

## Temporary trends of invasive uterine cancer in women between 20 and 39 years of age. Manizales, Colombia, 2003-2018.<sup>1</sup>

María del Pilar Arango Arango <sup>a</sup>

<sup>a</sup> MD. Gynecologist at Santillana Clinic, Manizales. Professor, Universidad de Manizales.

ORCID: <https://orcid.org/0000-0002-3119-283X>, [mariadelpilar.arango@yahoo.es](mailto:mariadelpilar.arango@yahoo.es)

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### Abstract

**Objective:** This article analyzes the invasive uterine cancer occurrences in women between 20 and 39 years old in Manizales, Colombia, 2003-2018.

**Materials and methods:** Observational, descriptive, retrospective, population-based study. Temporary trends of occurrences were evaluated (as referring to Population Segi, per 100,000 women / year) by using the Joinpoint regression (Joint Point Regression Program v. 4.7.0.0 of the National Cancer Institute of the USA), in order to estimate annual percentage changes and number of years of significant variation in trends.

**Results:** The study was carried out with a total of 116 patients, whose average age at the time of diagnosis was 33.7 years. Only 3 invasive cancer cases were found in women between the ages of 20 and 25. The greatest number of cases occurred in the group of women between 35 and 39 years old. The most frequent histological type was squamous cell carcinoma. 45.6% of cases were diagnosed in early stages. The Average Annual Percentage Change calculated using the Joinpoint regression model showed a 7.9% decrease in the incidence rate between 2003 and 2018, with a breaking point in 2010.

**Conclusions:** Cervical cancer in Manizales is infrequent in women under the age of 25; and, for ages between 20 and 39, it has shown a tendency to decrease over time, particularly from 2010 onwards.

**Key words:** Cervical cancer, women, adolescent, young adult, epidemiology, epidemiological studies, trends. (DeCS, BIREME).

### Tendencias temporales del cáncer de cuello uterino invasivo en mujeres entre 20 y 39 años en Manizales, Colombia. 2003-2018

#### Resumen

**Objetivo:** Analizar la tendencia de la incidencia de cáncer de cuello uterino invasivo en mujeres entre 20 y 39 años en Manizales, Colombia, 2003-2018.

**Materiales y métodos:** Estudio observacional, descriptivo, retrospectivo, de base poblacional. Se evaluaron las tendencias temporales en la incidencia (con referencia a Población Segi, por 100.000 mujeres/año) utilizando la regresión de Joinpoint (*Joint Point Regression Program* v. 4.7.0.0 del *National Cancer Institute* de los EEUU) para estimar los cambios porcentuales anuales y años de variación significativa en las tendencias.

**Resultados:** Se realizó el estudio con un total de 116 pacientes, cuya edad promedio al momento del diagnóstico fue 33.7 años. Sólo se hallaron 3 casos de cáncer invasivo en mujeres entre 20 y 25 años. El mayor número de casos se presentó en el grupo de mujeres de 35 a 39 años. El tipo histológico más frecuente fue el carcinoma escamocelular. El 45.6% de los casos se diagnosticaron en etapas tempranas. El Cambio Porcentual Anual Promedio calculado mediante el modelo de regresión *Joinpoint* mostró un descenso de 7,9% en la tasa de incidencia entre 2003 y 2018, con un punto de quiebre en el año 2010.

**Conclusiones:** El cáncer de cuello uterino en Manizales tiene escasa frecuencia en mujeres menores de 25 años y para edades entre 20 y 39 años muestra una tendencia a la disminución en el tiempo, en particular desde el año 2010 en adelante.

**Palabras clave:** Cáncer de cuello uterino, mujeres, adolescente, adulto joven, epidemiología, estudios epidemiológicos, tendencias (DeCS, BIREME)

## Introduction

According to GLOBOCAN, in 2018, there were 570,000 new cases and 311,000 deaths from cervical cancer in the world (1). In higher-income countries, mortality from cervical cancer has decreased by about half in the last 30 years, in part attributed to screening programs. But in low-income countries the rates have been stable or increased (1, two). In Latin America, in 2015, 74,488 cases and 31,303 deaths were reported, an increase of 45% in mortality is estimated for the year 2030 (3).

