

Article

Evolution, Distribution and Prediction of Cervical Cancer Mortality in a Central Mexican State Using a Dynamic Model

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Abstract

This study analyzes the evolution and spatial distribution of cervical cancer mortality. Furthermore, it develops a dynamic simulation model for estimating the evolution of the disease up to 2040. This manuscript details an ecological and retrospective study that analyzed official mortality, morbidity, and population data from the 58 municipalities that constitute the state of San Luis Potosi. We used Moran's index, linear correlation, structural equation modeling, Excel predictions, and Vensim PLE x64 simulation software to conduct this study. The evolution of deaths from cervical cancer shows a downward trend; mortality follows a clustered distribution pattern, and it is not random. The structural model showed standardized regression coefficients of 0.68 between syphilis cases and cervical cancer cases, with a coefficient of 0.35 for deaths; candidiasis cases with cervical cancer at a coefficient of 0.25 and with deaths from the same disease at a coefficient of 0.46. The coefficients of determination for cervical cancer cases and deaths were 0.74 and 0.91, respectively. This shows that these co-infections—syphilis and candidiasis—are a risk factor for cervical cancer mortality. The estimated mortality rates per 100,000 inhabitants for 2025, 2030, 2035, and 2040 were 5.5, 5.1, 4.8, and 4.4, respectively. The prediction indicates an increase in the number of CC cases and deaths from this cause.

Keywords: cervical cancer; mortality; dynamic model; sexually transmitted infections; risk factors



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1. Introduction

As is well known, cervical cancer (CC) is one of the most prevalent diseases and has one of the highest mortality rates among women, despite the introduction, in 2006, of the vaccine against the Human Papillomavirus (HPV), which is the causative agent of the disease [1]. Globally, it ranks fourth among cancers diagnosed in women and is the leading cause of death in women in low- and middle-income countries (LMICs) [2]. In 2022, the standardized incidence and mortality rates in Latin America and the Caribbean were 21.9 and 11.1, respectively, per 100,000 women aged between 15 and 85 years old, above those reported for Asia, Europe and Oceania and only below those reported for Africa [3]. In Mexico, in 2024, 5014 cases of severe cervical dysplasia and CC were recorded in situ, and

4540 cases of malignant cervical tumors were registered. In April 2025, 1343 and 953 cases were reported, respectively. For the same month in 2024, 1252 cases of malignant cervical tumors were registered [4]. The above data show that, in this country, there has been no decrease in the number of cases.

Precursor lesions of CC can be eliminated through timely detection using cervical cytology (PAP smear or cervical cytology) or HPV testing as secondary prevention; they can also be identified and treated via conization in a colposcopy clinic when necessary. It is clear that early diagnosis is vital for any disease, and CC is no exception, since reducing mortality from this disease depends on it [5,6].

The early detection and appropriate treatment of precursor lesions prevent progression to cervical cancer in 80% of cases. Considering this, why do so many women die from this disease? From a public health perspective, CC represents a significant problem in developing countries, not only because of its high incidence rate but also because it mainly affects people from the most disadvantaged social classes, who have less access to health services and gynecological care [7].

In Mexico, most cases of CC are detected in advanced stages, leading to long and very painful terminal illnesses for women and their families. Effective early detection programs have been shown to decrease the occurrence of new cases and mortality from this type of cancer; however, no reduction has occurred in Mexico even though an early detection program based on cytology (PAP) has been implemented for approximately half a century. This is due, as has been said on many occasions, to a lack of highly trained personnel to take samples and interpret cytological studies, a lack of infrastructure required to achieve broad coverage, long waiting times for both the PAP test and the delivery of results, delays in timely care and follow-up of cases, the beliefs of and social barriers against women, and inequality, resulting in high incidence and mortality rates, especially in regions with low socioeconomic development [8–10]. In this context, primary prevention through vaccination is the best option in developing countries such as Mexico, a country where the vaccine was introduced in 2008 and where CC is a significant public health problem [11].

It is important to mention that HPV, the causative agent of CC, refers to a group of viruses belonging to the Papillomaviridae family. These can infect the skin or mucous membranes and are mostly transmitted through sexual relations and genital skin-to-skin contact. HPV infection is the most common sexually transmitted infection (STI), in both heterosexual and same-gender relationships.

A total of 90% of cervical infections are asymptomatic and usually clear up on their own within one to two years without causing lesions; only 5% to 10% of cases lead to pre-neoplastic lesions or cancer, which is due to viral persistence. CC is considered to be the long-term result of an untreated STI caused by certain HPV genotypes [12–14].

On the other hand, there are widely described cofactors that favor HPV infection and the development of CC; these include co-infection with other sexually transmitted infections such as *Chlamydia trachomatis*, HIV, syphilis, or candidiasis, among others [12,15,16].

Taking into account the above, this study was carried out to analyze the evolution, geographic distribution, and prediction of CC mortality in the State of San Luis Potosí, Mexico, and to develop a dynamic simulation model to estimate it up to 2040. The importance of the results of studies of this type is that they help those involved in decision-making and the proposal, modification, and implementation of national programs and services offered by the health sector, as well as in understanding the presence of other risk factors.

2. Results

The evolution of mortality rates in 1979–2023 is shown in Figure 1, where we can see that, in 1979, the rate was 4.77, before increasing until peaking at 11.80 in 1990. Since this

year, the mortality rate has been decreasing, albeit with fluctuations; for example, in 2023, a rate of 5.4 per 100,000 women was recorded.

