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Trend Analysis of Cancer Mortality and Incidence in Panama, Using Joinpoint Regression Analysis

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Abstract: Cancer is one of the leading causes of death worldwide and its incidence is expected to increase in the future. In Panama, cancer is also one of the leading causes of death. In 1964, a nationwide cancer registry was started and it was restructured and improved in 2012. The aim of this study is to utilize Joinpoint regression analysis to study the trends of the incidence and mortality of cancer in Panama in the last decade.

Cancer mortality was estimated from the Panamanian National Institute of Census and Statistics Registry for the period 2001 to 2011. Cancer incidence was estimated from the Panamanian National Cancer Registry for the period 2000 to 2009. The Joinpoint Regression Analysis program, version 4.0.4, was used to calculate trends by age-adjusted incidence and mortality rates for selected cancers.

Overall, the trend of age-adjusted cancer mortality in Panama has declined over the last 10 years (−1.12% per year). The cancers for which there was a significant increase in the trend of mortality were female breast cancer and ovarian cancer; while the highest increases in incidence were shown for breast cancer, liver cancer, and prostate cancer. Significant decrease in the trend of mortality was evidenced for the following: prostate cancer, lung and bronchus cancer, and cervical cancer; with respect to incidence, only oral and pharynx cancer in both sexes had a significant decrease. Some cancers showed no significant trends in incidence or mortality.

This study reveals contrasting trends in cancer incidence and mortality in Panama in the last decade. Although Panama is considered an upper middle income nation, this study demonstrates that some cancer mortality trends, like the ones seen in cervical and lung cancer, behave similarly to the ones seen in high income countries. In contrast, other types, like breast cancer, follow a pattern seen in countries undergoing a transition to a developed economy with its associated lifestyle, nutrition, and body weight changes.

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Abbreviations: APC = Annual Percent Change, ICD-O-3 = International Classification of Diseases for Oncology, third edition, SEER = The Surveillance, Epidemiology, and End Result, WHO = World Health Organization.

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INTRODUCTION

Cancer is one of the leading causes of death worldwide and its incidence is expected to increase in coming years.¹ In developing countries, risk factors for cancer associated with behavioral, nutritional, and environmental changes continue to increase.²

Like in most developing countries,³ cancer in Panama has become one of the leading causes of death.⁴ In 1964 Panama implemented a nationwide cancer registry and in 2012, a new and improved electronic cancer registry database was established.⁵

Trend analysis is a tool that helps to visualize changes in the incidence and mortality of cancer and has been used primarily in developed countries.^{6,7} A few studies have applied trend analysis in the Americas.^{8–11} The aim of this study is to utilize Joinpoint regression analysis to study the trends of the incidence and mortality of cancer in Panama.

METHODS

Data Collection

We obtained all cancer mortality cases reported for the year 2001 to 2011 from the Panamanian National Institute of Census and Statistics (Instituto Nacional de Estadística y Censo), which is the repository of all death certificates issued nationwide. All registries for which the principal cause of death was cancer were included and identified using the codes of the 10th revision of the International Classification of Diseases.¹² The cancer types described in this study were chosen based on their mortality rank and their malignant behavior. Blood and skin cancer were not included in the analysis because of the difficulty in diagnostic consensus.

To estimate cancer incidence, we used the cases recorded by the Panamanian National Cancer Registry (Registro Nacional de Cancer),⁵ which is the national institution responsible for collecting information on all new cancer cases by clinical and pathological diagnosis from both the public and private health sectors. We compiled all available cases from the years 2000 to 2009 utilizing the International Classification of Diseases for Oncology, third edition.¹³

Statistical Analysis

Cancer rates were calculated as cases per 100,000 people and age-adjusted to the World Health Organization standard population¹⁴ using the SEER*Stat software version 8.0.4 (The Surveillance, Epidemiology, and End Result [SEER]).¹⁵ The Joinpoint Regression Analysis program version 4.04¹⁶ was used to examine trends in overall age-adjusted incidence and mortality rates for selected cancers. The Joinpoint program selects the best fitting piecewise continuous log-linear model. The permutation test was performed to determine the minimum number of “joinpoints” necessary to fit the data.¹⁷ A significance level of 0.05 was used for the permutation test with 4499 of randomly permuted datasets. For the study period, we utilized trend analysis for selected cancers, estimated and displayed graphically the annual percent change (APC) with 95% confidence intervals.

Ethics Statement

This study was approved by the National Bioethics Committee of the Gorgas Memorial Institute for Health Studies and has been conducted in accordance with the ethical standards laid down in the 1965 Declaration of Helsinki and its later amendments.

RESULTS

The overall trend of the age-adjusted cancer mortality rates in Panama have declined over the last 10 years (Table 1, Figure 2). In men, age-adjusted cancer mortality declined by 1.48% per year, while in women it remained unchanged (Table 1). The age-adjusted incidence of cancer has increased in women by 0.85% per year, while in men it has remained the same (Table 2).

