by Addis Ketema (14.8%, n=69) sub-cities. The majority of cases (55.8%, n=260) and controls (46.6%, n=217) were housewives. Additionally, a substantial portion of cases (68.9%, n=321) and controls (61.4%, n=286) reported having some form of social support within their community. Regarding family size, approximately two-thirds of cases (79.6%, n=371) and the majority of controls (86.3%, n=402) had households with five or fewer

members. The mean (±SD) average monthly income for households was 5656.6 (±5055.9) Ethiopian Birr (ETB) for cases and 5404.9 (±3918.9) ETB for controls, equivalent to 102.8 (±91.9) and 98.3 (±71.3) USD for cases and controls, respectively. A significant proportion, 61.4% of cases (n=286) and 62.4% of controls (n=291), reported earnings above the poverty line of 3567 ETB or 65 USD per month. Lastly, community-based health insurance emerged as the primary source of funding for medical expenses, with nearly two-thirds of both cases (70.0%, n=326) and controls (67.4%, n=314) reporting its utilization (Table 1).

Table 1. Sociodemographic and economic characteristics of study participants, Addis Ababa, Ethiopia (N=932)

Variable	Category	Cases		Controls	
		Frequency	Percent	Frequency	Percent
Hospital					
	SPHMMC	250	53.6	250	53.6
	TASH	216	46.4	216	46.4
Age (yrs.)					
	52 or less	271	58.2	225	48.3
	>52	195	41.8	241	51.7
Marital status					
	Married	348	74.7	324	69.5
	Widowed	67	14.4	70	15.0
	Others*	51	10.9	72	15.5
Able to read and write					
	No	141	30.3	133	28.5
	Yes	325	69.7	333	71.5
Level of education					
	No formal education	174	37.3	176	37.8
	Primary and middle school (grade 1-8)	142	30.5	117	25.1
	High school (grade 9-12)	89	19.1	88	18.9
	Tertiary level (College or University)	61	13.1	85	18.2
Sub city					
	Addis Ketema	67	14.4	69	14.8
	Akaki Kality	30	6.4	32	6.9
	Arada	31	6.7	30	6.4
	Bole	23	4.9	27	5.8
	Gulele	38	8.2	47	10.1
	Kirkos	37	7.9	41	8.8
	Kolfe Keranio	63	13.5	44	9.4
	Lemi Kura	56	12.0	22	4.7
	Lideta	37	7.9	70	15.0

	Nifas Silk	41	8.8	52	11.2
	Yeka	43	9.2	32	6.9
Occupation					
	Government employee	64	13.7	80	17.2
	Private employee	64	13.7	76	16.3
	Merchant	33	7.1	46	9.9
	Housewives	260	55.8	217	46.6
	Others**	45	9.7	47	10.1
Presence of social support					
	No	145	31.1	180	38.6
	Yes	321	68.9	286	61.4
Number of members in the household					
	5 or less	371	79.6	402	86.3
	>5	95	20.4	64	13.7
Average monthly income of the household					
	≤3567 ETB or 65US$	180	38.6	175	37.6
	>3567 ETB	286	61.4	291	62.4
Source of funding for medical expense* **					
	Health insurance	326	70.0	314	67.4
	Self	157	33.7	170	36.5
	Aid or social support	11	2.4	7	1.5
	Relatives or friends	29	6.2	31	6.7

*Includes separated, divorced or singles; **includes housemaids, jobless, students, retired or farmers; ***does not consider combination of sources. Sum of percentages may exceed 100.

Behavioral characteristics

The evaluation of the current behavioral characters of the respondents indicates that a relatively small percentage of both cases and controls reported consumption of substances, including tobacco products, excessive alcohol, and khat (a stimulant leaf also called ‘Catha edulis’ that contains the chemical compound known as ‘cathinone’ among others). Notably, more than half of both cases (56.9%, n=265) and controls (51.9%, n=242) reported engaging in either moderate or vigorous exercises. Likewise, a higher percentage of both cases (59.2%, n=276) and controls (59.0%, n=275) reported maintaining good dietary practices (Fig 1).

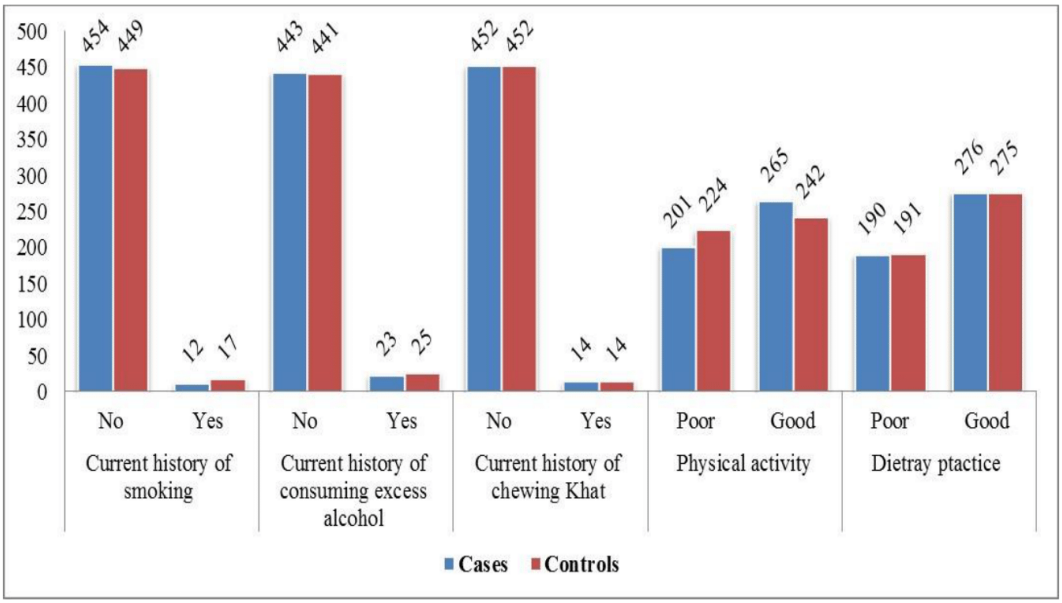


Fig 1. Behavioral practices of study participants, Addis Ababa, Ethiopia (N=932)

Clinical profiles

Most of the cases-controls pairs were from the outpatient department (95.3%, n=444). More number of cases reported history of hospitalization during the past 90 days (75, 16.1%) compared to the controls which was statistically significant (X^2=20.61, p<0.001). More than half of both the cases (54.3%, n=253) and controls (57.5%, n=268) did not have any chronic comorbidity. Among cases with comorbidities (n=2013), HIV/AIDS (19.5%, n=91) followed by hypertension (13.7%, n=64) constituted the highest proportions. In contrast, type 2 diabetes mellitus (17.6%, n=82) followed by cardiovascular diseases (CVDs) (10.9%, n=51) were the prevalent conditions among the controls with comorbidities (n=198) (Table 2).

Table 2. Clinical profile of study participants, Addis Ababa, Ethiopia (N=932)

Variable	Category	Cases		Controls	
		Frequency	Percent	Frequency	Percent
Admission classification					
	Outpatient	444	95.3	444	95.3
	Inpatient	22	4.7	22	4.7
History of hospitalization in the past 90 days*					
	No	391	83.9	435	93.3
	Yes	75	16.1	31	6.7
Presence of comorbidity					
	No	253	54.3	268	57.5

	Yes	213	45.7	198	42.5
Common comorbidities**					
	Type 2 diabetes mellitus	25	5.4	82	17.6
	Hypertension	64	13.7	NA	NA
	Chronic or End stage kidney disease	18	3.9	26	5.6
	HIV/AIDS	91	19.5	17	3.6
	Mental health problem	3	0.6	6	1.3
	Cardiovascular diseases	15	3.2	51	10.9
	Musculoskeletal problems	14	3.0	21	4.5
	Neurological problems	8	1.7	28	6.0

*Includes inpatients; **Percentage is computed out of all patients under each stratum and a case or control may report none or at least one comorbid illness other than the current condition.

In the current study, the assessment of clinical symptoms using the MD Anderson Symptom Inventory (MDASI) focused on five commonly reported dimensions: pain, fatigue, distress, sadness, and numbness [15]. The results revealed that a significant majority of both cases (87.6%, n=408) and controls (69.5%, n=324) experienced mild to severe pain. Moreover, a higher percentage of cases reported mild to severe fatigue (91.2%, n=425) compared to controls (85.4%, n=398). In terms of psychological symptoms, 88.4% of cases (n=412) and 82.8% of controls (n=386) reported mild to severe distress. Similarly, a substantial proportion experienced mild to severe sadness, with rates of 89.1% for cases (n=415) and 80.5% for controls (n=375). Lastly, it was observed that cases had a notably higher occurrence of mild to severe numbness (85.8%, n=400) compared to controls (61.8%, n=288) (Fig 2).

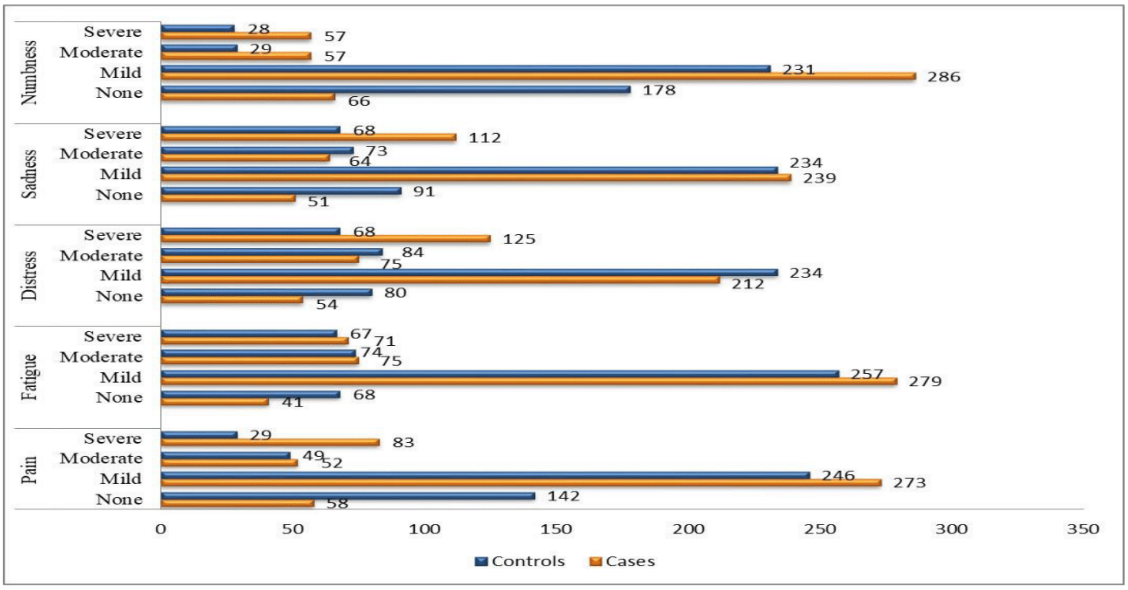


Fig 2. Current clinical symptoms reported by study participants based on the MD Anderson symptoms inventory, Addis Ababa, Ethiopia (N=932)

For the cases, the mean (±SD) duration from diagnosis to treatment initiation was 91.2 (±111.3) days, ranging from 0 to 762. The majority of patients underwent chemotherapy (63.3%, n=295), followed by surgery (52.6%, n=245), and radiotherapy (79.17%). Additionally, some patients reported receiving more than one type of treatment modality. As illustrated in figure 3, a quarter of the patients were diagnosed at either stage IB or IIB according to the International Federation of Gynecologic and Obstetrics (FIGO) classification [23]. The next highest percentages were stages IIA and IIIA, accounting for 17% and 16%, respectively (Fig 3).

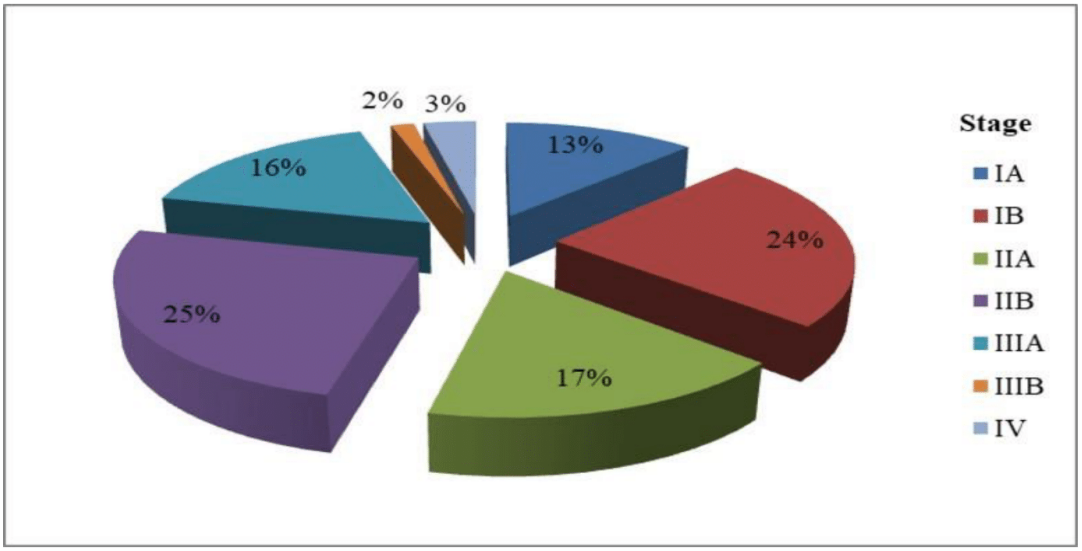


Fig 3. FIGO classification of cancer during diagnosis among patients with cervical cancer in Addis Ababa, Ethiopia (n=466)

Distribution of all costs during the past 90-days

As indicated in Table 3, the distribution of all costs over the past 90 days reveals significant variations in expenditure patterns between cases and controls. In terms of direct medical costs incurred at the current hospitals, the top three expenses for cases were attributed to drugs, imaging diagnoses, and hospital stays, with mean (±SD) amounts of 148.31 (±240.24), 71.23 (±121.25), and 44.47 (±91.49) INT$, respectively. Conversely, controls incurred the highest direct medical costs for drugs, laboratory diagnosis, and imaging services, with mean (±SD) values of 41.66 (±60.20), 29.15 (±27.12), and 14.41 (±34.95) INT$, respectively. When

examining direct medical costs outside the current hospitals, services related to any diagnostic methods (laboratory, computed tomography (CT) scan, magnetic resonance imaging (MRI), x-ray, ultrasound) took the highest expenditure with a mean (±SD) of 114.07 (±274.62) INT$ among cases. Among controls, services related to consultation or admission represented the top expenditure, with a mean (±SD) of 33.66 (±102.36) INT$. Turning to direct non-medical costs, travel to and from health facilities occupied the top rank in both cases and controls, with mean (±SD) amounts of 28.38 (±47.38) and 14.19 (±17.22) INT$, respectively. Finally, productivity loss due to absenteeism emerged as the highest indirect cost for both cases and controls, with mean (±SD) values of 36.69 (±120.31) and 14.05 (±99.83) INT$, respectively (Table 3).