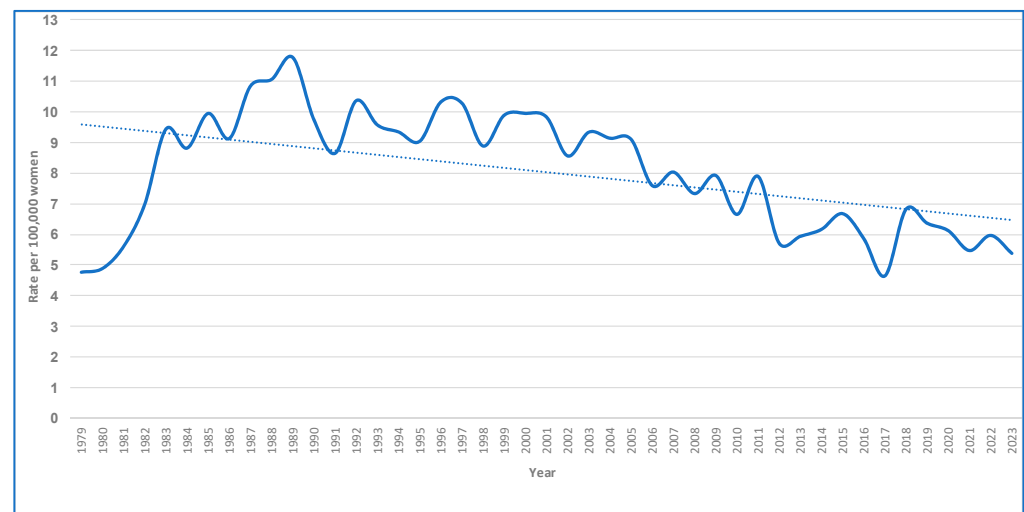


Figure 1. Evolution of CC mortality rates in the period 1979–2023 in the State of San Luis Potosí, Mexico. The dotted line indicates the trend, and the solid line indicates the observed rates.

The average mortality rate due to CC in the State of San Luis Potosí is presented in Figure 2a, and we can observe that it has not been distributed homogeneously throughout the state territory, since there are 12 municipalities with very high mortality, whose rates range between 10.93 and 16.42 deaths from CC per 100,000 women.

Tamasopo (036) was the municipality with the highest average CC-related mortality rate in the study period, with a value of 16.42, followed by Rayón (023), with 15.13; Lagunillas (019), with 14.22; Cerritos (008), with 13.76; Ciudad Fernández (011), with 13.56; Rioverde (024), with 13.10; Huehuetlán (018), with 12.73; Alaquines (002), with 15.52; Ciudad Valles (013), with 12.35; Ébano (016), with 12.08; San Nicolás Tolentino (030), with 11.90; and finally, Tierra Nueva (043), with 10.93. It should be noted that the municipalities with very high CC-related mortality rates are mainly located in Health Jurisdictions (HJs) IV (Rioverde) and V (Ciudad Valles). On the other hand, the municipality with the lowest average mortality rate between 1979 and 2023 was Vanegas (044), with only 3.95 deaths from CC per 100 thousand women.

The above information is relevant, given that the distribution of mortality due to CC is not random, as when performing a geostatistical analysis using the Moran Index test (Figure 2b), we found that mortality follows a clustered distribution pattern ($Z = 5.46$, $p\text{-value} < 0.001$), with less than 1% probability that this pattern is random.

On the other hand, all relationships between variables were statistically significant and positive, except for those between cases of CC and candidiasis, cases of CC and AIDS, and death from CC and AIDS. The model indicates that syphilis, AIDS, and candidiasis are correlated with coefficients of 0.71, 0.83, and 0.88, respectively. Syphilis has a standardized regression weight of 0.68 on CC cases, while CC cases, syphilis, and candidiasis have weights of 0.16, 0.35, and 0.46 on CC deaths, respectively. The coefficients of determination, representing the percentage that independent variables explain for dependent variables, are 0.74 for CC cases and 0.91 for CC deaths (Figure 3). The assumptions were fulfilled in both regression models:

- Linearity. The seven graphs clearly demonstrated a linear relationship.
- Independence. The Durbin-Watson statistic in the two models is between 1.5 and 2.5.
- Homoscedasticity. The scatter plot of standardized forecasts by standardized residuals in both models shows that the variation in the residuals is approximately uniform

across the forecast values, which indicates that the assumption of homoscedasticity has been met.

- Normality. The histograms and normal probability plots of both regression models show approximate normality.
- Non-collinearity. In each of the 7 variables, the VIF < 7.5.