According to the International Agency for Research on Cancer (IARC) in Colombia for the year 2018 there were 3,853 new cases and 1,775 deaths (4). For its part, Caldas, for the same year, reported 142 cases of which 98 were from Manizales (unpublished data - Manizales Health Secretariat). The incidence patterns reflect trends in behaviors associated with cancer risk and changes in medical practice, such as the use of cancer screening tests (5).

In order to reduce the incidence of invasive cervical cancer, primary prevention strategies have been developed through the use of HPV vaccines and secondary prevention through early detection of the risk due to infection by certain types of Papillomavirus Human (HPV), which is a necessary cause of cervical cancer (2,3,6,7,8).

Between 1990 and 2010, the world saw a 26.9% decrease in the mortality rate from cervical cancer, and in developed countries this reduction has been sustained since 1975 (9). In Colombia, the standardized rates for this tumor decreased from 13.2 per 100,000 women-years in the 1980s to 8.7 in 2013 (10).

In 2012, the American Society for Cervical Pathology and Colposcopy (ASCCP) published the new form of screening where all women must begin screening tests at age 21, those from 21 to 29 must be screened. cytology test every 3 years and after age 30 a combined Pap test with an HPV test every 5 years. This is called a joint test (or cotest) that must be continued until age 65 (7,11).

For Colombia, the Clinical Practice Guide of the Ministry of Health in 2014 established the performance of DNA tests for the detection of HPV between 30 to 65 years of age. In addition, it recommends the use of cytology for the diagnostic triage of patients positive to HPV-DNA tests. For women between 25 and 30 years of age, he suggests screening with cytology every 3 years for negative results. Taking into account the low incidence of cancer and precancerous lesions in women under 25

years of age. Experts suggest not to perform screening as part of an organized population program, leaving it up to the clinician to offer an opportunity diagnosis with cytology to women in this group old (12).

Likewise, according to data from the Surveillance, Epidemiology and End Results Program (SEER) of the National Cancer Institute (NCI), Benard et al. found that from 1999 to 2008, 21% of invasive cancers in women under 40 years of age corresponded to women between 20 and 29 years of age and 1% to women under 20 years of age (13).

In the Latin American context, a hospital-based study in Lima, Peru, found, among women under 35 years of age, that the most frequent age group was 30 to 35 years with 78.9% of cervical cancer, followed of the 25 to 29 age group with 16.0% and the 20 to 24 age group with 5.3% (14).

However, the screening strategy in Colombia could expose the female population between the ages of 15 and 25, to whom, according to current recommendations, no screening test should be applied. Therefore, the objective of this study is to analyze the temporal trends of invasive cervical cancer in women aged 20 to 39 years between 2003 and 2018 in Manizales, Colombia.

## Materials and methods

A retrospective, descriptive, observational cohort study of incident cases, which included 119 cases of invasive cervical cancer in women between 20 and 39 years old identified by the Manizales Population Cancer Registry.

The master database was consulted and filters were used by location C53 and age for those under 40 years of age. The date of birth of the patients was verified and the age was corrected at the time of diagnosis. Of the total number of cases, 2 that did not have invasive cancer and 1 that had more than 40 years were excluded. The data from the population registry were verified with medical reports and government information sources, in addition, data was completed to construct the clinical stage at the time of diagnosis based on the classification of the International Federation of Gynecology and Obstetrics (FIGO) 2018.

Information on the place of residence at the time of diagnosis (address or neighborhood) was provided, from which the socio-economic level was assigned based on the predominant stratum of the neighborhood of residence according to the Housing-Household-People database ( HIVOPE) of the National Administrative

Department of Statistics - DANE. The clinical stage and histological diagnoses were completed and validated, the latter based on the International Classification of Diseases for Oncology, first revision of the third edition (ICD-O 3.1).