Table 3. Description of all costs in INT$ incurred by the study participants during the previous 90 days, Addis Ababa, Ethiopia (N=932)

	Cases		**Controls**	
Direct medical costs incurred at the current hospitals				
Cost object	**Mean**	**±SD**	**Mean**	**±SD**
Hospital visits	6.46	11.91	5.53	4.37
Laboratory diagnosis	38.36	63.88	29.15	27.12
Imaging services	71.23	121.25	14.41	34.95
Drugs	148.31	240.24	41.66	60.20
Hospital stay	44.47	91.49	1.95	11.69
Intensive care unit or emergency stays	1.54	23.43	0.41	7.18
Surgery	10.26	31.74	0.00	0.00
Nursing or palliative care services	10.78	46.83	8.17	44.19
Total	331.40		101.28	
Direct medical costs incurred outside the current hospitals				
Services related to any or a combination of consultation, follow-up or admission	95.29	431.37	33.66	102.36
Services received related to any diagnosis (laboratory, CT scan, MRI, x-ray, ultrasound)	114.07	274.62	23.54	72.90
Traditional practitioner	14.36	57.06	9.52	51.04
Spiritual leader or care provider	7.84	57.78	1.51	12.24
Total	231.55		68.23	
Direct non-medical costs				
Travel	28.38	47.38	14.19	17.22
Food or supplementation	10.92	22.36	5.12	13.31
Paid care giver	4.29	44.11	1.62	12.16
Total	43.59		20.93	
Indirect costs				
Productivity loss/absenteeism	36.69	120.31	14.05	99.83
Productivity loss care-giver	32.78	94.44	11.58	107.91
Total	69.47		25.63	

Incremental costs during the past 90-days

During the first year of initiating treatment, cases incurred significantly higher mean direct medical costs compared to controls, with mean (±SD) values of 659.51 (±635.91) INT$ for cases and 169.18 (±249.15) INT$ for controls. The observed statistically significant difference in costs, with a mean difference (95% C.I) of 490.33 (404.99-575.63) INT$, suggests a notable distinction within the same cost categories. Overall, cases experienced a mean (±SD) total annual cost of 799.09 (±815.90) INT$, while controls incurred a mean (±SD) total cost of 206.26 (±276.43) INT$. This resulted in an incremental total cost of 592.83 INT$ (95% C.I: 485.21-700.51), indicating a statistically significant difference (p<0.001). Similarly, during the post-first year time frame, both cases and controls exhibited the highest mean expenditures from direct medical costs, with mean (±SD) values of 474.51 (±704.19) INT$ and 176.41 (±187.58) INT$, respectively. In total, cases had a mean (±SD) total cost of 558.99 (±747.09) INT$, while controls incurred a mean (±SD) total cost of 234.60 (±363.39) INT$. Consequently, cases incurred an incremental total cost of 324.39 INT$ (95% C.I: 213.65-435.05) (P<0.001) (Table 4).

Table 4. Incremental costs in INT$ incurred by the study participants during the previous 90 days, Addis Ababa, Ethiopia (N=932)

Time frame	Cost category	Cases	Controls	Mean Difference (95% C.I)	p-value
		Mean (±SD)	Mean(±SD)		
First year	Direct medical costs	659.51(635.91)	169.18(249.15)	490.33 (404.99-575.63)	p<0.001
	Direct non-medical costs	49.75(121.69)	19.53(33.36)	30.22(14.52-46.06)	p<0.001
	Indirect costs	89.83(225.17)	17.55(27.39)	72.28(43.89-100.65)	p<0.001
	Total costs	799.09(815.90)	206.26(276.43)	592.83(485.21-700.51)	p<0.001
Post first year					
	Direct medical costs	474.51(704.19)	176.41(187.58)	298.10(200.86-395.29)	p<0.001
	Direct non-medical costs	38.14(34.82)	23.35(24.67)	14.79(9.08-20.43)	p<0.001
	Indirect costs	46.34(124.30)	34.84(298.21)	11.50(-31.52-54.51)	p<0.001
	Total costs	558.99(747.09)	234.60(363.39)	324.39(213.65-435.05)	p<0.001

Annual Incremental costs

In the comparison of mean (±SD) total annual costs among cases, outpatients exhibited costs of 2597.37 (±2940.43) INT$, while inpatients reported 5766.57(±5498.89) INT$. The difference, indeed, was not statistically significant with a mean difference (MD) of -3169.20 INT$ (95% C.I: -5792.69 to -1130.55, p < 0.060). Similarly, controls reported total annual costs of 856.11 INT$ (±1247.24) and 1319.56 INT$ (±1803.56) at the outpatient and inpatient departments, respectively. The observed difference was not statistically significant (MD = -463.46 INT$, 95% C.I: -1374.58 to 265.16, p = 0.270). Further stratification based on admission classification

revealed that outpatient cases incurred significantly higher annual mean total costs compared to outpatient controls (MD = 1741.27 INT$, 95% C.I: 1469.25-2050.13) (p =0.001). Similarly, inpatient cases reported a statistically significant and higher annual mean total cost compared to inpatient controls (MD = 4447.01 INT$, 95% C.I: 2261.43 to 6864.28, p=0.023) (S1 Table).

As illustrated in Table 5, the yearly incremental costs were delineated based on the year of occurrence and major cost categories. In the first year, annual direct medical costs took the top position for both cases and controls, with mean (±SD) values of 2638.05 (±2543.64) INT$ and 676.78 (±996.71) INT$, respectively. The mean of incremental annual direct medical costs among cases was 1961.27 INT$ (95% C.I: 1619.97-2302.58) (p<0.001). The mean difference in total costs among cases during the first year of initiating treatment was 2371.42 INT$ (95% C.I: 1940.87-2802.03), indicating a statistically significant difference from controls (p<0.001). Similarly, during the post-first-year time frame, direct medical costs constituted a higher proportion of annual expenditures. Cases incurred a mean (±SD) cost of 1898.02 (±2816.72) INT$, whereas controls had an expenditure of 705.68 (±750.26) INT$. The incremental cost in direct medical costs for cases was 1192.34 INT$ (95% C.I: 803.50-1581.20). The mean incremental total cost among cases during the same timeframe was 1297.39 INT$ (95% C.I: 854.59-1740.26), revealing a statistically significant difference (p<0.001).

Table 5. Annual incremental costs in INT$ incurred by the study participants, Addis Ababa, Ethiopia (N=932)

Time frame	Cost category	Cases	Controls	Mean Difference (95% C.I)	p-value
		Mean (±SD)	Mean(±SD)		
First year	Direct medical costs	2638.05(2543.64)	676.78(996.71)	1961.27(1619.97-2302.58)	p<0.001
	Direct non-medical costs	198.99(486.78)	77.83(133.38)	121.16(58.08-184.25)	p<0.001
	Indirect costs	359.23(900.74)	70.24(109.51)	288.99(175.53-402.46)	p<0.001
	Total costs	3196.27(3263.62)	824.85(1105.69)	2371.42(1940.87-2802.03)	p<0.001
Post-first year					
	Direct medical costs	1898.02(2816.72)	705.68(750.26)	1192.34(803.50-1581.20)	p<0.001
	Direct non-medical costs	152.52(139.26)	93.45(98.70)	59.07(36.36-81.81)	p<0.001
	Indirect costs	185.32(497.17)	139.34(1192.87)	45.98(-126.28-218.02)	p<0.001
	Total costs	2235.86(2988.37)	938.47(1453.54)	1297.39(854.59-1740.26)	p<0.001

Drivers of total annual cost in cancer care

The main cost drivers in cancer care are diagnosis and treatment, which account for the largest expenses across both the first year and post-first year phases. In the first year, diagnosis costs are the highest, averaging INT$1548.16 (±SD INT$1946.87), followed by treatment costs at INT$1004.18 (±SD INT$1403.45). Post-first year, diagnosis costs remain significant at INT$1020.91 (±SD INT$2344.55), with treatment costs averaging INT$796.26 (±SD INT$1001.36). Indirect costs such as lost productivity also contribute notably, especially in the first year (INT$359.23, ±SD INT$900.72), although they decrease post-first year. Direct non-medical costs, such as transportation, are relatively smaller but still impactful, averaging

INT$199.00 (±SD INT$486.77) in the first year and reducing to INT$152.52 (±SD INT$139.27) afterward (Table 6).

Table 6. Major cost drivers in INT$ of cancer care by phase and time frame in Addis Ababa, Ethiopia

Time frame	Care phase and associated costs	Base case mean(±SD)	Sensitivity analysis range	
			Lower (-20%)	Upper (+20%)
First year	Diagnosis costs	1548.16 (1946.87)	1238.53	1857.79
	Treatment costs	1004.18(1403.45)	803.34	1205.02
	Nursing and palliative care	39.30(215.04)	31.44	47.16
	Direct non-medical costs	199.00(486.77)	159.20	238.80
	Indirect costs	359.23(900.72)	287.38	431.08
Post-first year	Diagnosis costs	1020.91(2344.55)	816.73	1225.09
	Treatment costs	796.26(1001.36)	637.01	955.51
	Nursing and palliative care	47.38(150.04)	37.90	56.86
	Direct non-medical costs	152.52(139.27)	122.02	183.02
	Indirect costs	185.33(497.17)	148.26	222.40

Predictors of total annual cost in cancer care

A Tukey's biweight regression analysis was conducted in R to identify predictors of total annual cost. Several steps were taken to refine the fitness of the final model. Dummy variables with minimal contribution, such as marital status and level of education categories, were excluded. Additionally, three dummy coded variables with a variance inflation factor (VIF) exceeding 2.5 were recoded to mitigate multicollinearity among predictors. Furthermore, nine observations with influential outliers were removed from the model. The residual standard error (RSE) of the robust model was found to be lower than that of the ordinary least square (OLS) model (RSE=1881.64 vs. 1332.04, for the OLS and Tukey's models respectively), indicating a favorable fit. The diagnosis of heteroscedasticity using the studentized Breusch-Pagan test suggested that the variance of residuals was constant (BP = 22.001, df = 15, p-value = 0.108).

The final model revealed that, keeping other variables constant, patients with households larger than 5 members are likely to incur a higher total annual cost of 492.82 INT$ compared to those with fewer members (β=492.82, p=0.016). Patients with comorbid conditions were more likely to incur an additional total annual cost of 834.96 INT$ compared to those without comorbidity

(β=834.96, p<0.001). The absence of social support significantly increases the total annual cost of patients by 627.48 INT$ (β=627.48, p=0.001). Patients with poor dietary habit are more likely to expend an additional 740.27 INT$ annually compared to those with good dietary practices (β=740.27, p<0.001). The total annual cost of cervical cancer during the first year of starting treatment increases by an average of 967.73 INT$ compared to the estimate during the post-first-year timeframe (β=967.73, p<0.001). An advanced stage of cancer during diagnosis is associated with an additional total annual cost of 1324.12 INT$ compared to those at an early stage (β=1324.12, p<0.001) (Table 7).

Table 7. Predictors of total annual cost in INT$ among patients with cervical cancer in Addis Ababa, Ethiopia (n=457)

Variables	Estimate	Std. Error	t value	Pr(>|t|)
(Intercept)	-7.0739	222.0823	-0.032	0.974604
Age >52 years	210.0943	173.9764	1.208	0.227847
Not able to read and write	-222.0755	200.9696	-1.105	0.269753
Employed to any organization	33.6234	218.5482	0.154	0.877799
Merchant	453.9785	354.6270	1.280	0.201163
More than 5 members in the household	492.8157	204.1674	2.414	0.016194*
Concomitant chronic comorbidity	834.9642	167.9186	4.972	9.49e-07*
Absence of social support	627.4826	184.6109	3.399	0.000738*
Poor physical activity	224.2978	177.8559	1.261	0.207932
Poor dietary habit	740.2696	185.9441	3.981	8.02e-05*
In the first year of starting treatment	967.7256	184.4599	5.246	2.42e-07*
Advanced stage of cancer	1324.1189	246.4117	5.374	1.25e-07*
Symptomatic per MDASI rating	39.7220	205.9067	0.193	0.847116
Admission to the inpatient	860.8666	590.0070	1.459	0.145255
Days of hospitalization in the past 90 days	92.0729	55.3280	1.664	0.096797
Days from diagnosis to treatment initiation	0.6230	0.9276	0.672	0.502154

*Statistically significant

Discussion

This research investigated the economic impact of cervical cancer in an urban context of Ethiopia. It placed emphasis on comprehending the direct medical costs, direct non-medical costs, and indirect costs faced by patients in accessing a diverse array of advanced healthcare services. The study also analyzed the incremental costs associated with cervical cancer compared to hypertension. The inclusion of hypertensive patients as a control group was essential for contextualizing the economic burden of cervical cancer. Hypertension, being a prevalent non-cancer chronic condition, serves as a meaningful comparator, allowing for a clear differentiation between the costs of cancer treatment and those of less intensive chronic disease management. As such, the study highlights the unique financial challenges faced by cervical cancer patients, especially in terms of diagnostic and treatment costs, which were significantly higher compared

to controls. These findings provide a robust foundation for policymakers to develop more effective cost-containment strategies and targeted public health interventions. In addition, the factors influencing the total annual costs incurred in this patient population were identified.

The main direct medical costs for cervical cancer cases at the studied hospitals were driven by expenses for drugs, imaging diagnostics, and hospital stays, making them the top contributors to total costs. These diagnosis and treatment costs were the primary drivers in both the first year and post-first-year periods. This is largely due to the high cost of medications commonly used in cancer management, which significantly elevates the overall cost of care. Additionally, the intricate nature of clinical decision-making in cancer treatment necessitates a comprehensive approach, with imaging diagnoses—primarily utilizing ultrasound, CT, and MRI evaluations—playing a significant role. Despite inpatient admissions constituting a substantial portion of direct medical costs, there was no statistically significant difference between outpatient and inpatient cases ($p=0.060$). This lack of significance could be primarily attributed to the smaller proportion of patients assessed in the inpatient group. However, the costs associated with hospitalization were markedly higher among the cases compared to the controls, potentially linked to frequent emergency unit admissions or visits by the cases. The results indicate a significantly higher incidence of hospitalization among cases, either at present or in the past 90 days, compared to the controls ($X^2=20.61$, $p<0.001$). A report from China also highlighted that inpatient care accounted for 58.6% of cancer treatment costs [24]. Even though medications stood out as the primary cost contributors for both cases and controls in this study, the challenge on availability and the elevated expense of individual drugs presents a substantial hurdle, particularly for cancer patients compared to controls. This is in line with reports indicating that anticancer medicines are poorly available [25] or more costly than other classes of drugs[26]. A study conducted by Kasahun and colleagues highlighted that nearly three-fourths of cancer patients in Addis Ababa faced catastrophic health expenditures [27]. Additionally, the reported high-cost may also be associated with the clinical symptoms experienced by patients, as a larger proportion of cases reported mild to severe clinical symptoms in contrast to the controls. A recent report underscored that addressing the relief of cancer-related symptoms significantly contributed to the financial burden borne by patients in terms of out-of-pocket expenditures[28].