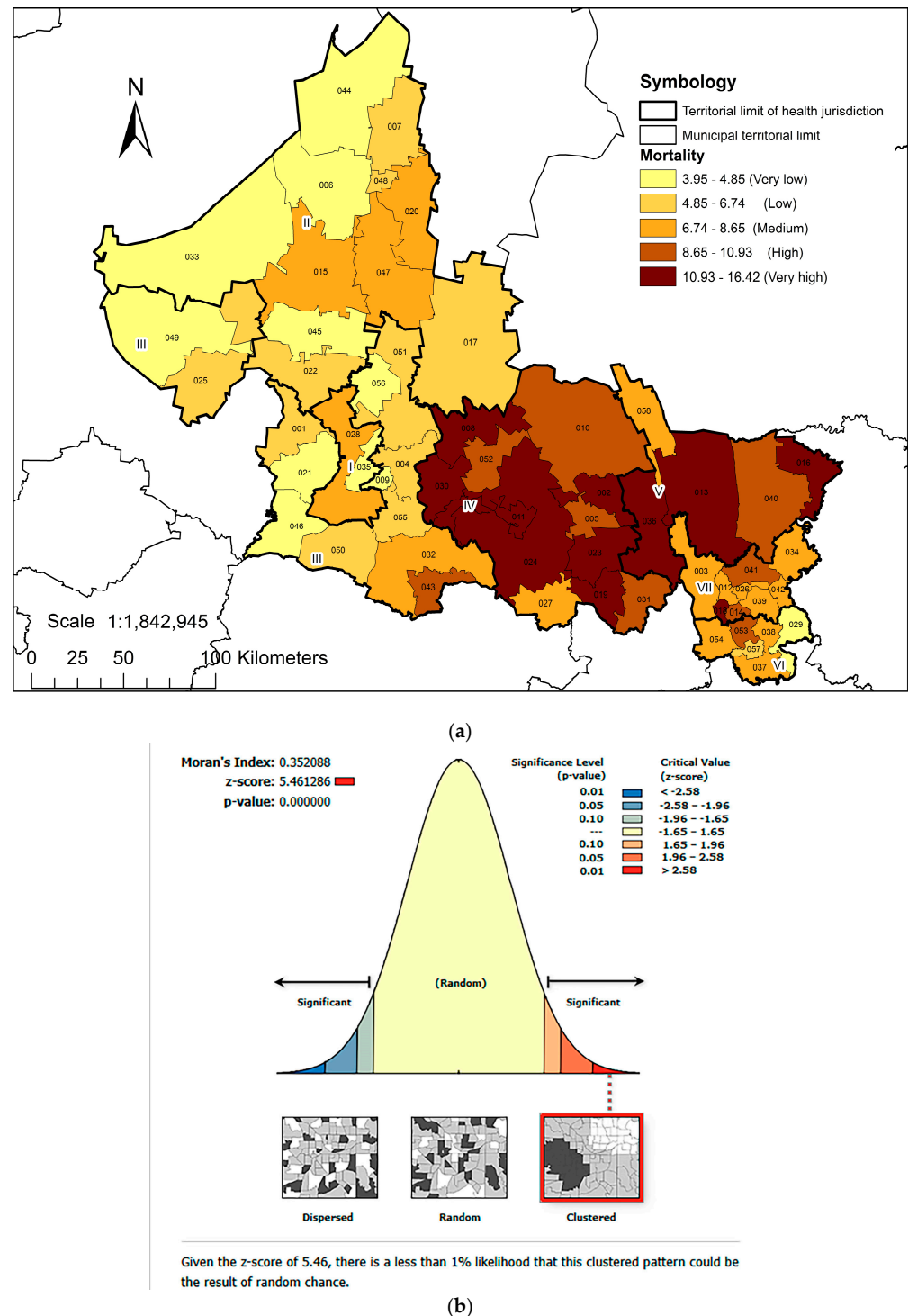


Figure 2. Geographic distribution of average mortality from CC in the state of San Luis Potosí, Mexico, during the period 1979–2023. (a) Map of the State of San Luis Potosí, Mexico; I–VII indicate Health Jurisdictions. (b) Spatial autocorrelation report. Rate per 100,000 women.

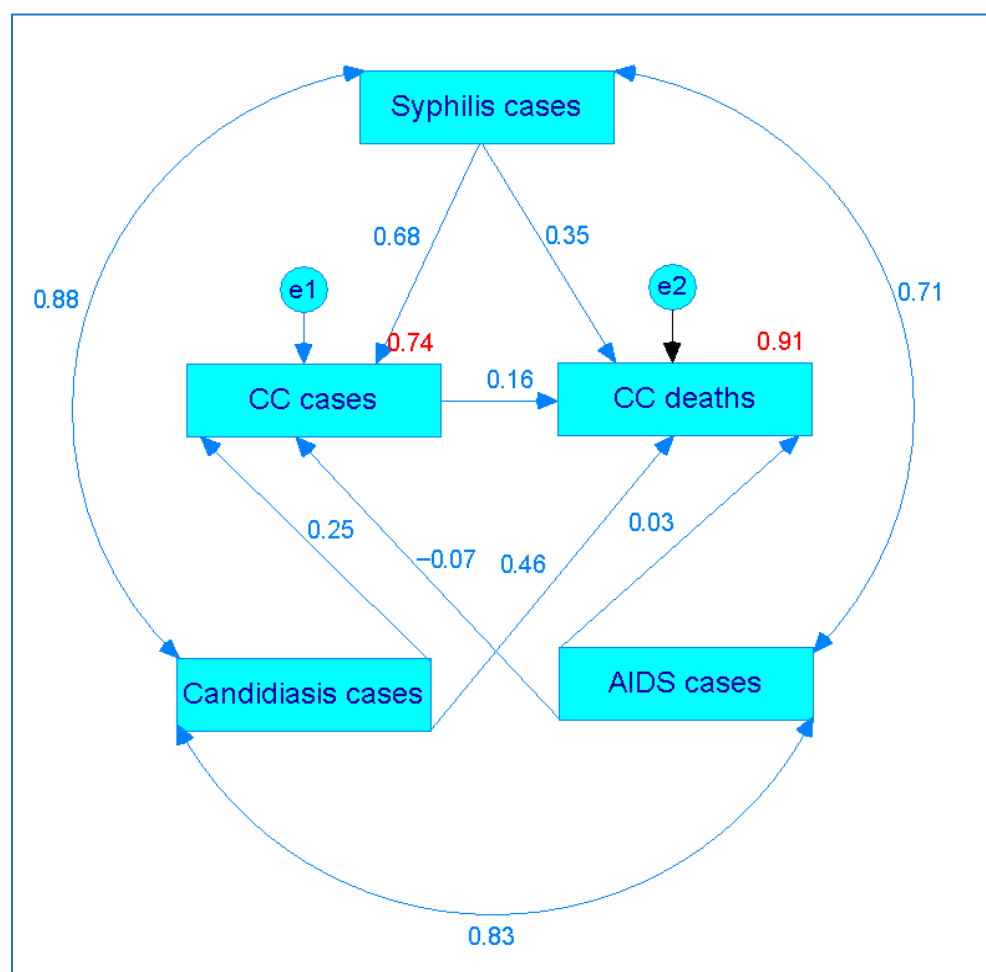


Figure 3. Structural model of the factors (2003), CC cases (2013) and CC deaths (2023) in the State of San Luis Potosí, Mexico.