A univariate description of the variables of interest was carried out, in addition to a bivariate analysis for the variables of clinical stage with age and socioeconomic status. The clinical stage variable was dichotomized as early stage for cases with FIGO stages I and II and as late stage for the others. The median age of the entire data set was used as the cut-off point for age, that is, under 34 years and 34 and over. The socio-economic level variable was categorized as an ordinal variable in three groups: high (strata 5 and 6), medium (strata 3 and 4) and low (strata 1 and 2).

For the adjustment of rates by age, the direct standardization method was used; Four selected strata were established for the purposes of this research (five-year age groups between 20 and 39 years) and the world population of Segi was used as a reference. The data on the population at risk were obtained from the official population projections of the National Administrative Department of Statistics.

The temporal trends in incidence were estimated using the Joinpoint regression, which uses log linear regression by parts to evaluate the annual percentage changes and identify any year in which a significant change in the trends occurs, version 4.7.0.0 of the Joinpoint Regression Program produced by the National Cancer Institute (NCI, USA).

Furthermore, for data processing and analysis, Microsoft Excel® packages were used; SPSS® version 22 (licensed for the University of Caldas) and Stata IC 14.2 (personal license).

## Results

The median age at diagnosis was 34.2 years (interquartile range - IQR = 6.6 years). It was found that most of the patients in this study belong to low and medium socioeconomic status in 38.8% and 39.7%, respectively. Only 4.3% of women belong to the high socioeconomic stratum. For this variable, the percentage of cases with missing data reached 17.2%. Regarding the distribution by age groups, it is evidenced that invasive cancer cases are concentrated in the 35 to 39 year old group followed by the 30 to 34 year old group. A minority of cases occur in women under the age of 30, and only 3 cases occurred under the age of 25. (Figure 1)

### AGE AT DIAGNOSIS

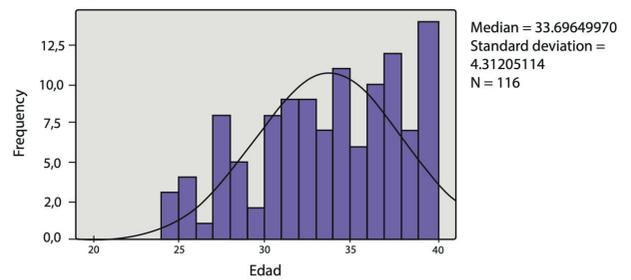


Figure 1. Distribution by age of patients with cervical cancer between 20 and 39 years. Manizales, Colombia, 2003-2018

Source: Own elaboration.

The absolute number of cases per year varied between the periods 2003 to 2010 and 2011-2018, observing a decrease in the last period. The years with the highest number of incident cases were 2005 and 2008-2009, while the lowest number of cases was observed in 2015.

According to the morphological classification, the most frequent histological type was squamous cell carcinoma, followed by adenocarcinoma. More than 10% of the cases did not have an adequate morphological classification.

Regarding the clinical staging at diagnosis, 45.6% of the patients were classified in the early stage, and 24.1% in the advanced stage. The distribution of incident cases by diagnostic stage was 33 (28.4%), 20 (17.2%), 21 (18.1%), and 7 (6.0%) for stages I to IV, respectively. ; but there was a volume of 35 cases (30.2%) in which this data could not be found.

Regarding the relationship between the stage at the time of diagnosis and the socioeconomic level, a higher proportion of women with early stages was observed in the group with high socioeconomic level and a greater proportion of late stages in the low level (Exact test of Fisher, p-value = 0.034). The association between clinical staging (early or late) and age groups was also explored, without finding a statistically significant association (Fisher's exact test, p value = 0.89).

AGE-ADJUSTED RATE ACCORDING TO HISTOLOGICAL TYPE

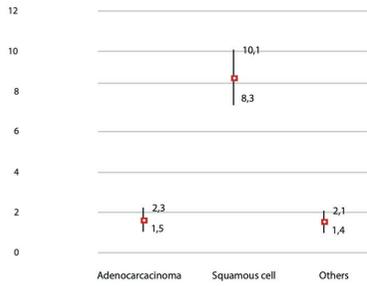


Figure 2. Age-Adjusted Incidence Rates (Segi World Population) per 100,000 Women-Years of Neck Cancer uterine according to histological type.