The analysis of costs incurred outside the present hospitals indicates that, among cases, imaging services took the top position, whereas costs related to consultation visits were highest among

controls. This observation underscores the substantial reliance on common cross-sectional imaging modalities, specifically CT and MRI in the diagnosis and monitoring of cancer [29]. Cases not only accumulated significant expenses for imaging services at the current hospitals but also sought similar services at other hospitals or centers during periods of non-functionality or extended waiting times in the present facilities. The challenges of high costs and prolonged waiting times for diagnostic tests have been reported as prominent obstacles facing cancer patients in Ethiopia [30]. Meanwhile, both outpatients and inpatients experienced substantial expenses, with a slight increase observed among the inpatients. However, both figures are notably lower when compared to findings reported a decade ago in the same setting by Hailu and Mariam [8]. The observed difference could be attributed to various factors, including changes in health infrastructure, changes in patient load, economic inflation, and methodological variations between the current study and the one reported a decade ago.

In the present study, we found that the estimated average of total annual expenses for cervical cancer per patient were 3196.27 INT$ or 1162.3 USD in the initial year of treatment commencement. For the subsequent post-first-year period following treatment initiation, the cost decreased to 2235.86 INT$ (813.04 USD). Upon comparing the cost estimates with controls (824.85 INT$ or 299.94 USD), a statistically significant difference emerged across all assessed cost objects, indicating an almost fourfold increase in total annual costs among cases. A nationwide study examining the costs associated with four prevalent cancers in the United States similarly reported a fourfold higher cost for cancer patients compared to non-cancer controls [31]. Another study in the same country highlighted that costs among cases were significantly higher compared to controls[32].

Cases consistently incurred higher costs, both in the first year of treatment initiation and in subsequent time frames. Interestingly, it was revealed that the per capita total annual costs among cases significantly decreased during the post-first year time frame (1162.30 USD vs. 813.04 USD). The accuracy of this estimate may vary throughout the later stages of patients' lives since the assessments conducted did not account for end-of-life care or mortality costs. Consequently, there is a potential for an upward trend in expenses or an increased likelihood of higher costs during the final year of life. Numerous studies have illustrated that both the initial and concluding years of life for individuals with cancer are linked to elevated healthcare expenditures [33-35]. Conversely, among controls, there was a slight increase in the same figure

(299.94 USD vs. 341.29 USD) (Table 5). This notable difference could be primarily attributed to the resource-intensive nature of initial aggressive treatments that patients receive during the early phases of cancer care, including surgeries, radiotherapy, or chemotherapy (either neo-adjuvant or adjuvant). Additionally, patients may undergo various diagnostic processes and repeated hospital treatments, such as chemotherapy, contributing to higher costs. This financial burden may decrease in subsequent phases of cancer care, essentially before end-of-life, as well as in comparison to other chronic illnesses.

It is noteworthy that, despite variations in years of follow-up, the overall cost in our study was considerably lower compared to a similar estimate reported in Ontario, which amounted to 29,027.7 USD [5]. Several factors may explain the observed differences, including variations in healthcare system structures and payment models, differences in treatment protocols and standards of care, and economic disparities. Additionally, differences in healthcare spending across populations could also play a role, among other influencing factors. These diverse elements may collectively influence the overall cost landscape and financial burden associated with cervical cancer care in the two settings. It is interesting to note that a study in Brazil reported a slightly higher figure (3591.72 INT$) for the total annual costs of cervical cancer per patient [36]. Additionally, this study emphasized that direct medical costs accounted for 81.2%, which is comparable to our finding of 82.5%. This similarity in the distribution of costs suggests a common trend in the dominance of direct medical costs in the overall economic burden of cervical cancer in both settings.

An analysis of factors influencing the total annual cost of cervical cancer indicated that certain patient characteristics—such as having more than five family members in the household, experiencing concomitant chronic comorbidity, lacking social support, practicing poor dietary habits, being in the initial year of treatment initiation, and being in an advanced stage of cancer—exhibited a statistically significant positive association. The impact of a larger household size on the yearly total expenditure might stem from either having more potential sources of financial support or facing elevated premiums for community-based health insurance. Another study in the current research setting indicated that individuals with a household size of five or more were more prone to encountering poor dietary diversity [37], which may have an indirect effect on total cost of cancer management. It is probable that chronic comorbidity can impact the overall costs of cervical cancer, either directly or indirectly. Directly, patients may

face intricate treatment regimens, prolonged hospitalizations, or additional imaging tests, all of which contribute to the total cost. Indirectly, there might be related costs associated with frequent transportation to hospitals, lost productivity, or expenses for paid caregivers, among other factors. A recent study in Taiwan demonstrated that cancer patients with mental health disorders incurred costs that were 50% higher than those without such issues [38]. A separate study conducted in China found that comorbidities in individuals with lung cancer led to frequent outpatient visits, hospitalizations, and increased expenditures [39].

The effect of absence of social support and poor dietary habit on the increasing annual expenditures in cervical cancer appears to be quite intricate and interactive. From the sample, patients with poor social support were found to be about 1.78 times more likely to have poor dietary habit (COR: 1.78: 95% C.I: 1.19 -2.67). The fact that cancer patients reported poor level of dietary diversity has been documented in a recent study [37]. This, in turn, may compromise patients' immune system and overall health, leading to increased side effects from cancer treatments. Prolonged recovery times and additional medical interventions to manage side effects can contribute to the higher costs reported. In a parallel note, poor diet has also been reported to significantly contribute in the incidence of new cases in the United States [40].

Furthermore, the implicit correlation between an advanced stage of cancer and increased overall costs is evident. This connection is influenced by various factors such as the necessity for sophisticated diagnostic methods, personalized treatment strategies, frequent hospitalizations, and the adverse effects of treatments. The progression to an advanced stage of cancer could be a predictor for the requirement of end-of-life care in cancer management which, indirectly, exacerbates total healthcare expenditures in this population [35] On a similar note, it is probable that the initial year of cancer diagnosis necessitates repetitive diagnostic procedures and extended treatment regimens spanning several months. Consequently, these factors are linked to increased overall costs.

While there may be potential deviations in the reported cost estimates due to factors such as recall bias, disease prognosis, and projections, this study aimed to provide a comprehensive and up-to-date assessment of the financial burden of cervical cancer in Ethiopia. The inclusion of a sensitivity analysis helps mitigate the effect of unreported cases, reducing the risk of deviation from realistic cost scenarios and improving the robustness of the findings. A series of endeavors, including design, modeling assumptions, and analysis techniques, were undertaken to enhance

the precision of the derived conclusions. To minimize recall bias, the cost estimation was conducted over a three-month period, with an additional stratification of patient groups into the first year and post the first year of diagnosis. However, there are limitations that may affect the generalizability of the findings. First, the study excluded patients referred from rural areas or other regions, which may present a different cost structure. Second, productivity losses related to mortality and reduced productivity (presenteeism) were not considered in the cost estimation. Third, intangible costs, such as pain and suffering, were not examined, as these subjective experiences are difficult to quantify monetarily. Additionally, the willingness-to-pay method, often used to measure intangible costs, was not included due to ethical concerns. [17].

Conclusion

The costs associated with cervical cancer in Addis Ababa were calculated to represent the yearly total expenditure, encompassing direct medical, non-medical, and indirect cost components. During the first and post-first year of diagnosis, the direct medical costs were assessed at 2638.05 and 1898.02 INT$ respectively, holding the highest rank among all cost categories and covering 82.5% and 84.9% of the average in total annual costs. In comparison to the control group, individuals with cervical cancer accrued additional mean total annual costs of 1961.27 and 1297.39 INT$ during the first and post-first year periods, respectively. Various patient characteristics, including having more than five family members in the household, experiencing concurrent chronic comorbidities, lacking social support, adopting poor dietary habits, being in the initial year of treatment initiation, and being in an advanced cancer stage were found to be statistically significant predictors of increase in total annual costs of cervical cancer management. It is crucial to implement policies that prioritize ensuring the availability and affordability of medicines, encourage the prescription of generic drugs, and emphasize the prevention and early detection of cervical cancer. Furthermore, there is a need to expand tertiary treatment center facilities, coupled with the introduction of cost-sharing schemes to guarantee the accessibility of services.

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Competing interests

The authors have declared that no competing interests exist.

Captions

Table 6. Sociodemographic and economic characteristics of study participants, Addis Ababa, Ethiopia (N=932)

Fig 4. Behavioral practices of study participants, Addis Ababa, Ethiopia (N=932)

Table 7. Clinical profile of study participants, Addis Ababa, Ethiopia (N=932)

Fig 5. Current clinical symptoms reported by study participants based on the MD Anderson symptoms inventory, Addis Ababa, Ethiopia (N=932)

Table 8. Description of all costs in INT$ incurred by the study participants during the previous 90 days, Addis Ababa, Ethiopia (N=932)

Table 9. Incremental costs in INT$ incurred by the study participants during the previous 90 days, Addis Ababa, Ethiopia (N=932)

Table 10. Annual incremental costs in INT$ incurred by the study participants, Addis Ababa, Ethiopia (N=932)

Table 6. Major cost drivers in INT$ of cancer care by phase and time frame in Addis Ababa, Ethiopia

Table 7. Predictors of total annual cost in INT$ among patients with cervical cancer in Addis Ababa, Ethiopia (n=457)

S1 Table. Cost difference by Patient and admission classification

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Appendix I: Information sheet-English version

Title of the study

‘Spatiotemporal dynamics of incidence cases, access to healthcare and the economic burden of cervical cancer in Addis Ababa, Ethiopia’

[Salutation]:

My name is _____. I am currently a member of data collectors for a research which is conducted by Tariku Shimels and his supervisor/s. This research is part of a Ph.D. study intended to map the incidence, assess the access to healthcare of patients diagnosed with cervical cancer in Addis Ababa, and the economic burden of the disease among this population. You are invited to take part in the study. However, before you are going to be part of this research, I kindly invite you to carefully read/hear on why the research is being conducted, and what it involves as described below.

Purpose of the study

The aim in this study is to assess spatial distribution of incident cases, determine access to healthcare of patients, determine the overall cost and explore the determinants of access and cost.

Why you are selected to take part

The output of the study is expected to help make appropriate recommendations to concerned stakeholders, especially the ministry of health, and inform decision making and policy in the management of cervical cancer in Ethiopia in general, and in Addis Ababa in particular. You are also expected to have sufficient information on the proposed aims of the study. As a result, it is highly essential and valuable that you take part in this study, and that your inputs are included to achieve the aims.

Procedure

We invite you to participate in this project. If you are willing to participate in this project, you need to understand and sign the agreement form. Then, you will be interviewed by data collectors. You do not need to write your name to data collector and all your responses, and the results obtained will be kept confidential by using coding system whereby no one will have access to your response.

Risk/Discomfort

By participating in this project, you may fill that it has some discomfort especially on wasting 15-20 minutes. We hope you will participate in the study for the sake of the benefit of the research result. There is no risk in participating in this research project.

Benefits

If you participate in this project, there may not be direct benefit to you, but your participation is likely help us to meet the research objectives. This will enable to uncover healthcare access and economic issues that patients like you face because of cervical cancer. And this will help us to recommend for and inform policy makers to improve services for the patients in the same problem.

Incentives

You will not be provided any incentives or payment to take part in this project.

Confidentiality

The information collected from this research project will be kept confidential. Information will be stored in a file, without your name, only code number is used. It will not be revealed to anyone except the principal investigator, and it will be kept locked with code.

Right to refuse or withdraw

You have full right to refuse from participating in this project. You can choose not to respond to some or all questions if you do not want to give your response. You have also full right to withdraw from this study at any time you wish without losing any of your right in the health facility.

Persons to contact

This research project is reviewed and approved by the ethical review committees of Addis Ababa University and Saint Paul's Hospital Millennium Medical College. If you have any question, you can contact any of the following individuals and you may ask any time you want.

Contact address of principal investigator:

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Appendix II: Informed consent form-English version

I hereby confirm that:

I confirm that I have read and understand the Participant Information Sheet

I have had the opportunity to ask questions and had them answered

I understand that all personal information will remain confidential and that all efforts will be made to ensure I cannot be identified (except as might be required by law)

I agree that data gathered in this study may be stored anonymously and securely, and may be used for future research

I understand that my participation is voluntary and that I am free to withdraw at any time without giving a reason.

I agree to take part in this study

Signature of participant:---------- date _____

Signature of Enumerator taking the consent:----------date----------

Appendix III: Information sheet- Amharic version

የመረጃ ቅጽ

[ሰላምታ]፤

ስሜ----------ይባላል። አቶ ታሪኩ ሽመልስና የጥናት ኣማካሪው/ዎቹ በሚሰሩትና ‹የማህጸን ጫፍ እጢ በአዲስ አበባ ከተማ ያለው የቦታና የጊዜ ስርጭት፤ ለታካሚዎች ያለ የጤና አገልግሎት ተደራሽነት፤ እንዲሁም ኢኮኖሚያዊ ጫናው› በሚል ጥናት ላይ መረጃ ሰብሳቢ ስሆን ጥናቱ ደግሞ የፍልስፍና ዶክትሬት ጥናት (ፒ.ኤች.ዲ) አካል ነው። እርስዎም በዚህ ጥናት እንዲሳተፉ ተጋብዘዋል። ይሁን እንጂ፤ በጥናቱ ለመሳተፍ ከመወሰንዎ በፊት ጥናቱ ለምን እንደሚሰራና በሂደቱም ምን ምን ክንዋኔ እንዳለ ለመረዳት ያግዘዎት ዘንድ የሚከተሉትን ሃሳቦች እንዲያደምጡ በአክብሮት እጋብዝዎታለሁ።

የዚህ ጥናት ዓላማ

የዚህ ጥናት ዋነኛ ዓላማዎች የማህጸን ጫፍ እጢ በአዲስ አበባ ከተማ ያለውን አካባቢያዊ ስርጭት መለየት፤ ታካሚዎችን የህክምና ተደራሽነት፤ ህመሙ የሚያደርስባቸውን ኢኮኖሚያዊ ጫና መገመትና መመርመር ፤ ብሎም እንደጤና ጥበቃ ያሉ ለሚመለከታቸው አካላት ውሳኔ መስጫነት ግብዓት የሚሆን ማስረጃ ማቅረብ ነው።

እርስዎ ለምን ተመረጡ?