Figure 4 shows a dynamic model used for estimating mortality predictions up to 2040, developed via Vensim. We observed that syphilis cases will more than double in 10 years and almost quadruple in 15 years starting from 2025 (Figure 5a), while CC cases are expected to increase by double to nearly triple in 15 years. However, CC deaths and mortality rates are expected to undergo a sustained decrease (Figure 5b).

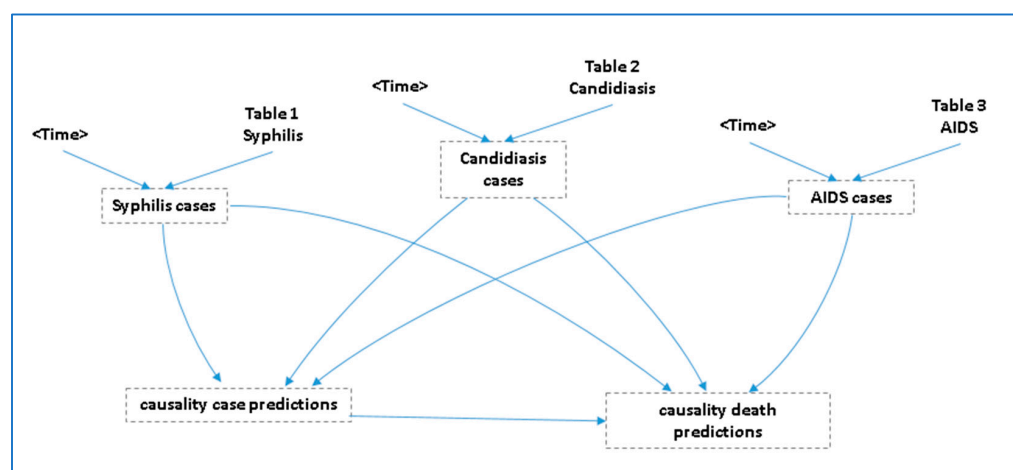


Figure 4. Dynamic model of the factors (2003), CC cases (2013) and deaths (2023) in the State of San Luis Potosí, Mexico.

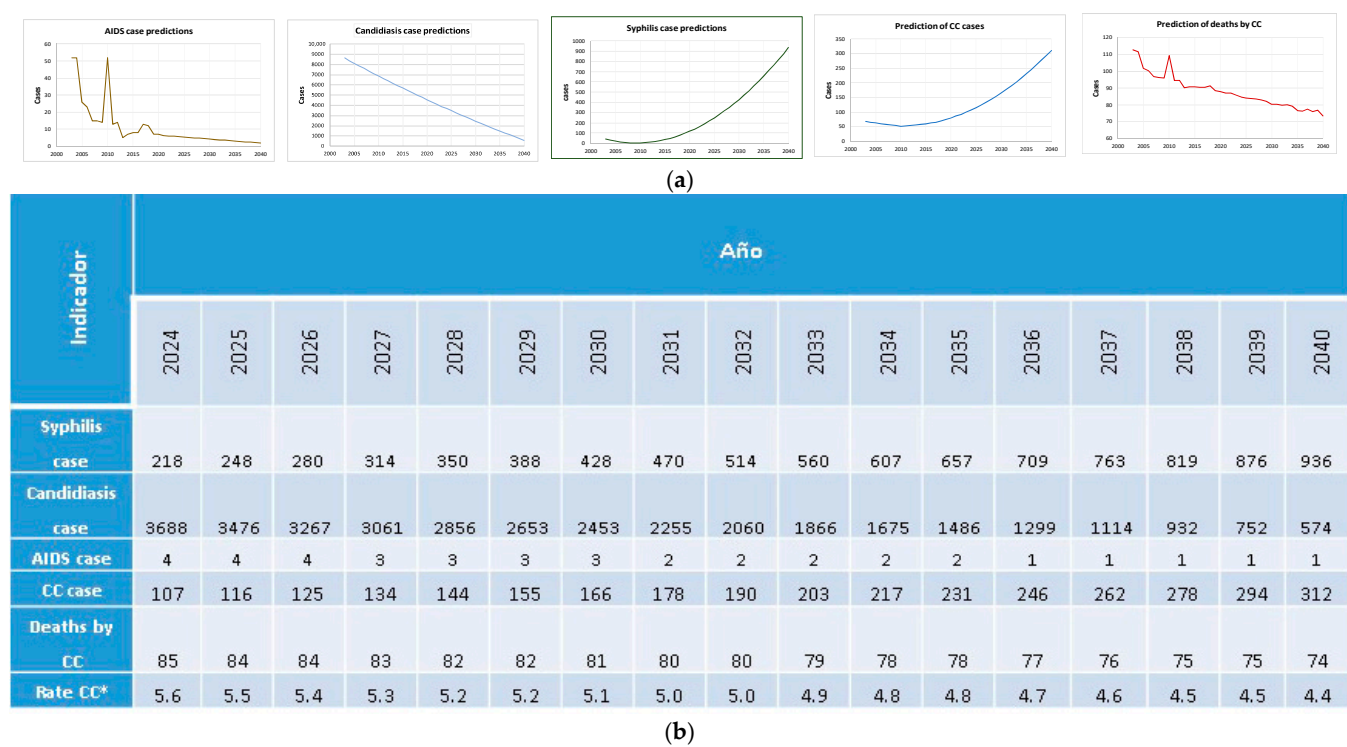


Figure 5. Predictive values of the analyzed factors, cases of cervical cancer, deaths from CC, and the mortality rate from CC in the State of San Luis Potosí, Mexico. In (a) Projections up to 2040 shown graphically every 5 years and in (b) the same projections showing detailed values by year. * per 100,000 women.