Figure 2 shows the age-adjusted cervical cancer incidence rates (Segi world population) per 100,000 women / year according to histological type. The specific rates by age groups stand out, whose distribution in all the aggregated histological types was: 1.2 between 20 to 24 years; 7.2 between 25 to 29 years old; 18.6 between 30 to 34 years; and 22.7 between 35 to 39 years.

Likewise, in relation to the behavior of the incidence by age groups, in squamous cell carcinoma, the rate was 0.4 per 100,000 between 20 and 24 years; 6.1 in the 25 to 29 age group; 14.3 between 30 and 34 years; and 15.9 between 35 and 39 years. For adenocarcinoma, the specific rates in these same age groups were 0.4; 0.0; 3.0; and 3.6 respectively. Regarding the other histological types, the rates were very similar to those of adenocarcinoma.

ANNUAL PERCENTAGE CHANGE

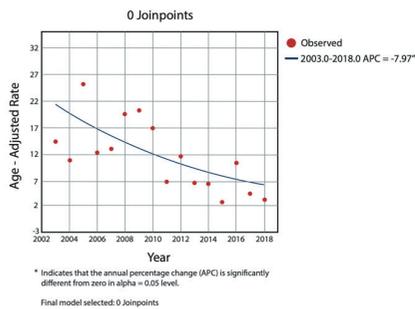


Figure 3. 0 Joint point . It shows a 7.97 annual percentage decrease in the age-adjusted incidence rate in women with cervical cancer between the ages of 20 and 39.

Source: Own elaboration.

TEMPORAL TRENDS

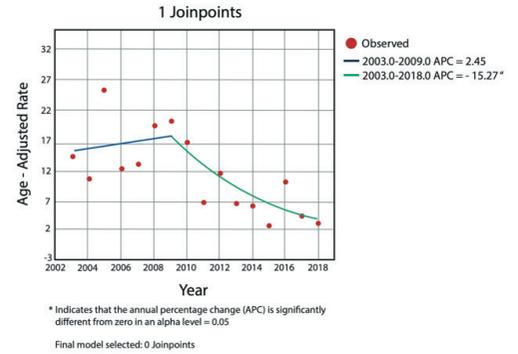


Figure 4. Joint point break points of the annual percentage value in the age-adjusted incidence rate in the women with cervical cancer between the ages of 20 and 39.

Source: Own elaboration.

Figures 3 and 4 show a 7.97% annual decrease in the age-adjusted incidence rate in women with invasive cervical cancer between 20 and 39 years of age. Alternative models showed 2 break points that were not significant. The significant decline in the rate is seen more clearly from 2010.

Discussion

The results of this research, in terms of the distribution of cases by age groups, are similar to those found in the United States between 1999 and 2008, where 78% of cervical cancer cases were diagnosed in women aged 30 a 39, 21% were diagnosed in women between 20 and 29 years old and 1% in those under 20 years of age. Up to age 14 the incidence rates were close to 0 and were removed from the tables due to low case counts (13).

In this study, the concentration of cases in the age group 30 to 39 years reinforces the need to implement screening with cytology detection as soon as possible in young women over 25 years of age and HPV typing in those over 30 years of age also using care models that allow adequate coverage of the population at risk. Organized cervical cancer screening programs are effective and powerful tools that can prevent deaths as has been shown in Europe, North America, and Asia (15).

A descriptive investigation of the behavior of cervical cancer in young people under or equal to 35 years of age between 1990 and 2012 in the US, of 126 patients with whom the study was carried out, 15% were aged less than or equal to 25 years and 85% were aged from 26 to 35 years (16). In this study, the percentage of cases was

lower in the youngest of 116 patients, 3% of the cases occurred in women under 25 years of age and 97% of the cases in those over 25 years of age.