የጥናቱ ዉጤት የማህጸን ጫፍ እጢ ህክማናና ቁጥጥርን በተመለከተ በሀገር-አቀፍ ድረጃ በተለይ ደግሞ በአዲስ አበባ ደረጃ ለሚመለከታቸው አካላት ምክረ-ሃሳብ ለመስጠትና የፖሊሲ ውሳኔ እንዲቀመጥ ለማድረግ እንደሚያግዝ ይጠበቃል። እርስዎም በተቀመጡት የጥናቱ አላማዎች ላይ በቂ የሆነ መረጃ እንዳለዎት ይገመታል። ስለሆነም የእርስዎ በዚህ ጥናት ውስጥ መካከተት በጣም ጠቃሚና ዋጋ የሚሰጠው ጉዳይ ሲሆን፤ ይህ በመሆኑም የጥናቱን ዓላማ ለማሳካት አስተዋጽኦ ያበረክታሉ።

ሂደት

የተሳታፊነት ፈቃድዎን በፊርማ ካረጋገጡልን በቀጥታ ወደ መረጃ ስብሰባ እንሄዳለን። በዚህም ወቅት መረጃ ሰብሳቢው እርስዎን የተወሰኑ ጥያቄዎች ያቀርብለዎታል፤ ወይም የሚሞሉት መጠይቅ ይሰጠዎታል።የሚሰጡት ምላሽ ምስጢራዊነቱ የተጠበቀ ይሆናል።

በመሳተፍዎ ምን ጉዳት ሊያጋጥምዎ ይችላል?

በዚህ ጥናት በመሳተፍዎ የተወሰነ መሰላቼት በተለይም ከ15-20 ደቂቃ ጊዜዎትን ሊያባክኑ ይችላሉ። ሆኖም በመሳተፍዎ ለጥናቱ ውጤታማነት ከፍተኛ አስተዋጽኦ እንደሚያበረክቱ ተስፋ እናደርጋለን። ከዚህ ያለፈ በጥናቱ ሚጋጥምዎት ምንም አይነት ጉዳት የለም።

ጥቅም

በዚህ ጥናት በመሳተፍዎ የሚያገኙት ቀጥተኛ ጥቅም አይኖርም። ይሁን እንጂ ለጥናቱ ውጤታማነትና ዓላማ መሳካት ጠቀሜታ አለው።በመጠይቁ የስነ ልቦና ጤና ችግር የሚያመላክት ችግር ካለብዎና

ፈቃደኛ ከሆኑ ከስነ አእምሮ ባለሙያ ጋር ተገናኝተው የምክር አገልግሎት የሚያገኙበት ሁኔታ ይመቻቻል። በመጨረሻም ጥናቱ እንደእርስዎ አይነት ታካሚዎችን ጤናና አገልግሎት አሰጣጥ ለማሻሻል ይጠቅማል; ታካሚዎች የሚገጥማቸውን የኢኮኖሚ ጫና መረጃ ለሚመለከታቸው አካላት በማድረስ ለፖሊሲ ግብዓት እደሆን ይደረጋል።

ምስጢራዊነት

በዚህ ጥናት የሚሰበሰበው መረጃ ምስጢራዊነቱ የተጠበቀ ይሆናል።መረጃው ያለስምዎ በመረጃ ቋት ይቀመጣል።ለዚህም የምስጢር መለያ ብቻ የምንጠቀም ይሆናል።ከዋና ተመራማሪው ውጪ ማንም ሰው የሚያገኘው አይሆንም።

ከተሳታፊነት የመቃወም ወይም አቋርጦ የመውጣት መብት

በዚህ ጥናት ያለመሳተፍ ሙሉ መብት አለዎት።ለአንዳንድ ጥያቄዎች ምላሽ ያለመስጠት መብትም አለዎት። በተጨማሪም በፈለጉበት ጊዜ መጠይቁን አቋርጦ የመሄድ ሙሉ መብት አለዎት።

የሚያናግሩት ሰው ቢፈለጉ

ይህ ጥናት በቅ/ጳ/ሆ/ሚ/ሜ/ኮ እና በአዲስ አበባ ዩኒቨርሲቲ የጥናትና ምርምር ኢቲክስ ኮሚቴ የፀደቀ ነው። ስለጥናቱ ምንም አይነት ጥያቄ ካለዎት፤ የጥናቱን ዋና ተመራማሪ ወይም አማካሪውን በሚከተለው አድራሻ ማግኘትና ማናገር ይችላሉ።

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Appendix IV: Informed consent form-Amharic version

የተሰጠ የተሳታፊነት ፈቃድ ቅጽ

የጥናቱን መረጃ ቅፅ ስለማንበቤና እና መረዳቴ፤

የነበሩኝን ጥያቄዎች ስለመጠየቄና ተገቢ ምላሽ ስለማግኘቴ፤

የምሰጠው መረጃ ግላዊነት እንደሚጠበቅ እና ማንነቴ እንዳይታወቅ አስፈላጊው ሁሉ ጥረት እንደሚደረግ፤

የዚህ ጥናት ተሳታፊ ግላዊ ማንነት እንዲሁም የሚሰበሰበው መረጃ ምስጢራዊነት ተጠብቆ እንደሚቀመጥ፤

በጥናቱ የሚኖረኝ ተሳትፎ ሙሉ በሙሉ በራሴ ፍላጎት ላይ የተመሰረተ እንደሆነና በፈለግሁበት ጊዜም ከጥናቱ መውጣት ወይም ማቋረጥ እንደምችል ተገንዝቢያለሁ።

በዚህ መሰረትም በጥናቱ ለመሳተፍ ተስማምቻልሁ።

የተሳታፊው ፊርማ፤----------ቀን----------

የመረጃ ሰብሳቢ ፊርማ፤ ----------ቀን----------

Appendix V: Access to healthcare services questionnaire-English version

Part I: Socio-demographic and economic characteristics		
Q101	Source facility /hospital	1. Public 2. Private
Q102	Service classification	1. OPD 2. Inpatient 3. ICU
Q103	Age (in yrs.)---	----------
Q104	Marital status	1. Single 2. Married 3. Divorced 4. Widowed 5. Separated
Q105	Sub-city	1. Arada 2. Akaki Kality 3. N/S/Lafto 4. Lideta 5. Kirkos 6. Addis Ketema 7. Gulele 8. Bole 9. Yeka 10. Kolfe Keranyo 11. Lemi kura
Q106	Able to read and write	1. Yes 2. No ------> Q107
Q107	Level of education	1. No formal education 2. Grade 1-8(primary schoo1) 3. Grade 9-12 (secondary school)

		4. Higher education (college/university)
Q108	Occupation	1. Government employee 2. Private employee 3. Merchant 4. House wife 5. Housemaid 6. Student 7. Jobless 8. Other, specify----------
Q109	Status of community health insurance coverage	1. Yes 2. No
Q110	Average monthly income of the household (in ETB)	----------
Q111	Number of family members	----------
Q112	Presence of social support (any form of help from community, family, friends…)	1. Yes 2. No
	Part II: Behavioral/life-style practice Questions	
Q113	Do you currently use (smoked or non-smoked) cigarettes?	1. Yes 2. No
Q114	Do you currently drink excess alcohol (i.e > bottle a day)?	1. Yes 2. No
Q115	Do you currently chew Khat or other stimulant substances (Hashish, Ganja…etc)?	1. Yes 2. No
Q116	Do you engage in a minimum of 150-minutes of moderate exercise (example: waking) per week?	1. Yes 2. No
Q117	Do you engage in a minimum of 75-minutes of vigorous exercise (example: gym sport) per week?	1. Yes 2. No
Q118	Which of this list is part of your dietary practice? (select all that apply)	1. Grains 2. Fruits

		3. Low fat 4. Vegetables 5. Processed foods 6. Sweetened beverages 7. Refined grains 8. Excess salt (> 1 spoon) 9. Other, specify ---------- ----------
Part III: Clinical characteristics		
Q119	Presence of any chronic Comorbidity	1. yes 2. No ----------□Q121
Q120	If yes, which (check all that apply)	1. DM 2. Hypertension 3. Chronic/end stage kidney disease 4. HIV/AIDS 5. Mental illness 6. Cardiovascular disease 7. Musculoskeletal 8. Neurological 9. Other, specify----------
Q121	Date of first cancer diagnosis in EC.	----------(mm/yyyy)
Q122	Date of initiation of treatment in EC.	----------(mm/yyyy)
Q123	Stage of cancer at diagnosis (FIGO classification)	1. I 2. II 3. III 4. IV
Q124	Which treatments did you receive/are you receiving for the current diagnosis?(select all that apply)	1. Radiation 2. Chemotherapy/medications 3. Surgery 4. Hormonal therapy

		5. Traditional treatment 6. Other, specify----------
Q125	Ever history of cancer screening	1. Yes 2. No
Q126	History of HPV immunization	1. Yes 2. No

Part IV: Objective measures of access to healthcare in cervical cancer

Domain	**Indicator variables**		**Responses**	**Data collection method**
Geographic accessibility	127	On average, how much time on walk do you travel from your home to get the nearest health facility for getting medical care services (follow-up visits, consultations, surgery, or emergencies etc.) in your current illness? (answer in minutes)	-------minutes	Patient exit-interview
	128	On average, how much time on walk do you travel from your home to get the nearest health facility for getting drugs for your current illness? (answer in hour)	------minutes	Patient exit-interview, Mapping patient residence
	129	On average, how much time on walk do you travel from your home to get the nearest health facility for getting laboratory diagnosis services for your current illness? (answer in hour)	-------minutes	
	130	On average, how much time walk do you travel from your home to get the nearest health facility for getting imaging diagnostic (ultrasound, x-ray…) services for your current illness? (answer in hour)	--------minutes	
	131	On average, how much time on walk do you travel from your home to get the nearest health facility for getting radiotherapy for your current illness? (answer in hour)	--------minutes	
Availability	132	Are any of the essential generic drugs (cisplatin, carboplatin, bleomycin, paclitaxel/docetaxel, rituximab, bevacizumab, gemcitabine) or their brand counterparts	1. Yes 2. No	Observation checklist, exit-interviews

		prescribed on the current visit available at the health facility?		
	133	Are basic diagnostic services (laboratory, ultrasound, histopathology…) required for the current illness available at the current health facility?	1. Yes 2. No	Observation checklist, exit-interviews
	134	Are surgical services of any level for the current illness available at the current health facility?	1. Yes 2. No	Observation check-list
	135	Have you ever received any education and support services (health education, care and support) provided to patients?	1.Yes 2. No	Patient exit-interviews
	136	Have the health professionals (doctors and nurses) providing the oncology services (ex. providing chemotherapy) received any related training?	1. Yes, all 2. Yes, but not all 3. No	Observation checklist, interview of providers
	137	Are palliative care services available at the current health facility?	1. Yes 2. No	Observation checklist
Affordability	138	What is your estimated monthly expenditure for medicines in relation to the current illness? (deduct coverage by health insurance)	---------Birr	Patient exit-interview, record review

Part V: Questionnaire on perceived access to healthcare services in patients with cervical visiting health facilities in Addis Ababa, Ethiopia, 2022

Domains	**Item constructs**		**Responses**				
			1 (absolutely disagree)	2 (disagree)	3 (neutral)	4 (agree)	5 (absolutely agree)
Reachability	Q139	The distance from the health facility to my house is appropriate.					
	Q140	The time required to reach the health facility is appropriate.					
	Q141	Getting to and from the health facility is easy for me.					
Availability	Q142	The health services (including consultation, laboratory tests, imaging etc.) I need are provided at the health facility.					
	Q143	I get medicines or supplies prescribed to me at the health facility.					
	Q144	There is adequate number of health professionals (doctors, nurses) to my need at the health facility.					
	Q145	Health professionals (doctors, nurses…) have the appropriate skill to my healthcare needs.					
Acceptability	Q146	The quality of services provided in the health facility is acceptable.					
	Q147	The health facility staff meets the needs of the					

		clients in various ways, such as education, care and support.					
	Q148	Health workers listen carefully to what I have to say.					
	Q149	The health workers give me enough time.					
	Q150	I trust the statements of the treatment team (doctor, nurse, etc.) about my health and illness.					
	Q151	My preference for same sex health care professionals is taken into account.					
	Q152	I accept other screening services and tests (such as colon cancer) at this health facility.					
	Q153	The treatment team at the health facility is respectful.					
	Q154	The health workers (doctors, nurses etc.) are familiar with the culture and religion of clients and communicate with them appropriately.					
Affordability	Q155	To solve my health problem, I first see a general practitioner.					
	Q156	With the guidance of a general practitioner, I use specialized and sub-specialized services.					
	Q157	Cost is a serious barrier to using health care.					
Accommodation	Q158	It is easy to make an appointment at a health facility.					

	Q159	The expected time to receive the services I need is appropriate.					
	Q160	I can discuss health issues and changes in my condition over the phone (in person) with the treatment team (doctor, nurse, midwife, etc.).					
	Q161	The working hours of the health facility are suitable for receiving healthcare services.					
	Q162	The physical space of the health facility is suitable for receiving services.					
	Q163	Access to some facilities such as wheelchairs, benches, walkers, etc. is easy when needed.					
Awareness	Q164	The education that is given to me is such that I understand them.					
	Q165	The information I need is expressed in simple language without the use of specialized words.					
	Q166	Communication of health workers (doctor, nurse etc.) with clients is appropriate.					
	Q167	Health workers try to make sure I fully understand the health information provided.					
	Q168	My living conditions are taken into accounts, such as marital status, ability to pay, and cultural differences.					

Appendix VI: Cost of illness measurement tool-English version

Group ID: --------(cases and controls will be coded identically making sure that they match for residence, sex, service classification, age (±5 years) and hospital).