3. Discussion

3.1. Methodological Insights

Within the natural history of a disease and for intervention with treatments, there are many different aspects that make it difficult to understand specific prognosis, survival, or mortality within populations; these factors are varied, so understanding them is essential to guide or redirect treatments and, thus, improve patient outcomes, which, for obvious reasons, is reflected in health. Traditionally, these types of problems have been addressed using statistical tools of limited robustness, such as bivariate analyses, applied primarily to data from cross-sectional studies. While these approaches are useful in initial exploratory phases and allow for the description of simple associations between variables, their capacity is limited when the aim is to perform in-depth analyses or construct predictive or causal models in contexts characterized by high complexity [17,18].

A more robust methodological alternative is provided by multiple linear regression models, which allow for the simultaneous evaluation of the effect of several independent variables on a dependent variable. These models offer a more comprehensive and accurate representation of the interaction between various factors that influence a specific outcome, strengthening both the theoretical interpretation and the practical applicability of the statistical results. However, they have significant limitations, including the assumption of linear relationships between variables and the need to meet strict statistical assumptions to guarantee the validity of the inferences [19].

From an advanced methodological alternative, structural equation models (SEMs) offer the advantage of incorporating latent variables and simultaneously examining multiple variables, considering crossed, direct, indirect, and total relationships. They also allow for the inclusion of more than one dependent variable along with their respective measurement errors, as well as modeling both correlations between variables and between the errors

themselves. However, this methodology has certain limitations: it requires relatively large sample sizes—generally greater than 200 observations—although a minimum criterion of at least ten cases for each free parameter or observed variable has been proposed. Additionally, SEM can be affected by overfitting problems, difficulties in correctly specifying the model, ambiguities in interpreting fit indices, and high sensitivity to violations of statistical assumptions, such as data normality [20].

In this context, the application of structural equation models is proposed for the comprehensive analysis of CC, given the complexity and interdependence of its risk factors. Complementarily, dynamic models are especially valuable for planning in both clinical services and public health, as they allow for the simultaneous evaluation of the temporal evolution of risk factors, as well as changes in the incidence and mortality associated with CC.

3.2. Contextual Analysis: Incidence and Mortality from CC

The highest rates of incidence and mortality from CC occur in low- and middle-income countries LMICs. This reflects significant inequalities stemming from a lack of access to national HPV vaccination programs and CC screening and treatment services, as well as social and economic determinants [21]. In 2022, it was established that the mortality rate from CC in Latin America and the Caribbean was three times higher than that in North America, highlighting the inequalities in access to and quality of health care in different areas of the Region of the Americas [22]. Indeed, Mexico has the highest mortality rate due to CC of the member countries of the Organization for Economic Cooperation and Development (OECD) [23].

3.3. Mortality from CC and Policy Implications

Thus, there is a greater burden from CC and other gynecological cancers on women living in LMICs than on those living in high-income countries. Socioeconomic inequalities and inequalities in access to health services have considerable impacts on CC mortality [24,25]. Our study found a general decreasing trend in observed mortality rates from CC, although it has fluctuated. This may be due to HPV vaccination campaigns and health service coverage for early detection. Deaths are expected to decrease by 12.9% by 2040. However, in cases of CC, an upward trend was observed; if a woman's living conditions do not improve, an increase of 329.4% is expected by 2020.

It is necessary to consider that the model does not explain 100% of the variation in incidence rates. Therefore, the low estimated incidence was not derived from an official database, and no specific reason can be identified to explain the low incidence expected during the initial years. Nevertheless, it can be assumed that underreporting may be present due to infrastructure limitations in some municipalities of the state.

It can be hypothesized that the decrease in mortality is due to earlier detection of the disease or to the appropriate and effective treatment provided to women with the disease. The increase in the number of cases is explained by the improved coverage of early detection and by the appropriate treatment of patients, the decrease in mortality.

Cervical cancer survival rates in Mexico are primarily due to early detection (Pap smear, HPV test) and HPV vaccination, which dramatically increase cure rates (>90% in early stages) [26].

Likewise, Cervical cancer (CC) mortality rates were found to be neither uniformly nor randomly distributed across the studied area, a finding confirmed by Moran's Index. This type of spatial pattern has been previously reported in research conducted [27–29]. CC mortality is determined by individual and contextual factors [30]. Among individual factors, age is particularly relevant, as the risk of dying from CC increases in older women [31].

Contextual factors include socioeconomic inequality and difficulties accessing healthcare services [21,32].

In the 12 municipalities with the highest CC mortality rates, the female population represents more than 50% of the inhabitants, and a considerable proportion are women of reproductive age (15 to 49 years). In socioeconomic terms, 41.6% of these municipalities have illiteracy rates between 7.55% and 10.94%, higher than the state average of 6.22% [33], in addition to varying levels of development and marginalization. More than half have a medium Human Development Index (HDI) [34], and the rest have a high HDI; however, the three municipalities with the highest mortality rates have a medium HDI. Regarding the Marginalization Index, several municipalities show medium or high levels [35], with Tamasopo standing out with a high level.

Finally, in most of these municipalities, the proportion of people not enrolled in health services is higher than the state average, indicating limitations in access to medical care. This is compounded by factors such as cultural barriers and beliefs about cervical cancer screening, which negatively impact the early detection of cervical cancer [36,37].

The authors state that there are marked geographical and socioeconomic disparities, since in countries with a low human development index (HDI), incidence rates were twice as high and mortality rates five times higher than those in countries with a very high HDI. On the other hand, CC was among both the three most frequent cancers and the main causes of cancer death in women between 15 and 44 years old, highlighting the persistence and widening of inequalities at the global level and the need to establish national strategies to reduce the gap and move towards the elimination of cervical cancer, which is the WHO's objective [38,39]. The above is also reflected in countries such as Mexico, where CC is a public health problem.