In men, the mortality of prostate cancer ranked first (21.1 per 100,000), followed by lung and bronchus cancer (13.2 per 100,000), and stomach cancer (12.2 per 100,000) (Table 1, Figure 1). With respect to incidence, prostate cancer also ranked first throughout the study period (58.1 per 100,000), followed by stomach cancer (14.1 per 100,000), lung and bronchus cancer (12.0 per 100,000), colon and rectum cancer (11.8 per 100,000), oral and pharynx cancer (4.3 per 100,000), liver cancer (3.7 per 100,000), and finally, esophageal cancer (2.2 per 100,000) (Table 2, Figure 1).

In women, mortality from breast cancer ranked first (10.1 per 100,000), followed by cervical cancer (8.7 per 100,000), stomach cancer (7.0 per 100,000), and lung and bronchus cancer (5.2 per 100,000) (Table 1, Figure 1). The incidence followed the same pattern as mortality, with breast cancer ranking first (28.5 per 100,000), followed by cervical cancer (20.7 per 100,000), colon and rectum cancer (10.4 per 100,000), stomach cancer (8.1 per 100,000), lung and bronchus cancer (5.3 per 100,000), and ovarian cancer (4.8 per 100,000) (Table 2, Figure 1).

Colon and rectum cancer had a slightly higher mortality rate for males (7.9 vs 6.3 per 100,000) while pancreatic cancer

mortality (3.4 vs 3.3 per 100,000) was similar for males and females (Table 1, Figure 1). Pancreatic cancer (2.7 vs 2.8 per 100,000) and brain and central nervous system (CNS) cancer (3.6 vs 3.2 per 100,000) had similar male and female incidence rates (Table 2, Figure 1).

Trend Analysis and APC

The following results have been described as increasing or decreasing trends based on the respective positive or negative sign of the APC. Results with no significant value were considered as stable and, therefore, were not included in this section (Tables 1 and 2, Figure 2).

Increasing Trends

Mortality

During the study period, 2 types of cancer had a significant increase in the age-adjusted mortality trend. These were breast cancer (1.66% per year) and ovarian cancer (3.21% per year) (Table 1, Figures 1 and 2).

Incidence

There was a significant increase in the incidence trend of breast cancer (2.62% per year), liver cancer (4.43% per year), as well as prostate cancer (2.68% per year) (Table 2, Figure 1).

Decreasing Trends

Mortality

In men, despite the increasing trend in the age-adjusted incidence of prostate cancer, mortality has been decreasing (−2.56% per year), as well as the age-adjusted mortality trend

TABLE 1. Mortality Trends and Age Adjusted Rates Panama 2001 to 2011

	Male				Female				Total						
	APC	95% CI	ASR	No.	APC	95% CI	ASR	No.	APC	95% CI	ASR	No.			
Stomach	−1.9	−4	0.26	12.2	1726	−1.07	−3.33	1.25	7	1117	−1.63*	−3.08	−0.15	9.5	2843
Prostate	−2.56*	−4.18	−0.91	21.1	2973						−2.56*	−4.18	−0.91	9.7	2973
Lung and Bronchus	−1.94*	−3.61	−0.25	13.2	1833	−1.97	−5.02	1.17	5.2	812	−2.06*	−3.8	−0.29	9	2645
Colon and Rectum	−0.24	−2.5	2.07	7.9	1112	−0.78	−2.08	0.53	6.3	1002	−0.53	−2.06	1.03	7	2114
Breast			0.1	14		1.66*	0.69	2.64	10.1	1601	1.66*	0.69	2.64	5.3	1615
Cervix Uteri						−4.23*	−6.44	−1.98	8.7	1407	−4.23*	−6.44	−1.98	4.5	1407
Gallbladder	−0.72	−10.3	9.89	0.3	46	−2.93	−9.98	4.68	1	154	−2.13	−8.09	4.23	0.7	200
Esophagus	−3.01	−7.11	1.28	2.1	291	−4.08	−13.08	5.84	0.5	79	−3.42	−8.02	1.41	1.3	370
Oral cavity and pharynx	−2.91	−6.66	1	2.7	383	−1.78	−5.51	2.09	1.1	184	−2.62*	−5.13	−0.04	1.9	567
Liver	2.11	−0.79	5.09	3.8	537	0.68	−2.16	3.61	2.8	441	1.41	−1.09	3.98	3.2	978
Pancreas	−1.3	−6.25	3.93	3.4	483	0.04	−3.74	3.96	3.3	513	−0.58	−4.02	2.99	3.3	996
Ovary						3.21*	0.15	6.36	3	474	3.21*	0.15	6.36	1.6	474
Brain and CNS	−1.88	−6.43	2.9	3.1	492	−3.6	−9.29	2.44	2.5	416	−2.64	−7.16	2.08	2.8	908
All sites	−1.48*	−2.29	−0.66	97.1	13925	−0.64	−1.67	0.41	73.5	11746	−1.12*	−1.89	−0.35	84.2	25671

Rates are per 100,000 and age-adjusted to the World (WHO 2000–2025) Std Million (19 age groups) standard; confidence intervals are 95% for trends (Tiwari mod). No:Count. APC = annual percent change, ASR = age standardized rate.