A study conducted in the United Kingdom showed that the incidence of cervical cancer in young women aged 20 to 29 years increased by 10.3% annually between the years 2000 and 2009 (17). Similarly, for Japanese women, between 1985 and 2012, an increase in the incidence rates for cervical cancer in women aged 25 to 49 years and in South Korea at that time increased the incidence rate in young women between 20 and 29 years old (18). Likewise, several epidemiological studies show that the incidence of cervical cancer in young women was increasing (16, 19, 20, 21, 22)

In Costa Rica, they found an increase in the incidence of cervical cancer since 2012. The age group most affected globally (in situ ca and invasive ca) was between 26 and 30 years old. But for invasive cancer it was the 46-50 age group (23). It is necessary to consider that, by including carcinomas in situ, the incidence in this study could have increased as a result of a good functioning of the screening programs and not due to a real increase in incidence.

A study in a London hospital reported that of 108 cases of invasive cancer diagnosed between 1999 and 2006, 2 cases occurred in women aged 20-24 years, 12 between 25 and 29 years and 18 between 30 and 34 years; 62.1% were detected in stage I according to FIGO classification (24). These results are also consistent with those found for this investigation.

Cervical cancer screening in women under 21 is considered to be less effective than in older age groups, so the age to start screening has been increased regardless of the onset of sexual activity. An American study comments that, although detection occurs less frequently in younger age groups (15-19 years), 2.7 million cytology tests were performed to detect an average of 14 cancers that occurred annually (13).

Low socioeconomic status is associated with an increased risk of cervical cancer. From 1988 to 1992 in the United States, the incidence of cervical cancer was higher in women living in communities with higher poverty levels ( $\geq 20\%$  or more of the population below the poverty level: 19.2 cases per 100,000 women versus  $< 10\%$  below the poverty level: 8.8 per 100,000). Women in high-poverty counties, compared to low-poverty ones, had a 71% higher cervical cancer death rate (25). This is similar to what was found in this study, where more than two thirds of the patients included in the study belong to

the middle and lower strata.

With particular reference to invasive adenocarcinoma and its histological variants, its incidence has increased in recent decades, especially in younger women. In fact, in the past 35 years, there has been a 32 percent increase in adenocarcinoma and a 16 percent increase in adeno-squamous histologies among newly diagnosed cervical cancer patients (25). In contrast, in this research different data was found in women between 20 and 30 years old, for these young women the predominant histological type was squamous cell carcinoma and not adenocarcinoma or other histological types.

The incidence of cervical cancer, including squamous cell carcinoma, has been declining in developed countries. However, adenocarcinoma has increased among young people as demonstrated by Birgitte and Col in the study carried out between 1997 and 2011 in Denmark (26).

In South Korea, an annual percentage change of 3.9% (95% CI: -4.2 to -3.6) has been reported between 1993 and 2012, in addition to the presence of a cohort effect and a slight increase in the incidence rate in women under 30 years of age (14).

Thus, for Manizales, the reduction in the annual percentage change was almost double than that of Korea, which can be explained first, in 2018 the data collection of the Population Registry has not been closed, and the data collection may not have been completed. Completion of the population registry, with which the rate for the last year may be falsely low, secondly because Manizales had higher rates than Korea at the beginning of the registry and therefore the change is more visible than in Korea, which started from lower rates in 1993 and third because the department of Caldas has had a decentralized screening program with Colposcopy in primary care since 2000, with 17 deaths per year per 100,000 women per year less when compared to the centralized care program (27) which could be related to the notable decrease in the incidence of invasive cancer in Manizales.

## Conclusions

Given that historical data from the years 2003 to 2018 from the Manizales population cancer registry were used in this research, it is recommended for other studies to continue studying these variables with the information provided in the municipal registry since 2016 that has the notification mandatory of invasive cervical cancer cases in Colombia; and therefore, could complement the data captured by the Population Registry.

It is concluded that cervical cancer in Manizales is

infrequent in women under 25 years of age and for ages between 20 and 39 it shows a decreasing trend over time, particularly since 2010. There is a greater number of Squamous cell cancers in young women. There is a greater number of invasive cancers in the group of women aged 30-39 years, so interventions for cancer prevention should be reinforced.

In recent decades, cervical cancer incidence rates have decreased in Manizales, probably due to decentralized population-based screening programs. New public policies are required in addition to research that provide feedback to the health provider in order to provide safe and quality care to young patients.

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