3.4. Mortality from CC and HIV, Syphilis and Candidiasis Like Risk Factors

Although it has already been reported that there is a low prevalence of preneoplastic lesions compared to a high prevalence of microbial infection in the cervix [40], inflammation of the lower genital tract in all women is commonly caused by vaginal infections, whose anatomical proximity implies the infection of the cervix. One of these infections is vaginal candidiasis. In a study conducted in 2014, it was observed that, for 25.4% of women, the presence of *Candida* in the vagina was the specific cause of inflammation [39]. In other studies addressing the same problem, different percentages of *Candida* presence are reported [41,42], and although it is argued that the increase in vaginal candidiasis is due to it being an emerging infection considered an opportunistic mycosis, despite the indiscriminate use of antifungals and the increased numbers of both women using hormonal contraceptives and immunocompromised individuals, these research studies do not establish a relationship between infection and the development of preneoplastic lesions of the cervix or CC, much less establish it as a risk factor for mortality from CC.

The interplay between human microbiota and cancer is increasingly being recognized [43]. For some time now, it has been proposed that microbiome communities play a role in the development, progression, and metastasis, as well as in the response to treatment, of various types of cancer. The genus *Candida* constitutes a group of opportunistic pathogens present as part of the microbiota of different typographic areas in humans, such as the skin, oropharyngeal cavity, gastrointestinal tract, and genital system [44]. Specifically, the relationship between *C. albicans* and cancer has been recognized for many years. It is still debated whether this yeast infection is merely a consequence of the cancer or if it actively contributes to its development [45]. Recently, research has suggested that *C. albicans* may be involved in the development of some types of cancer by increasing host susceptibility through several processes, including inflammation, the stimulation of im-

immune responses mediated by type 17 helper T cells (Th17), the production of compounds with carcinogenic potential, and the ability to mimic the compositions of the molecular structures of human cells [46]. Although the association between *C. albicans* and varied cancers, such as oral cavity, esophageal, stomach, colorectal, liver, skin and even breast cancer, has been described, as have the potential mechanisms of carcinogenesis by this microorganism [47,48], there is no evidence regarding the relationship and possible involvement of any member of the *Candida* genus in the development of CC. Population-based studies generally conclude that there is no association between *C. albicans* and the detection of preneoplastic and neoplastic lesions in CC [49–51]. However, these studies do not consider the impact of using a dynamic model. In our study, we found that vaginal candidiasis has a standardized regression weight on deaths from CC of 0.460, which is statistically significant, meaning that it could represent a risk factor for mortality. Due to the lack of supporting literature, this finding should be taken with caution as further investigation is required.

Another agent considered a risk factor for the development of CC, and which in our study is shown to be a determinant in the mortality of women experiencing this disease, is HIV. HIV-associated cancers are more severe and cause increased mortality in the infected population due to loss of control of the immune system [52,53]. People infected with HIV are more susceptible to developing cancer than uninfected individuals, and they usually have coinfection with oncoviruses such as Human Herpesvirus 8, Epstein–Barr Virus, Hepatitis B and C Viruses, or HPV [54]. This last causative agent of CC is considered a definitive cancer-causing factor in AIDS, since it is traditionally distinctive in patients with HIV, in whom it is common to observe a drop in the CD4 lymphocyte count, an indicator of the quality of the immune system [55,56]. Thus, HIV infection, coupled with immunosuppression, inflammation, and coinfection with oncogenic viruses, predisposes patients to the development of cancers, such as, in the case at hand, CC [57].

A previous study found that the prevalence of HPV infection is not higher in patients with syphilis, nor does it affect the evolution of preneoplastic lesions of the cervix. The relationship between these factors has been investigated because both infections are sexually transmitted [58]. In another study, it was found that in patients with CC, the prevalence of STIs was higher, with syphilis being present in 7.2% of the studied patients [59]. Studies that explain whether or not there is a relationship have not been conducted, and neither have studies that combine several risk factors. In our study, syphilis was identified as a risk factor, with standardized regression weights of 0.680 and 0.350 for CC cases and deaths; both relationships are statistically significant. This risk factor proved to be the most important, and it is expected that the number of cases will increase by 324% by 2040.

3.5. Limitations and Future Scenarios

Furthermore, the model used does not explain 100% of the variation in CC cases and deaths.

The predictions of the future scenarios produced using the model in our study show a sustained three-time increase in the number of CC cases, rising from 116 in 2025 to 312 in 2040. For mortality rates, a sustained, though very small, decrease is predicted, decreasing from 5.5 to 4.4 per 100,000 women between 2025 and 2040. Considering this, in a study conducted in 2025, Li et al. mention that, of the CC cases reported in 2022, 52.67% of patients died from this disease. Their study describes the global demographic projections of the incidence and mortality of CC worldwide for 2030, estimating increases of 14.8% in the number of new cases and 17.8% in mortality.

An exhaustive literature review was conducted to support the relationship between syphilis, candidiasis, and cervical cancer-related outcomes; however, no evidence was

found to support a direct association between these factors. Nevertheless, both conditions are associated with AIDS and may therefore be considered indirect factors [60].

4. Materials and Methods

4.1. Type of Research Methods and Data Used

This study was a retrospective ecological study. Secondary databases were used with data from the 58 municipalities making up the State of San Luis Potosí, Mexico, in 1979–2023. The trend was estimated by obtaining data on deaths from CC for 1979–2011 from the dynamic cubes of the General Directorate of Epidemiology (DGE) [61] and for 2012–2023 from the National Institute of Statistics and Geography (INEGI) of Mexico [33]. The population data were obtained from the National Population Council (CONAPO) [62]. Rates were estimated per 100,000 women.

4.2. Spatial Analysis

The modeling of both the average rates of CC deaths for 1979–2023 and their spatial distribution was carried out via ArcMap software version 10.1 using the World Geodetic System (WGS) 1984 coordinate system. To do this, the territorial limits of the State of San Luis Potosí, as well as its 58 individual municipalities, were derived from the state and municipal political division maps of Mexico at a scale of 1:250,000 from INEGI; these maps were in Shape File (SHP) format. Cartographic data from the polygonal entities of both the state and the municipalities were extracted and saved in an SHP.