Part I: Socio-demographic and economic characteristics		
Q200	Patient classification?	1. Cervical ca 2. Non-ca
Q201	Source facility /hospital;	1. Public 2. Private
Q202	Service classification;	1. OPD 2. Inpatient 3. ICU
Q203	If your classification is in inpatient or ICU, how long is it been in days since you were admitted in the past 3 months?	----------
Q204	Age (in yrs.);	----------
Q205	Marital status;	1. Single 2. Married 3. Divorced 4. Widowed 5. Separated
Q206	Sub-city;	1. Arada 2. Akaki Kality 3. N/S/Lafto 4. Lideta 5. Kirkos 6. Addis Ketema 7. Gulele 8. Bole 9. Yeka 10. Kolfe Keranyo

		11. Lemi kura
Q207	Able to read and write	1. Yes 2. No ------> Q108
Q208	Level of education	1. No formal education 2. Grade 1-8(primary schoo1) 3. Grade 9-12 (secondary school) 4. Higher education (college/university)
Q209	Occupation	1. Government employee 2. Private employee 3. Merchant 4. House wife 5. Housemaid 6. Student 7. Jobless 8. Other, specify----------
Q210	Which source is your medical expense covered by? (select all that apply)	1. health insurance 2. self (selling assets, savings, salary etc) 3. aids or social support 4. relatives or friends
Q211	Average monthly income of the household (in ETB)	----------
Q212	Number of family members	----------
Q213	Presence of social support (any form of help from community, family, friends…)	1. Yes 2. No
Part II: Behavioral/life-style practice Questions		
Q214	Do you currently use (smoked or non-smoked) cigarettes?	1. Yes 2. No

Q215	Do you currently drink excess alcohol (i.e > bottle a day)?	1. Yes 2. No
Q216	Do you currently chew Khat or other stimulant substances (Hashish, Ganja…etc)?	1. Yes 2. No
Q217	Do you engage in a minimum of 150-minutes of moderate exercise (example: waking) per week?	1. Yes 2. No
Q218	Do you engage in a minimum of 75-minutes of vigorous exercise (example: gym sport) per week?	1. Yes 2. No
Q219	Which of this list is part of your dietary practice? (select all that apply)	1. Grains 2. Fruits 3. Low fat 4. Vegetables 5. Processed foods 6. Sweetened beverages 7. Refined grains 8. Excess salt (> 1 spoon) 9. Other, specify ---------- --------

Part III: Clinical characteristics

Q220	Presence of any chronic Comorbidity	1. Yes 2. No ----------□Q222
Q221	If yes, which (check all that apply)	1. DM 2. Hypertension 3. Chronic/end stage liver disease 4. HIV/AIDS 5. Mental illness 6. Cardiovascular disease 7. Musculoskeletal 8. Neurological

		9. Other, specify----------

People with cancer frequently have symptoms that are caused by either their disease or their treatment. We ask you to rate how severe the following symtoms have been in the last 24 hours. Please fill in the circle below from 0(no symptoms were present) to 10 (the symptopm was as bad as you can imagine it could be) for each item.

	0 (Not present)	1	2	3	4	5	6	7	8	9	10 (as BAD as you can imagine)
222. Your pain score at its WORST?	○	○	○	○	○	○	○	○	○	○	○
223. Your fatigue (tiredne s) at its ORST?	○	○	○	○	○	○	○	○	○	○	○
224. Your feeling of be ng distres ed (up et) a its WORST?	○	○	○	○	○	○	○	○	○	○	○
225. Your feeling sad at its WORST?	○	○	○	○	○	○	○	○	○	○	○
226. Your numbness or tingling at its W RST?	○	○	○	○	○	○	○	○	○	○	○

Please Check following for cases only (patients with cervical ca)

Q227	Date of first cancer diagnosis in EC.	----------(mm/yyyy)
Q228	Date of initiation of treatment in EC	----------(mm/yyyy)
Q229	Stage of cancer at diagnosis (FIGO	1. IA 2. IB

	classification)	3. IIA 4. IIB 5. IIIA 6. IIIB 7. IV
Q230	Which treatments did you receive/are you receiving for the current diagnosis?(select all that apply)	1. Radiation 2. Chemotherapy/medications 3. Surgery 4. Hormonal therapy 5. Traditional treatment 6. Other, specify----------

Part IV: Direct medical costs in the past 3 months		**Cost details**				**Gross cost of specific drivers**
		Mention name of cost object	**Quantity (Q)**	**Unit cost (UC)**	**Total cost(Q *UC)**	
Q231	Payments made to physician visits/card at the current hospital	Visit1				
		Visit2				
		Visit 3				
		Visit n (add more visits if any)				
Q232	Payments made to laboratory tests at the current hospital	Test 1				
		Test 2				
		Test 3				
		Test n (add more tests if any)				
Q233	Payments made to other diagnosis (imaging, x-ray…etc)	Imaging 1				
		Imaging 2				
		Imaging 3				
		Imaging n (add if other imaging/x-ray)				
Q233	Payments made to drugs	Drug1				

	prescribed at the current hospital in relation to the main diagnosis or side effect of anticancer medicines	Drug2				
		Drug3				
		Drug 4 Drug 5				
		Drugs n (add if more drugs prescribed)				
Q234	Payments made to hospital stays/admission	Stay 1				
		Stay n (add if more admissions occurred)				
Q235	Payments made to intensive care unit (ICU) stays	ICU1				
		ICU n (add if more ICU admissions occurred)				
Q236	Payments made to surgery and related procedures	Procedure 1				
		Procedure n				
Q237	Payments made to chemotherapy administration/radiotherapy /physiotherapy /related nursing care services (cases)	Service 1				
		Service 2				
		Service 3				
		Service n (add if more services received)				
Q238	Payments made to physician visits outside the current hospital	Visit 1				
		Visit 2				
		Visit n (add if more visits made to other hospital)				
Q239	Payments made to diagnostic services obtained outside the current hospital	Diagnosis 1				
		Diagnosis 2				
		Diagnosis n (add if more diagnosis services received in other hospital)				
Q240	Payments made to related	Diagnosis 1				

	investigation services (laboratory, CT scan, ultrasound, MRI, X-ray) at other facilities/hospitals	Diagnosis 2				
		Diagnosis n (add if more diagnosis services received in other hospital)				
Q241	Payments made to traditional healers	Healer 1				
		Healer n (add if visited more traditional healers)				
Q242	Payments made to spiritual healers	Healer 1				
		Healer n (add if more spiritual healers visited)				
Part V: Direct non-medical costs in the past 3 months						
Q243	Payments made to travels to and from hospitals or/and traditional/spiritual healers	Travel 1				
		Travel 2				
		Travel 3				
		Travel n (add if more travels reported)				
Q244	Payments made to food /medical supplements	Food/sup1				
		Food/sup 2				
		Food/sup n (add if more food/sups reported)				
Q245	Payments made to caregivers	Caregiver/cost1 Caregiver/cost n (add if more caregivers/costs reported)				
Part VI: Indirect costs						
Q246	Have you been absent from job due to the illness in the past 3 months?	1. Yes 2. No				
Q247	If Yes to Q242 above,	Number of days you were absent ---------- Your average monthly income on the job(in ETB)----------|				

Q248	Has your caregiver been absent from job due to your illness in the past 3 months?	1. Yes 2. No	
Q249	If yes to Q244 above, what is the cost of absence?	1. Number of days your caregiver was absent-------- 2. His/her average monthly income (in ETB)----------	

Appendix VII: Access to healthcare services questionnaire- Amharic version

ክፍል 1: የታካሚ ስነ-ህሰባዊ፤ማህበራዊ እና ኢኮኖሚያዊ ሁኔታዎች መለኪያ		
ጥ101	የታካሚዋ ምድብ፤	1. የካንሰር ታካሚ ናቸው 2. የካንሰር ታካሚ አይደሉም
ጥ102	የሚታከሙበት ጤና ተቋም/ሆስፒታል ዓይነት፤	1. የመንግስት 2. የግል
ጥ103	የሚታከሙበት የአገልግሎት ዘርፍ፤	1. ተመላላሽ ህክምና 2. ተኝቶ ህክምና 3. ጽኑ ህሙማን
ጥ104	እድሜ (በዓመት)፤	----------
ጥ105	የጋብቻ ሁኔታ፤	1. ያላገባች 2. ያገባች 3. ፍች የፈጸመች 4. ባሏ የሞተባት 5. ተለያይተው የሚኖሩ
ጥ106	ክፍለ ከተማ፤	1. አራዳ 2. አቃቂ 3. ንፋስ/ላፍቶ 4. ልደታ 5. ቂርቆስ 6. አዲስ ከተማ 7. ጉለሌ 8. ቦሌ 9. የካ 10. ኮልፌ 11. ለሚ ኩራ
ጥ107	ማንበብ እና መጻፍ ይችላሉ፤	1. አዎ 2. አይ
ጥ108	የትምህርት ደረጃ፤	1. መደበኛ ትምህርት ያልተማሩ 2. 1-8 ክፍል (የመጀመሪያ ደረጃ) 3. 9-12 ክፍል (ሁለተኛ ደረጃ) 4. ኮሌጅ/ዩኒቨርሲቲ የገቡ/የጨረሱ (ከፍተኛ ትምህርት)
ጥ109	ስራ፤	1. የመንግስት ተቀጣሪ 2. የግል ተቀጣሪ 3. ነጋዴ

		4. የቤት እመቤት 5. የቤት ሰራተኛ 6. ተማሪ 7. ስራ የሌለው 8. ሌላ፤ ካለ ይጠቀስ፤----------
ጥ110	የማህበረሰብ-አቀፍ ጤና መድህን ተጠቃሚ ነዎት፤	1. አዎ 2. አይ
ጥ111	የቤተሰቡ አማካይ ወርሀዊ ገቢ (በብር)	----------
ጥ112	አንድ ላይ የሚኖሩ የቤተሰብ አባላት ብዛት	----------
ጥ113	የማህበረሰብ ድጋፍ መኖር (በአካባቢ ፤ ጎረቤት ወይም ቤተሰብ ወዘተ የሚገኝ) ማንኛውም እርዳታ አለዎት፤	1. አዎ 2. አይ
ክፍል 2፤ ስነ-ባህርያዊ ወይም የዓኗኗር ዘዴን የተመለከቱ መጠይቆች		
ጥ114	አሁን ላይ የሲጋራ ውጤቶችን (የሚጨሱ ወይም የማይጨሱ) ይጠቀማሉ፤	1. አዎ 2. አይ
ጥ115	አሁን ላይ ማንኛውም የአልኮል መጠጦችን አብዝተው (በቀን ከ1 ጠርሙስ በላይ) ይጠቀማሉ፤	1. አዎ 2. አይ
ጥ116	አሁን ላይ ጫት ወይም ሌሎች አነቃቂ መድሀኒቶችን (ሀሽሽ፤ ጋንጃ/ሺሻ፤ ወዘተ) ይጠቀማሉ፤	1. አዎ 2. አይ
ጥ117	በሳምንት ውስጥ ቢያንስ ለ150 ደቂቃ ወይም 2 ሰዓት ከ30 ደቂቃ የሚወስድ መጠነኛ የአካል እንቅስቃሴ (ለምሳሌ የእግር ጉዞ…) ያደርጋሉ?	1. አዎ 2. አይ
ጥ118	በሳምንት ውስጥ ቢያንስ ለ 75 ደቂቃ ወይም 1 ሰዓት ከሩብ የሚወስድ ከባድ አካላዊ እንቅስቃሴ (ምሳሌ፤ ጂም ስፖርት…) ያደርጋሉ?	1. አዎ 2. አይ
ጥ119	ከእነዚህ ውስጥ የትኞቹ በምግብ ዝርዝርዎ ውስጥ ይካተታሉ? (መልስ የሚሆነውን ሁሉ ይምረጡ)	1. ጥራጥሬዎች 2. ፍራፍሬዎች 3. አነስተኛ ስብ 4. አትክልቶች 5. በፋብሪካ የተቀነባበሩ ምግቦች 6. ጣፋጭ መጠጦች 7. አሰር የሌላቸው ጥራጥሬዎች 8. ከፍተኛ ጨው (በቀን ከ1 የሻይ

		ማንኪያ በላይ) 9. ሌላ ካለ, ይገለጽ ---------- ----------
ክፍል 3: ጤና-ነክ መጠይቆች		
ጥ120	ማንኛውም ዓይነት ተጓዳኝ የረጅም ጊዜ የጤና ችግር አለብዎት፤	1. አዎ 2. አይ -----□ጥ122
ጥ121	ለጥያቄ 120 መልስዎ አዎ ከሆነ፤ የትኛው፤(መልስ የሚሆኑትን ሁሉ ይምረጡ)	1. የስኪር ህመም 2. የደም ግፊት ህመም 3. የኩላሊት ህመም 4. አች.አይ.ቪ/ኤድስ 5. የአእምሮ ህመም 6. የልብና ደም ዝውውር ጤና ችግር 7. የጡንቻና አጥንት 8. የነርቭ ህመም 9. ሌላ ካለ፤ ይገለጽ----------
ጥ122	ለመጀመሪያ ጊዜ ካንሰር እንዳለብዎት በምርመራ ያወቁበት ቀን (በኢትዮጵያ አቆጣጠር)፤	----------(ወር/አ.ም)
ጥ123	ለመጀመሪያ ጊዜ መድሃኒት የጀመሩበት ቀን (በኢትዮጵያ አቆጣጠር)፤	----------(ወር/አ.ም)
ጥ124	መጀመሪያ ሲመረመሩ የካንሰሩ ደረጃ ምን ነበር ፤	1. I 2. II 3. III 4. IV
ጥ125	አሁን ላለብዎት የጤና ችግር እስካሁን ድረስ የትኞቹን ህክምናዎች ወስደዋል፤(የወሰዱትን ሁሉ ይምረጡ)	1. የጨረር 2. የመድሀኒት 3. የቀዶ ህክምና 4. የሆርሞን/የሰውነት ቅመም 5. ባህላዊ ህክምና 6. ሌላ፤ ይጠቀስ----------
ጥ126	የቅድመ-ካንሰር ምርመራ ተደርጎልዎት ያውቃል፤	1. አዎ 2. አይ
ጥ127	የማህጸን ጫፍ ካንሰር መከላከያ ክትባት	1. አዎ