Subsequently, a health administration layer was constructed for the State of San Luis Potosí, specifically for the seven Health Jurisdictions (HJs) comprising the state. Using information from the Unique Health Establishment Code (CLUES) catalog of the Ministry of Health [63], average mortality rates due to CC were modeled at the municipal level.

Finally, the “Join Data” tool was used to add the average mortality rate data for the municipalities to the attribute table of the previously mentioned municipal territorial boundaries layer. The rate values were represented using colors in 5 categories, classified via the “Natural Breaks (Jenks)” method.

A geostatistical analysis of the average death rates for CC was carried out to determine if there was a clustered, dispersed, or random distribution pattern [64]; in this case, the average rates were analyzed as a numerical attribution of the polygons making up the municipalities of the State of San Luis Potosí.

According to the scientific literature, clinical indicators were considered as direct and indirect risk factors for deaths from congenital heart disease. Based on the factors showing significant correlations in previous analyses, the following indicators were used: For the health services of the State of San Luis Potosí, data on new cases of the following diseases in women in 2003 were obtained: urogenital candidiasis (candidiasis), acquired syphilis (syphilis), acquired immunodeficiency syndrome (AIDS), and malignant tumor of the cervix (CC cases). The development of cervical cancer after an HPV infection can take between 10 and 20 years, although in people with weakened immune systems, it can be faster (between 5 and 10 years) [65]; these years were taken into account when developing the dynamic model. Deaths due to CC in 2023 were considered, statistics for which were obtained from data reported by INEGI, since it has been found that average survival is approximately 10 years [24].

CC has multiple interrelated risk factors. SEM allows for the simultaneous analysis of these complex cause-and-effect networks, unlike traditional statistical methods that typically analyze variables in isolation.

Holistic models using software such as Vensim are important in the context of CC because they enable a systems dynamics approach to analyzing the complexity of the

disease and its interrelated factors, which is crucial for designing effective public health strategies. They allow estimating future scenarios of variables and their evolution over time.

Based on these factors, a structural equation model, specifically a path analysis (structural model), was built via AMOS 26 software for analyzing multiple relationships between the included factors. In this model, AIDS, syphilis, and candidiasis were considered explanatory (exogenous) factors, while CC cases and CC deaths were defined as endogenous (dependent) variables. This approach made it possible to evaluate both the direct effects of and the cross-interactions between the factors, offering a comprehensive view of the dynamics influencing the behavior of CC-related mortality. In this structural model, standardized coefficients were used to express the effects on a common scale of standard deviations, allowing for comparison of the relative influence of each variable.

It is a recursive model, with X^2 value = 0 and degrees of freedom = 0, also known as saturated. When a structural equation model is saturated, global model fit cannot be evaluated because the model reproduces the observed covariance matrix exactly. Nevertheless, saturated models remain useful for estimating and interpreting the magnitude and significance of structural relationships among variables, particularly in exploratory or path-analytic contexts [66].

The structural model was integrated by two linear regression models. Model 1 used CC cases as the dependent variable and syphilis, candidiasis, and AIDS as independent variables. Model 2 used CC-related deaths as the dependent variable and CC, syphilis, candidiasis, and AIDS as independent variables. The assumptions were tested in both models:

Linearity. Partial regression plots, one for each independent and dependent variable.

Independence. Tested using the Durbin-Watson statistic, with acceptable values between 1.5 and 2.5 [20].

Homoscedasticity. Tested using a scatter plot with standardized forecasts (x) and standardized residuals (y).

Normality. Histogram of the standardized residuals and normal probability plot of the residuals.

Multicollinearity. Tested using the variance inflation factor (VIF); values < 10 are acceptable [67].

4.3. Future Scenario for the Factors Considered

To conduct the prospective analysis, a dynamic model was developed using Vensim PLE x64, <https://vensim.com/software/> (accessed on 10 January 2025). This is a specialized simulation software that was used as a methodological tool to estimate future scenarios regarding the evolution of cervical cancer cases and related deaths. For the modeling process, parameters were entered into Vensim PLE x64. The analysis covered 2003–2040, considering a 24 year horizon to estimate the long-term evolution of the phenomenon. The Euler integration method was applied. The time step entered in the software was set to 1, with the year as the temporal unit [68].

The dynamic model was structured through equations and feedback loops, which replicate the interaction among the explanatory variables and their effects on mortality (Figure 4). The polarity and linkages between variables were defined based on statistical analysis and literature review [69]. To identify trends and simulate the future evolution of candidiasis and syphilis, historical time series from 2003 to 2023 were compiled. In the case of AIDS, time series for the period 2004–2020 were analyzed. Quadratic regression models were fitted to project candidiasis and syphilis cases, while a decreasing exponential model was applied to AIDS cases.

These types of models were selected as it allows the capture of the nonlinear trends identified in the historical series. Quadratic models reproduced phases of increase or decel-

eration. The decreasing exponential model was consistent with processes of progressive reduction associated with public health interventions and epidemiological changes [70].

The models used for predicting the exogenous variables tendency were as follows:

- (A) For candidiasis, we used “cases of candidiasis = $1.11209286 \times (\text{year}^2) - 4714.17087 \times (\text{year}) + 4,989,396.71$ ”. This model showed a strong match between the real data and the simulated values ($R^2 = 0.923$).
- (B) For syphilis, we used “syphilis cases = $0.98684211 \times (\text{year} - 2003)^2 - 12.33721805 \times (\text{year} - 2003) + 41.57857143$ ”, with this model showing an acceptable degree of similarity with respect to the observed series ($R^2 = 0.802$).
- (C) For AIDS, we used “ $(t) = 6.1191 \cdot e^{-0.0895} (t - 2020)$ ”, where t denotes year. The model achieved an $R^2 = 0.92$ between observed and simulated data.

The equations were processed in Excel and subsequently integrated into the dynamic model in Vensim PLE x64. For validation and calibration, the maximum likelihood method was applied through an iterative process aimed at maximizing the correspondence between the observed time series and the values generated by the model [71]. The projections were considered valid when R^2 values between 0.75 and 0.80 were achieved between observed and simulated data [72].

The standardized coefficients of the structural model were converted to non-standardized values, since it was necessary to express them in the original scale of the data to apply them to real cases. The converted values were adjusted and two equations were created and integrated into the dynamic model to estimate the predictions of CC cases and CC deaths:

- (D) Cases of CC = $29.8303 + (\text{cases of candidiasis} \times 0.0035) + (\text{cases of syphilis} \times 0.299) + (\text{cases of AIDS} \times -0.07)$.
- (E) Deaths due to CC = $-2.21765 \times 10^6 + (74,344.8 \times \text{cases of CC}) - (22,229.1 \times \text{cases of syphilis}) + (5204.51 \times \text{cases of AIDS}) - (260.205 \times \text{cases of candidiasis})$.

A sensitivity analysis was conducted through controlled variation in the coefficients associated with the exogenous variables candidiasis, syphilis, and AIDS, in order to assess their influence on the simulated trajectories of cervical cancer cases and mortality and to evaluate the robustness of the model.

4.4. Statistical Analysis

For the geostatistical analysis, the “Moran’s Index” test was used. This tool measures spatial autocorrelation using both the geographic locations and numerical attributes of different entities. A 95% confidence level was considered, with $Z = 1.96$ and a probability of 0.05. Using AMOS software, a structural equation model was developed to analyze multiple relationships, including the cross-relationships between the endogenous and exogenous variables used.

5. Conclusions

Mortality from CC in the state of San Luis Potosí exhibits a non-random spatial pattern with statistically significant clustering.

The structural equation model showed that CC deaths are 91% dependent on syphilis, candidiasis, AIDS, and CC cases combined.

Prospective scenarios indicate a substantial increase in syphilis cases, with a trend toward a near quadrupling between 2025 and 2040, as well as an increase in CC cases and a moderate decrease in mortality rates.

Overall, the results confirm the value of integrated approaches that combine spatial analysis, structural modeling, and dynamic simulation to generate information that can

support the planning of prevention strategies. These interventions should consider the integrated control of multiple sexually transmitted infections, strengthen HPV vaccination, and improve early detection programs, recognizing the combined influence of clinical and social factors on CC mortality.

Although syphilis exhibited the highest association coefficients, its effect is interpreted in the context of its interaction with other relevant sexually transmitted infections, such as HIV and candidiasis, as well as with social determinants related to access to health services, coverage of early detection programs, geographic barriers, and socioeconomic conditions.

Health authorities in the State of San Luis Potosí, Mexico, as well as those in any country, can rely on this study's geographical results to design strategies, primarily those from the 12 municipalities with very high mortality rates from CC.

Sexually transmitted diseases must be reduced or at least controlled, especially syphilis, candidiasis, and HIV/AIDS, which are particularly important, as their combined analysis revealed them to be risk factors for CC cases, and these four variables also contribute significantly to CC-related deaths.

Establishing relationships between risk factors and CC is extremely important to optimally propose prevention and management strategies; however, researchers must consider that the disease is multifactorial and that the factors present must be analyzed using robust techniques that allow for identifying multiple linear and cross-dependency relationships, as this will achieve the most accurate results.

The importance of structural equation models and dynamic models that allow us to generate future scenarios for both morbidity and mortality from CC is clear.

Training in implementing the correct Pap smear technique is a powerful tool in prevention, but it should be remembered that the process for performing cervical cytology allows for evaluating the health status of the vulvovaginal anatomical region and the collection of simple samples that, together with the signs and symptoms, allow for the rapid detection of candidiasis and syphilis; therefore, comprehensively preparing and training the health personnel in charge of taking samples for Pap is essential.

CC in Mexico is a public health problem; whether due to social inequality, economic backwardness, geographical distances acting as a barrier to accessing health services, the limited number of educational campaigns with a cultural focus on both men and women, etc., it is important to think about effective prevention strategies and their immediate application. It is advisable to continue the study and, through the dynamic model, conduct a what-if analysis to simulate optimistic scenarios that could result from an increase in vaccination coverage. It is recommended to further investigate the link between candidiasis.

Limitations

The sample size is small. The models do not incorporate all the factors that may determine CC cases and mortality from this disease. They were constructed based on a specific set of explanatory variables selected according to the availability of official information and their statistical significance. Only three sexually transmitted infections were included, although others were initially considered, such as herpes, chancroid, and lymphogranuloma; however, their correlations with CC cases and mortality were not statistically significant. The absence of other individual risk factors (e.g., family history of cervical cancer, smoking, use of hormonal contraceptives, nutrition, and lifestyle factors) reflects the fact that the data were obtained at the municipal level. As this is an ecological study, it is subject to the ecological fallacy, whereby group-level characteristics are attributed to individuals.

Projections up to 2040 are subject to uncertainty due to the assumed continuity of historical trends and potential inaccuracies in epidemiological records. Moreover, future

changes in public policies or early detection practices are not considered, which may alter the projected trajectories.

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Abbreviations

The following abbreviations are used in this manuscript:

CC	Cervical Cancer
HPV	Human Papillomavirus
STI	Sexually Transmitted Infection
HIV	Human Immunodeficiency Virus
AIDS	Acquired Immunodeficiency Syndrome
DGE	General Directorate of Epidemiology
INEG	National Institute of Statistics and Geography
CONAPO	National Population Council
WGS	World Geodetic System
SHP	Shape File
HJs	Health Jurisdictions
CLUES	Unique Health Establishment Code

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