	ወስደው ያውቃሉ፤	2. አይ

ክፍል 4፡ የአቅርቦት እና ተደራሽነት መለኪያ መጠይቆች

ስውር ልኬት	ጠቋሚ መለኪያዎች		ምላሽ	መረጃው የሚሰበሰብበት መንገድ
ቅርበት	ጥ128	ለአሁኑ ህመምዎ የህክምና አገልግሎቶችን (ምሳሌ፤ ክትትል ለማድረግ፤ የምክር አገልግሎት፤ ቀዶ-ህክምና ወይም ድንገተኛ ህክምና ወዘተ) ለማግኘት ከቤትዎ በአማካይ ለምን ያህል ጊዜ በእግር ጉዞ ያስኬዳል? (መልሱ በደቂቃ ይቀመጥ)	------ደቂቃ	ታካሚው ህክምና ጨርሰው ሲወጡ በሚደረግ ቃለ-መጠይቅ፤
	ጥ129	ለአሁኑ ህመምዎ የታዘዘልዎትን መድሀኒት ለማግኘት ከቤትዎ በአማካይ ለምን ያህል ጊዜ በእግር ጉዞ ያስኬዳል? (መልሱ በደቂቃ ይቀመጥ)	------ደቂቃ	ታካሚው ህክምና ጨርሰው ሲወጡ በሚደረግ ቃለ-መጠይቅ፤
	ጥ130	ለአሁኑ ህመምዎ የታዘዘልዎትን የላቦራቶሪ ምርመራዎችለማድረግ ከቤትዎ በአማካይ ለምን ያህል ጊዜ በእግር ጉዞ ያስኬዳል? (መልሱ በደቂቃ ይቀመጥ)	------ደቂቃ	
	ጥ131	ለአሁኑ ህመምዎ የታዘዘልዎትን የጨረር ምርመራዎች (አልትራ ሳውንድ፤ ራጂ…ወዘተ) ለማግኘት ከቤትዎ በአማካይ ለምን ያህል ጊዜ በእግር ጉዞ ያስኬዳል? (መልሱ በደቂቃ ይቀመጥ)	------ደቂቃ	
	ጥ132	ለአሁኑ ህመምዎ የታዘዘልዎትን የጨረር ህክምና ለማድረግ ከቤትዎ በአማካይ ለምን ያህል ጊዜ በእግር ጉዞ ያስኬዳል? (መልሱ በደቂቃ ይቀመጥ)	--------ደቂቃ	
የአገልግሎት መኖር	ጥ133	ማንኛውም ከእነዚህ ውስጥ (cisplatin, carboplatin, bleomycin, paclitaxel/docetaxel, rituximab, bevacizumab, gemcitabine) በምርት ወይም ንግድ ስም አቻቸው የታዘዙልዎት መድሃኒቶች በአሁኑ ሰኣት በጤና ተቋሙ ይገኛሉ?	1. አዎ 2. አይ	ታካሚው ህክምና ጨርሰው ሲወጡ በሚደረግ ቃለ-መጠይቅ፤እና የክትትል ቅጽ ምልከታ፤
	ጥ134	ለአሁኑ ህክምና የሚታዘዙ መሰረታዊ የምርመራ አገልግሎቶች (ላቦራቶሪ፤ አልትራሳውንድ፤የጉበት ናሙና ምርመራ ወዘተ) በጤና ተቋሙ ይገኛሉ?	1. አዎ 2. አይ	ታካሚው ህክምና ጨርሰው ሲወጡ በሚደረግ ቃለ-መጠይቅ፤ የክትትል ቅጽ ምልከታ፤
	ጥ135	ለአሁኑ ህክምና የሚሰሩ ማንኛውም ደረጃ የቀዶ-ህክምናዎች	ነ. አዎ	የክትትል ቅጽ

		አግልግሎቶች በጤና ተቋሙ ይሰጣሉ?	2. አይ	ምልከታ፤የጤና ባለሙያ ቃለ-መጠይቅ
	ጥ136	ማንኛውም አይነት ትምህርት እና ድጋፍ (የጤና ትምህርት፤ ማህበራዊ ድጋፍ ወይም እንክብካቤ) አግኝተው ያውቃሉ?	1.አዎ 2. አይ	የታካሚው ቃለ-መጠይቅ በማድረግ፤
	ጥ137	የጤና ባለሙያዎቹ (ሀኪም፤ ነርስ…ወዘተ) አሁን ለሚሰጡት የካንሰር ጤና አግልግሎት ተያያዥ ስልጠና ወስደው ያውቃሉ?	1. አዎ፤ ሁሉም 2. አዎ፤ በከፊል 3. አይ	የክትትል ቅጽ ምልከታ፤ የክፍል ሀላፊዎች ቃለ-መጠይቅ
	ጥ138	በጤና ተቋሙ ለማህጸን ጫፍ እጢ ታካሚዎች የህመም መቋቋሚያ ህክምና ይሰጣል?	1. አዎ 2. አይ	የታካሚውን መረጃ በመመልከት፤ጤና ባለሙያዎች በመጠየቅ
የመግዛት አቅምን ያገናዘበ መሆን	ጥ139	በአማካይ በወር ከአሁኑ ህክምናዎ ጋር ተያያዘ ምን ያህል ገንዘብ ያወጣሉ? (የጤና መድህን ተቀናሽ ይደርግ)	---------ብር	የታካሚውን መረጃ በመመልከት፤ ለታካሚው ቃለ-መጠይቅ በማድረግ

ክፍል 5፡ አገልግሎት አሰጣጥ፤ አቅርቦትና ተደራሽነት የተመለከቱ መጠይቆች

ውድ ታካሚ፡ ከዚህ በመቀጠል ደግሞ የማህጸን ጫፍ ካንሰር ህክምና አገልግሎት አሰጣጥ፤ አቅርቦትና ተደራሽነት በተመለከተ እይታዎን እንዳጋሩኝ አንዳንድ ጥያቄዎችን አነብልዎታለሁ። የእርስዎ ምላሽ ምን ያህል እንደሚሰማሙ ማለትም፤ “በጣም አልስማማም”፤ “አልስማማም”፤ “ልዩነት የለኝም”፤ “እስማማለሁ” ወይም “በጣም እስማማለሁ” በማለት ይሆናል።							
ወካይ መለኪያ	መጠይቆች		ምላሽ				
			1 በጣም አልስማማም	2 አልስማማም	3 ልዩነት የለኝም	4 እስማማለሁ	5 በጣም እስማማለሁ
ተደራሽነት	ጥ140	ከጤና ተቋሙ እስከ ቤቴ ያለው ርቀት መጠነኛ ነው።					
	ጥ141	ወደ ጤና ተቋሙ ለመድረስ የሚወስድብኝ ጊዜ መጠነኛ ነው።					
	ጥ142	ወደ ጤና ተቋሙ እንደፈለኩ መግባትና መውጣት ለኔ ቀላል ነው።					
በቅርበት መገኘት	ጥ143	የምፈልጋቸው የጤና አገልግሎቶች (የሀኪም ምክር፤ ላቦራቶሪ ምርመራ፤ ራጅ ወዘተ) በሙሉ በተቋሙ ይሰጣሉ።					
	ጥ144	በሀኪም የታዘዙልኝን መድሀኒቶችም ሆነ የህክምና ግብዓቶች ከጤና ተቋሙ አገኛለሁ።					

	ጥ145	የተቋሙ ጤና ባለሙያች (ሀኪም፤ ነርስ ወዘተ) ቁጥርና ስብጥር ለምፈልገው የጤና አገልግሎት ምቹ ነው።					
	ጥ146	የጤና ባለሙያዎቹ (ሀኪም፤ ነርስ ወዘተ) በምፈልገው አገልግሎት ላይ በቂ የሙያ ክህሎት አላቸው።					
ቅቡልነት	ጥ147	በተቋሙ የሚሰጠው አገልግሎት ጥራቱን የጠበቀ ነው።					
	ጥ148	የተቋሙ ሙያተኞች የታካሚዎችን ፍላጎት በተለያዬ መልኩ፤ለምሳሌ ትምህርት፤ እንክብካቤ እና እርዳታ በመስጠት የሚያሟሉ ናቸው።					
	ጥ149	ጤና ባለሙያዎች እኔም የማነሳውን ሀሳብ በአግባቡ ያዳምጡኛል።					
	ጥ150	የጤና ባለሞያዎቹ በቂ ጊዜ ይሰጡኛል።					
	ጥ151	የጤና ባለሙያ ቡድኑ (ሀኪም፤ ነርስ፤ ወዘተ) ስለጤናም ሆነ ህመም ሁኔታዬ ለሚሰጡኝ ምክር እምነት አለኝ።					
	ጥ152	የህክምና አገልግሎት የሚሰጠኝ እንደምፈልገው በተመሳሳይ ፆታ (ሴት የጤና ባለሙያ) ነው።					
	ጥ153	በጤና ተቋሙ የቅድመ-ምርመራ (ምሳሌ አንጀት					

		ካንሰር ወዘተ) አግልገሎቶችን አገኛለሁ።					
	ጥ154	የህክምና ቡድኑ ለታካሚዎች አክብሮት አላቸው።					
	ጥ155	ጤና ባለሙያዎቹ (ሀኪሞች፤ ነርሶች፤ ወዘተ) የታካሚዎችን ባህል እና እምነት የሚያውቁና በተገቢው መንገድ የሚያሰተናግዱ ናቸው።					
የመክፈል አቅምን ያገናዘበ መሆን	ጥ156	የጤና ችግሬን ለመፍታት መጀመሪያ በጠቅላላ ሀኪም እታያለሁ።					
	ጥ157	በጠቅላላ ሀኪም ምክር መሰረት የስፔሻሊስት ወይም ሰብ ስፔሻሊስት ሀኪም አገልግሎት እጠቀማለሁ።					
	ጥ158	የጤና አገልግሎት ለማግኘት ወጪ ትልቅ እንቅፋት ሆኖብኛል።					
አካታችነት	ጥ159	በጤና ተቋሙ ቀጠሮ ለመያዝ ቀላል ነው።					
	ጥ160	በተቋሙ የጤና አገልግሎት ለማግኘት የሚወስደውና የሚጠበቀው ጊዜ ተመጣጣኝ ነው።					
	ጥ161	ስለጤናዬ ሁኔታና ለውጥ በተመለከተ ከህክምና ቡድኑ (ሀኪም፤ ነርስ፤ ወዘተ) ጋር በስልክ በነጻነት እወያያለሁ።					
	ጥ162	የጤና ተቋሙ የስራ ሰዓት ሁሉንም አገልግሎቶች ለማግኘት ምቹ ነው።					
	ጥ163	የተቋሙ ግቢ የሚሰጡትን አገልገሎቶች ለማግኘት					

		ምቹ ነው።					
	ጥ164	በተቋሙ እንደ ተሸከርካሪ ወንበር (ዊል ቸር) እና ለመሄድ የሚያግዝ የቁም-መደገፊያ (ወከር) ወዘተ ይቀርባሉ።					
ለግንዛቤ የሚቀል	ጥ165	የጤና ትምህርት ሲሰጠኝ እኔ በቀላሉ በምረዳው መልኩ ተደርጎ ነው።					
	ጥ166	የሚሰጠኝ መረጃ ቀላል በሆነ ቋንቋ እና ለመረዳት የሚያስቸግሩ ቃላት የሌሉበት ነው።					
	ጥ167	የጤና ባለሙያዎቹ (ሀኪም፤ ነርስ፤ ወዘተ) ከታካሚ ጋር ያላቸው ተግባቦት ጥሩ ነው።					
	ጥ168	የጤና ባለሙያዎች የተሰጠኝን የጤና መረጃ በአግባቡ ስለመረዳቴ ለማረጋገጥ ይጥራሉ።					
	ጥ169	በህክምና አገልግሎት አሰጣጥ ወቅት የአኗኗር ሁኔታዬ ማለትም፤ የትዳር ሁኔታ፤ የመክፈል አቅም፤ የባህል ልዩነት ወዘተ ግምት ውስጥ ይገባልኛል።					

Appendix VIII: Cost of illness measurement tool-Amharic version

ክፍል 1: የታካሚ ስነ-ህዝባዊ፤ማህበራዊ እና ኢኮኖሚያዊ ሁኔታዎች መለኪያ		
ጥ201	የታካሚዋ ምድብ፤	1. የካንሰር ታካሚ ናቸው 2. የካንሰር ታካሚ አይደሉም
ጥ202	የሚታከሙበት ጤና ተቋም/ሆስፒታል ዓይነት፤	1. የመንግስት 2. የግል
ጥ203	የሚታከሙበት የአገልግሎት ዘርፍ፤	1. ተመላላሽ ህክምና 2. ተኝቶ ህክምና 3. ጽኑ ህሙማን
ጥ204	እድሜ (በዓመት)፤	----------
ጥ205	የጋብቻ ሁኔታ፤	1. ያላገባች 2. ያገባች 3. ፍች የፈጸመች 4. ባሏ የሞተባት 5. ተለያይተው የሚኖሩ
ጥ206	ክፍለ ከተማ፤	1. አራዳ 2. አቃቂ 3. ንፋስ/ላፍቶ 4. ልደታ 5. ቂርቆስ 6. አዲስ ከተማ 7. ጉለሌ 8. ቦሌ 9. የካ 10. ኮልፌ 11. ለሚ ኩራ
ጥ207	ማንበብ እና መጻፍ ይችላሉ፤	1. አዎ 2. አይ
ጥ208	የትምህርት ደረጃ፤	1. መደበኛ ትምህርት ያልተማሩ 2. 1-8 ክፍል (የመጀመሪያ ደረጃ) 3. 9-12 ክፍል (ሁለተኛ ደረጃ) 4. ኮሌጅ/ዩኒቨርሲቲ የገቡ/የጨረሱ (ከፍተኛ ትምህርት)
ጥ209	ስራ፤	1. የመንግስት ተቀጣሪ 2. የግል ተቀጣሪ 3. ነጋዴ

		4. የቤት እመቤት 5. የቤት ሰራተኛ 6. ተማሪ 7. ስራ የሌለው 8. ሌላ፤ ካለ ይጠቀስ፤----------
ጥ210	የማህበረሰብ-አቀፍ ጤና መድህን ተጠቃሚ ነዎት፤	1. አዎ 2. አይ
ጥ211	የቤተሰቡ አማካይ ወርሀዊ ገቢ (በብር)	----------
ጥ212	አንድ ላይ የሚኖሩ የቤተሰብ አባላት ብዛት	----------
ጥ213	የማህበረሰብ ድጋፍ መኖር (በአካባቢ ፤ ጎረቤት ወይም ቤተሰብ ወዘተ የሚገኝ) ማንኛውም እርዳታ አለዎት፤	1. አዎ 2. አይ
ክፍል 2፤ ስነ-ባህርያዊ ወይም የዓኗኗር ዘዴን የተመለከቱ መጠይቆች		
ጥ214	አሁን ላይ የሲጋራ ውጤቶችን (የሚጨሱ ወይም የማይጨሱ) ይጠቀማሉ፤	1. አዎ 2. አይ
ጥ215	አሁን ላይ ማንኛውም የአልኮል መጠጦችን አብዝተው (በቀን ከ1 ጠርሙስ በላይ) ይጠቀማሉ፤	1. አዎ 2. አይ
ጥ216	አሁን ላይ ጫት ወይም ሌሎች አነቃቂ መድሀኒቶችን (ሀሽሽ፤ ጋንጃ/ሺሻ፤ ወዘተ) ይጠቀማሉ፤	1. አዎ 2. አይ
ጥ217	በሳምንት ውስጥ ቢያንስ ለ150 ደቂቃ ወይም 2 ሰዓት ከ30 ደቂቃ የሚወስድ መጠነኛ የአካል እንቅስቃሴ (ለምሳሌ የእግር ጉዞ…) ያደርጋሉ?	1. አዎ 2. አይ
ጥ218	በሳምንት ውስጥ ቢያንስ ለ 75 ደቂቃ ወይም 1 ሰዓት ከሩብ የሚወስድ ከባድ አካላዊ እንቅስቃሴ (ምሳሌ፤ ጂም ስፖርት…) ያደርጋሉ?	1. አዎ 2. አይ
ጥ219	ከእነዚህ ውስጥ የትኞቹ በምግብ ዝርዝርዎ ውስጥ ይካተታሉ? (መልስ የሚሆነውን ሁሉ ይምረጡ)	1. ጥራጥሬዎች 2. ፍራፍሬዎች 3. አነስተኛ ስብ 4. አትክልቶች 5. በፋብሪካ የተቀነባበሩ ምግቦች 6. ጣፋጭ መጠጦች 7. አሰር የሌላቸው ጥራጥሬዎች 8. ከፍተኛ ጨው (በቀን ከ1 የሻይ ማንኪያ በላይ) 9. ሌላ ካለ, ይገለጽ ---------- --------

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ክፍል 3: ጤና-ነክ መጠይቆች		
ጥ220	ማንኛውም ዓይነት ተጓዳኝ የረጅም ጊዜ የጤና ችግር አለብዎት፤	1. አዎ 2. አይ -----□ጥ122
ጥ221	ለጥያቄ 220 መልስዎ አዎ ከሆነ፤ የትኛው፤(መልስ የሚሆኑትን ሁሉ ይምረጡ)	1. የስኪር ህመም 2. የደም ግፊት ህመም 3. የኩላሊት ህመም 4. አች.አይ.ቪ/ኤድስ 5. የአእምሮ ህመም 6. የልብና ደም ዝውውር ጤና ችግር 7. የጡንቻና አጥንት 8. የነርቭ ህመም 9. ሌላ ካለ፤ ይገለጽ----------
ጥ222	የቅድመ-ካንሰር ምርመራ ተደርጎልዎት ያውቃል፤	1. አዎ 2. አይ
ጥ223	የማህጸን ጫፍ ካንሰር መከላከያ ክትባት ወስደው ያውቃሉ፤	1. አዎ 2. አይ
ቀጥሎ ጥ224-ጥ227 ለሴዞች (የማህጸን ካንሰር ታማሚዎች ብቻ) ይሙሉ፤		
ጥ224	ለመጀመሪያ ጊዜ ካንሰር እንዳለብዎት በምርመራ ያወቁበት ቀን (በኢትዮጵያ አቆጣጠር)፤	----------(ወር/ዓ.ም)
ጥ225	ለመጀመሪያ ጊዜ መድሃኒት የጀመሩበት ቀን (በኢትዮጵያ አቆጣጠር)፤	----------(ወር/ዓ.ም)
ጥ226	መጀመሪያ ሲመረመሩ የካንሰሩ ደረጃ ምን ነበር፤	1. IA 2. IB 3. IIA 4. IIB 5. IIIA 6. IIIB 7. IV
ጥ227	አሁን ላለብዎት የጤና ችግር እስካሁን ድረስ የትኞቹን ህክምናዎች ወስደዋል፤(የወሰዱትን ሁሉ ይምረጡ)	7. የጨረር 8. የመድሀኒት 9. የቀዶ ህክምና 10. የሆርሞን/የሰውነት ቅመም 11. ባህላዊ ህክምና 12. ሌላ፤ ይጠቀስ----------

ከዚህ ቀጥሎ ባለፉት 3 ወራት ያጋጠመዎትን ልዩ ልዩ ወጪዎች የሚመለከቱ መጠይቆችን እጠይቅዎታለሁ።።

ክፍል IV: ባለፉት 3 ወራት ህክምና ጋር ተያያዘ የተፈጸሙ ቀጥተኛ ወጪዎች		**የወጪ ዝርዝር**				**ድምር**
		የክፍያው ምክንያት	**ብዛት (Q)**	**ያንዱ ዋጋ (UC)**	**ጠቅላላ ዋጋ(Q* UC)**	
ጥ228	በዚህ ጤና ተቋም ሀኪም ጋ ለመቅረብ ወይም ካርድ ለማስወጣት የተፈጸሙ ክፍያዎች፤	ካርድ/ሀኪም 1				
		ካርድ/ሀኪም 2				
		ካርድ/ሀኪም 3				
		ካርድ/ሀኪም n (ተጨማሪ ካለ ይደመር)				
ጥ229	በዚህ ጤና ተቋም ለተለያየ የላቦራቶሪ ምርመራዎች የተፈጸመ ክፍያ፤	ምርመራ 1				
		ምርመራ 2				
		ምርመራ 3				
		ምርመራ n (ተጨማሪ ካለ ይደመር)				
ጥ230	በዚህ ጤና ተቋም ለተለያዩ የጨረር ምርመራዎች (ሲቲ፤ ኤክስ-ሬይ፤ ኤም አር አይ፤አልተራሳውንድ…) የተፈጸመ ክፍያ፤	ኢሜጅንግ 1				
		ኢሜጅንግ 2				
		ኢሜጅንግ 3				
		ኢሜጅንግ n (ተጨማሪ ካ ይደመር)				
ጥ231	በዚህ ጤና ተቋም የታዘዙ የተለያዩ መድሐኒቶችን (ኬሞቴራፒ ወይም ተያያዥ ስቴሮይድ መድሀኒቶች) ለመግዛት የተፈጸመ ክፍያ፤	መድሐኒት 1				
		መድሐኒት 2				
		መድሐኒት 3				
		መድሐኒት 4 መድሐኒት 5				
		መድሐኒት n (ተጨማሪ ካለ ይደመር)				
ጥ232	በዚህ ጤና ተቋም በተኝቶ ህክምና አገልግሎት ለአልጋ የተፈጸመ ክፍያ፤	ቆይታ 1				
		ቆይታ n (ከ1 ጊዜ በላይ ሆስፒታል ከተኙ				

		ይደመር)				
ጥ233	በዚህ ጤና ተቋም በጽኑ ህሙማን ህክምና አገልግሎት (ICU) stays የተፈጸመ ክፍያ፤	ጽኑ 1				
		ጽኑ n (ከ1 ጊዜ በላይ ICU ገብተው ከነበረ ይደመር)				
ጥ234	በዚህ ጤና ተቋም ለቀዶ-ህክምና አገልግሎት የተፈጸመ ክፍያ፤	ፕሮሲጀር 1				
		ፕሮሲጀር n (ከ1 ጊዜ በላይ ፕሮሲጀር ካለ ይደመር)				
ጥ235	በጤና ተቋሙ ውስጥ ለልዩ ልዩ የህክምና አገልግሎቶች ማለትም፤ መድሀኒት በደም ስር ሲሰጥ፤ በባለሙያ የታገዘ እንክብካቤ ሲደረግ፤ ለፊዚዮቴራፒ አገልግሎት፤ ወይም ተያያዥ በነርስ የታገዘ እንክብካቤ ሲደረግ የተፈጸመ ክፍያ፤	አገልግሎት 1				
		አገልግሎት 2				
		አገልግሎት 3				
		አገልግሎት n (ሌሎች ካሉ ይደመር)				
ጥ236	ሌላ ጤና ተቋም/ሆስፒታል ለተደረገ ማንኛውም የሀኪም ማማከር; ተመላላሽ፤ ወይም ተኝቶ ህክምና የተፈጸመ ክፍያ፤	ህክምና 1				
		ህክምና 2				
		ህክምና n (ተጨማሪ ህክምናዎች ከተደረጉ ይደመር)				
ጥ237	ሌላ ጤና ተቋም/ሆስፒታል ለተደረገ ማንኛውም ተያያዥ የህክምና ምርመራ አገልገሎት(ላቦራቶሪ፤ አልትራሳውንድ፤ ሲቲ…) የተፈጸመ ክፍያ፤	ምርመራ 1				
		ምርመራ 2				
		ምርመራ n (ተጨማሪ ምርመራዎች ካተደረጉ ይደመር)				
ጥ238	ለባህል ህክምና አዋቂዎች የተፈጸመ ክፍያ፤	ባህላዊ 1				
		ባህላዊ n (ተጨማሪ ህክምናዎች ካተደረጉ ይደመር)				
ጥ239	ለመንፈሳዊ መሪዎች ወይም መንፈሳዊ ህክምና ሰጪዎች የተፈጸመ ክፍያ፤	መንፈሳዊ 1				
		መንፈሳዊ n (ተጨማሪ ህክምናዎች ካተደረጉ				

		ይደመር)				
ክፍል V:ባለፉት 3 ወራት ከህክምና ውጪ የተፈጸሙ ቀጥተኛ ወጪዎች						
ጥ240	ከትራንስፖርት ጋር ተያይዞ (ወደ ሆስፒታል፤ ባህላዊ ህክምና ወይም መንፈሳዊ ቦታ ለደርሶ መልስ) የተፈጸመ ክፍያ፤	ትራንስፖርት 1				
		ትራንስፖርት 2				
		ትራንስፖርት 3				
		ትራንስፖርት n (ተጨማሪ ካለ ይደመር)				
ጥ241	ከተጨማሪ ምግብ ወይም በሀኪም የታዘዘ የምግብ ሰፕልሜንት ለመግዛት የተፈጸመ ክፍያ፤	ምግብ/ሰፕልሜንት 1				
		ምግብ/ሰፕልሜንት 2				
		ምግብ/ሰፕልሜንት n (ተጨማሪ ካለ ይደመር)				
ጥ242	በቤት ወይም ከህክምና ተቋም ውጪ እንክብካቤ ለሚያደርጉ ረዳቶች የተፈጸመ ክፍያ፤	ረዳት 1				
		ረዳት n (ተጨማሪ ካለ ይደመር)				
ክፍል VI: ቀጥተኛ ያልሆኑ ወጪዎች						
ጥ243	ባለፉት 3 ወራት በህመምዎ የተነሳ ከስራ ቀርተው ያውቃሉ?	1. አዎ 2. አይ---›ጥ245				
ጥ244	ከላይ ለጥ243 መልስዎ አዎ ከሆነ፤	ከስራው የቀሩባቸው ቀናት ብዛት ----------				
		ከስራው የሚያገኙት አማካይ ወርሀዊ ገቢ(በብር)----------				
ጥ245	ባለፉት 3 ወራት እርስዎን ለመርዳት ከስራቸው የቀሩ የቤተሰብ አባላት፤ዘመድ ወይም ግለሰቦች ነበሩን?	1. አዎ 2. አይ				
ጥ246	ከላይ ለጥ245 መልስዎ አዎ ከሆነ፤ በቀኝ በኩል ያሉትን ጥያቄዎች ይመልሱ፤	ከስራው የቀሩባቸው ቀናት ብዛት ----------				
		ከስራው የሚያገኙት አማካይ ወርሀዊ ገቢ(በብር)----------				

Appendix IX: Study tool validity assessment instrument

Dear Expert:

*You are kindly invited to put your expert opinion over the following list of translated items for their inclusion in an ''access to healthcare services'' psychometric questionnaire we are currently aiming to validate for utilization in broader patient populations, particularly, in patients with cervical cancer. The items are adapted from an earlier validated and published work by (Hoseini-Esfidarjani et al., 2021), and you are selected in this panel of experts because of your familiarity with the Ethiopian healthcare system, knowledge on the subject under investigation and experience in research. The questionnaire contains 6 domains and 30 items (Q140-169) that is going to be administered in a five-point Likert scale (strongly disagree to strongly agree). When rating, you are kindly asked to consider the essence, relevance and appropriateness of each item. Please read the scoring orders in all the three assessment columns and mark either as ''√''or ''**x**'' under your rating.*

***A quick definition of each criterion**:*

***Essentiality:** refers to whether the item is essential to be included under the given domain and the scale.*

***Relevance**: refers to the degree of relevance of each indicator to the measured latent variable.*

***Item appropriateness**: refers to your view of the respective item, whether it appears to be appropriate on the surface (its face-value) and the respondents' side to assess the given domain.*

ወካይ መለኪያ/Latent Variable	ጠቋሚ መለኪያዎች(Indicator variables)		**Item essentiality** (1=item is not essential, 2= Item is useful but not essential, 3= Item is essential)			**Item's relevance** (1=not relevant , 2= somewhat relevant, 3=quite relevant, 4=highly relevant)				**Item appropriateness** (1=unimportant, 2=slightly important, 3= relatively important, 4=important, and 5= highly important)				
			1	2	3	1	2	3	4	1	2	3	4	5
ቅርበት	ጥ140	ከጤና ተቋሙ እስከ ቤቴ ያለው ርቀት												

		ተመጣጣኝ ነው።												
	ጥ141	ወደ ጤና ተቋሙ ለመድረስ የሚወስድብኝ ጊዜ ተመጣጣኝ ነው።												
	ጥ142	ወደ ጤና ተቋሙ እንደፈለኩ መግባትና መውጣት ለኔ ቀላል ነው።												
በቅርበት መገኘት	ጥ143	የምፈልጋቸው የጤና አገልግሎቶች (የሀኪም ምክር፤ ላቦራቶሪ ምርመራ፤ ራጂ ወዘተ) በሙሉ በተቋሙ ይሰጣሉ።												
	ጥ144	በሀኪም የታዘዙልኝን መድሀኒቶች ሆነ የህክምና ግብዓቶች ከጤና ተቋሙ አገኛለሁ።												
	ጥ145	የጤና ባለሙያው (ሀኪም፤ ነርስ ወዘተ) በበቂ ቁጥርና በሚያስፈልገኝ አገልግሎት ልክ የተሰባጠረ ነው።												
	ጥ146	የጤና ባለሙያዎች (ሀኪም፤ ነርስ ወዘተ) በሚያስፈልገኝ አግልገሎት ላይ በቂ የሙያ ክህሎት አላቸው።												
ቅቡልነት	ጥ147	በተቋሙ የሚሰጠው አገልግሎት ጥራቱን የጠበቀ ነው።												
	ጥ148	የተቋሙ ሙያተኞች የታካሚዎችን ፍላጎት በተለየዬ መልኩ፤ለምሳሌ ትምህርት”፤ እንክብካቤ እና እርዳታ በመስጠት የሚያሟሉ												

		ናቸው።												
	ጥ149	ጤና ባለሙያዎች የምለውን ሀሳብ በአግባቡ ያዳምጡኛል።												
	ጥ150	የጤና ባለሞያዎቹ በቂ ጊዜ ይሰጡኛል።												
	ጥ151	የጤና ባለሙያው ቡድን (ሀኪም፤ ነርስ፤ ወዘተ) ስለጤናም ሆነ ህመም ሁኔታዬ ለሚሰጡኝ ምክር እምነት አለኝ።												
	ጥ152	የህክምና አገልግሎት የሚሰጠኝ በመረጥኩት የባለሙያ ፆታ ነው።												
	ጥ153	በጤና ተቋሙ የቅድመ-ምርመራ (ምሳሌ፤ ጡት ካንሰር፤ አንጀት ካንሰር) አግልገሎቶችን አገኛለሁ።												
	ጥ154	የህክምና ቡድኑ ለታካሚዎች አክብሮት አላቸው።												
	ጥ155	ጤና ባለሙያዎቹ (ሀኪሞች፤ ነርሶች፤ ወዘተ) የታካሚዎችን ባህል እና እምነት የሚያውቁና በተገቢው መንገድ የሚያሰተናግዱ ናቸው።												
የመክፈል አቅምን ያገናዘበ መሆን	ጥ156	የጤና ችግሬን ለመፍታት መጀመሪያ በመንግስት ተቋም ወይም ጤና ጣቢያ ሀኪም እታያለሁ።												
	ጥ157	በጤና ጣቢያ ሀኪም ምክር መሰረትም በስፔሻሊስት ወይም ሰብ ስፔሻሊስት ሀኪም												

		የሪፈራል አገልግሎት እጠቀማለሁ።												
	ጥ158	የጤና አግልግሎት ለማግኘት ክፍያ ትልቅ እንቅፋት ነው።												
አካታችነት	ጥ159	በጤና ተቋሙ ቀጠሮ ለመያዝ ቀላል ነው።												
	ጥ160	በተቋሙ የጤና አገልግሎት ለማግኘት የሚወስደውና የሚጠበቀው ጊዜ ተመጣጣኝ ነው።												
	ጥ161	ስለጤናዬ ሁኔታና ለውጥ በተመለከተ ከሀክምና ቡድኑ (ሀኪም፤ ነርስ፤ ወዘተ) ጋር በስልክ በነጻነት እወያያለሁ።												
	ጥ162	የጤና ተቋሙ የስራ ሰዓቶች ሁሉንም አግልገሎት ለማግኘት ምቹ ናቸው።												
	ጥ163	የተቋሙ ግቢ የሚሰጠውን አገልገሎት ለማግኘት ምቹ ነው።												
	ጥ164	በተቋሙ እንደ ተሸከርካሪ ወንበር (ዊል ቸር) እና ለመሄድ የሚያግዝ ወንበር (ወከር) ወዘተ ማግኘት ቀላል ነው።												
ለግንዛቤ የሚቀል	ጥ165	የሚሰጡኝ የጤና ትምህርቶች እኔ በቀላሉ በምረዳው መልኩ ነው።												
	ጥ166	የሚሰጠኝ መረጃ ቀላል በሆነ ቋንቋ እና												

		ለመረዳት የሚያስቸግሩ ቃላት የሌሉበት ነው።												
	ጥ167	የጤና ባለሙያዎቹ (ሀኪም፤ ነርስ፤ ወዘተ) ከታካሚ ጋር ያላቸው ተግባቦት ጥሩ ነው።												
	ጥ168	የጤና ባለሙያዎች የተሰጠኝን የጤና መረጃ በአግባቡ ስለመረዳቴ ያረጋግጣሉ።												
	ጥ169	በህክምና አገልግሎት አሰጣጥ ወቅት የአኗኗር ሁኔታ ማለትም፤ የትዳር ሁኔታ፤ የመክፈል አቅም፤ የባህል ልዩነት ወዘተ ግምት ውስጥ ይገባልኛል።												

Appendix X: Miscellaneous files

Ref. No. ፓጤጋጋ/284

Date: 18/11/2022

Institutional Review Board (IRB) of St. Paul's Hospital Millennium Medical College (SPHHMC)

Ethical Clearance

Research Title: - Access to Healthcare, Economic Burden and Associated Factors in Patients with Cervical Cancer and Visiting Oncology Centers in Addis Ababa, Ethiopia

Principal Investigator: - Tariku Shimels

The IRB of SPHMMC has reviewed the above mentioned research proposal and made the following decision:

- Approved:- _____x_____
- Approved with recommendation:- _____
- Approved on condition :-_____
- Disapproved:- _____

The decision is valid for __12__ months and the research should be conducted in compliance with the protocol/proposal approved by the IRB of SPHMMC. Any subsequent revision/amendment of the protocol/proposal needs approval before conduct of the research. The researcher should also submit written summaries of the research status to the IRB every __03__ months. Upon the conclusion of the study, manuscripts and thesis work to the final/completed research project needs to be submitted to the IRB.

IRB Chair:

Signature: _____

Date: November18/2022

Cc:

- Vice Provost for Academic and Research
- IRB
- Tariku Shimels
  SPHMMC

St. Paul's Hospital
Millennium Medical College
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Ref.No PM23/29
Date 29/11/2023

To:

Tikur Anbessa Specialized Hospital

Teklehaimanot General Hospital

Hallelujah General Hospital

Addis Hiwot General Hospital

Addis Ababa

Subject: Request to access health facility to conduct an approved study

The letter of support is written to **Tariku Shimels** who is an academic staff of Saint Paul's Hospital Millennium Medical College (SPHMMC). Currently, he is conducting a research a research entitled: "**Access to Healthcare, Economic Burden and Associated Factors in Patients with Cervical Cancer and Visiting Oncology Centers in Addis Ababa, Ethiopia**". The study proposal has been duly reviewed and approved by the institutional review board (IRB) of Saint Paul's Hospital Millennium Medical College. The principal investigator has also been informed, with a copy of this letter, to report any changes in the study procedures, and submit an activity report every three months to the ethical review committee.

Therefore, we request your health facility and staffs to provide the necessary support to the principal investigator during the conduct of the above mentioned study.

With Regards,

for

Dr Sisay Sirgu
Academic and Research Vice Provost

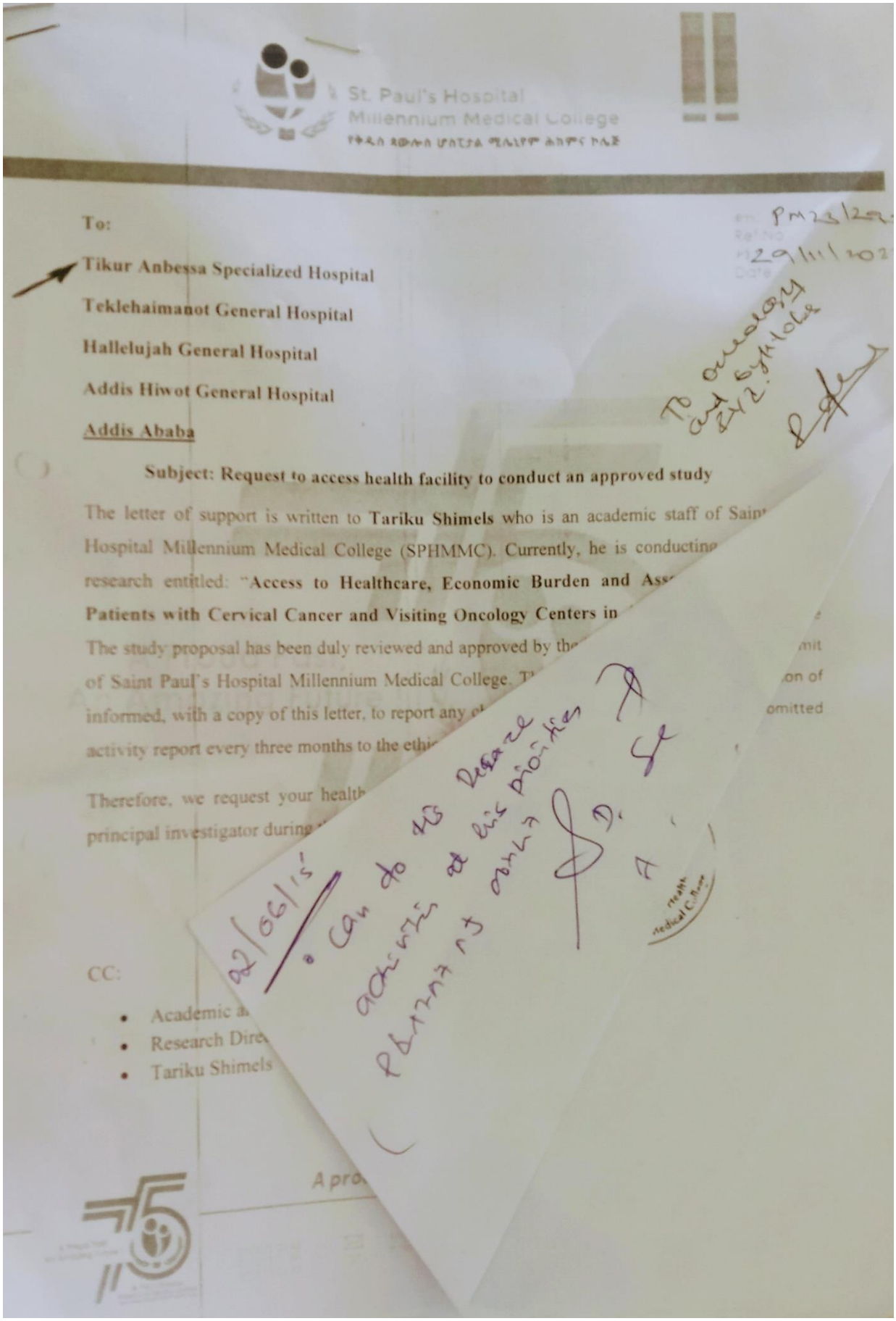
CC:

- Academic and research Vice provost
- Research Directorate
- Tariku Shimels

Federal Ministry of Health St. Paul's Millennium Medical College

Tariku S.

A proud Past, An Amazing Future !



St. Paul's Hospital
Millennium Medical College

To:

Tikur Anbessa Specialized Hospital

Teklehaimanot General Hospital

Hallelujah General Hospital

Addis Hiwot General Hospital

Addis Ababa

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activity report every three months to the ethi

Therefore, we request your health
principal investigator during

CC:

- Academic a
- Research Dire
- Tariku Shimels

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Addis Ababa University

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School of Pharmacy
Ethical Review Committee

ቀን Date: June 22, 2023

ቁጥር Ref. No.: ERB/SOP/543/15/2023

To: **Tariku Shimels**
School of Pharmacy

Re: Ethical Clearance

It is to be recalled that you submitted a research project proposal entitled "**Spatiotemporal Modelling of Incidence cases, Access to Healthcare and the Costs of Cervical Cancer in Addis Ababa, Ethiopia**". The committee thoroughly reviewed the proposal based on its operational guideline and found that, it fulfills the ethical requirements stipulated in the guideline. This is, therefore, to inform you that the proposal is ethically approval for implementation.

With best regards,

Shemsu Umer (PhD)
Chairperson, ERC
School of Pharmacy
College of Health Sciences
Addis Ababa University

☎ 00251156 02 12 ✉ 1176 ቴሌክስ Telex: 21205 ፋክስ Fax: 00251(11)1558566 ቴሌግራም Cable: AAUNIV

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Addis Ababa University

School of Pharmacy
Ethical Review Committee

Minute of the School Ethical Review Committee

Date: June 20, 2023.
Venue: Office, School of Pharmacy
Time 10:00-11:00a.m

Members present
1. Dr. Shesmsu Umer: Chair person
2. Eyerusalem Berhanemeskel: Secretary
3. Eskinder Ayalew: Member
4. Alemayehu Teshale: Member
5. Alemu Tadesse: Member
6. Dr. Legesse Chelkeba: Member
7. Tesfaye Gabreil: Member

Agendas of the Meeting
1. Mr. Tariku Shimelis's PhD Proposal for Ethical Clearance
2. AOB

The chairperson welcomed members and requested if there were any other agenda items to be included under AOB. As there were none, the presented agenda item was approved and the meeting was started at 10:00 am.

1. Mr. Tariku Shimelis's PhD Proposal for Ethical Clearance

Mr. Tariku Shimelis has submitted a research proposal entitled "Spatiotemporal Modelling of Incidence cases, Access to Healthcare and the Costs of Cervical Cancer in Addis Ababa, Ethiopia" for ethical approval. The chairperson assigned experts to review the proposal based on the committee's operational guideline. After thoroughly discussing on the proposal submitted and the experts' recommendations, the committee decided that the proposal submitted is ethically sound and the proposal is ethically approved for implementation as of 20 June 2023 with protocol number ERB/SOP/543/15/2023.

2. AOB

As there were no other issues to be discussed the meeting was adjourned at 11:00 am.

Dr. Shemsu Umer
Chairperson

Eyerusalem Berhanemeskel
Secretary

☎ 00251156 02 12 ✉ 1176 ቴሌክስ Telex: 21205 ፋክስ Fax: 00251(11)1558566 ቴሌግራም Cable: AAUNIV

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ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES (IRB)
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Institutional Review Board

ANNEX 3
Form AAUMF 03-008

IRB's Decision

Meeting No: 07/2023 Date: August 16, 2023
Protocol number: 055/23/SoP

Protocol Title: Spatio-temporal Modelling of Incidence cases, Access to Healthcare and the Costs of Cervical Cancer in Addis Ababa, Ethiopia	
Principal Investigator:	Tariku Shimels Mekonnon
Institute:	College of Health Sciences, AAU
Elements Reviewed (AAUMF 01-008)	☑ Attached ☐ Not Attached
Review of Revised Application ☐ Yes ☐ No	Date of the Previous Review:
Decision of the meeting:	☑Approved ☐Approved with Recommendation ☐Resubmission ☐ Disapproved

I. Elements approved-
1. Protocol Version No: 2
2. Protocol Version Date:
3. Informed consent Version No.
4. Informed Consent Version Date: 2

II. Obligations of the PI-
1. Should comply with the standard international & and national scientific and ethical guidelines
2. All amendments and changes made in protocol and consent form need IRB approval
3. The PI should report SAE within 10 days of the event
4. End of the study, including manuscripts and thesis works should be reported to the IRB
5. The PI should report non-compliance and unanticipated events

III. TO NERC ☐

Institution Review Board (IRB) Approval: Period from October 4, 2023, to October 3, 2024
Follow-up report expected in 3 Months ___6 months ___ 9 months__✔___one year____

Chairperson, IRB
Dr. Adamu Addissie

Institutional Review Board Office (IRB) Faculty of Medicine
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ADDIS ABABA UNIVERSITY

Signature
Date: October 4, 2023