*The APC is significantly different from zero at alpha = 0.05.

TABLE 2. Incidence Trends and Age Adjusted Rates, Panama 2000 to 2009

	Male				Female				Total						
	APC	95% CI	ASR	No.	APC	95% CI	ASR	No.	APC	95% CI	ASR	No.			
Stomach	-1.59	-3.92	0.79	14.1	1717	1.11	-2.02	4.34	8.1	1108	-0.6	-2.19	1.01	11.0	2825
Prostate	2.68*	0.07	5.36	58.1	6867				0.0	0	2.68*	0.07	5.36	27.6	6867
Lung and Bronchus	-0.43	-3.26	2.49	12.0	1430	0.67	-4.11	5.69	5.3	706	-0.12	-2.97	2.82	8.5	2136
Colon and Rectum	0.7	-0.76	2.19	11.8	1438	0.72	-1.22	2.7	10.4	1399	0.65	-0.26	1.56	11.0	2837
Breast			0.2	28	262*	1.47	3.78	28.5	3887	2.62*	1.47	3.78	14.7	3915	
Cervix Uteri			0.0	0	-0.85	-3.73	2.12	20.7	2971	-0.85	-3.73	2.12	10.5	2972	
Gallbladder	-1.99	-12.63	9.95	0.5	61	-3.26	-9.34	3.24	1.1	140	-2.55	-7.24	2.37	0.8	201
Esophagus	0.31	-3.23	3.97	2.2	265	4.39	-5.64	15.49	0.7	94	1.31	-1.69	4.41	1.4	359
Oral cavity and pharynx	-4.01*	-6.19	-1.77	4.3	530	1.22	-2.12	4.68	2.1	286	-2.27*	-4.37	-0.11	3.1	816
Liver	2.91	-1.38	7.38	3.7	452	6.32*	2.52	10.26	2.8	377	4.43*	1.29	7.67	3.2	829
Pancreas	0.33	-5.59	6.63	2.7	332	-1.09	-6.67	4.82	2.8	378	-0.31	-4.77	4.37	2.8	710
Ovary			0.0	0	0.56	-2.26	3.46	4.8	670	0.56	-2.26	3.46	2.4	670	
Brain and CNS	2.96	-2.15	8.35	3.6	503	1.09	-5.16	7.74	3.2	467	1.98	-3.1	7.32	3.4	970
All sites	1.09	-0.22	2.42	154.4	18993	0.85*	0.07	1.63	132.5	18352	0.97	-0.01	1.96	142.0	37345

Rates are per 100,000 and age-adjusted to the World (WHO 2000–2025) Std Million (19 age groups) standard; Confidence intervals are 95% for trends (Tiwari mod). APC = annual percent change, ASR = age standardized rate, No: count.

*The APC is significantly different from zero at alpha = 0.05.

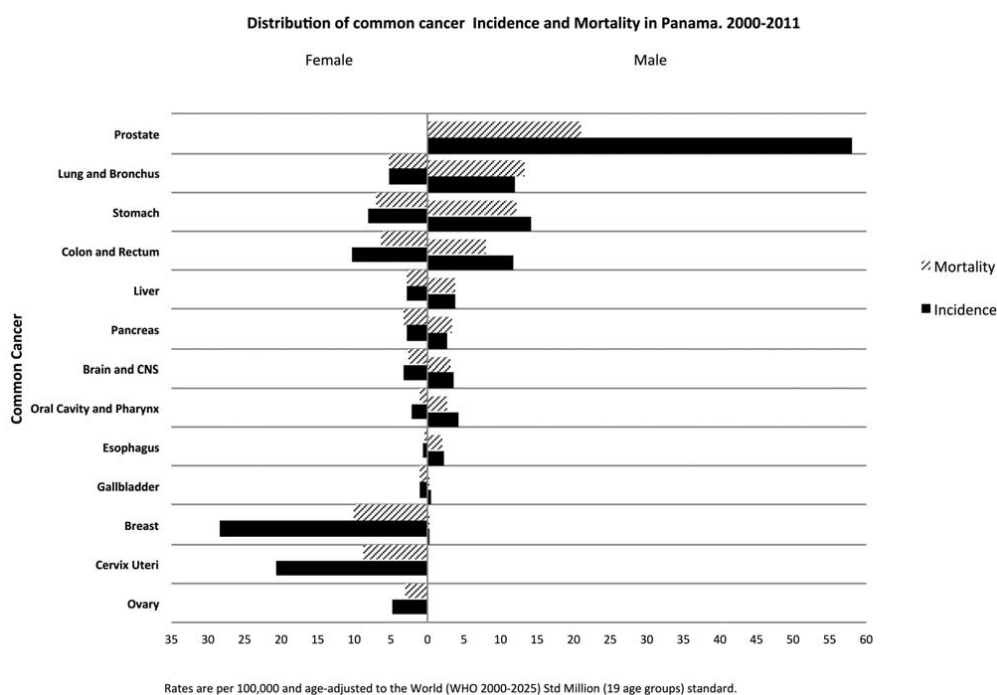


FIGURE 1. Distribution of common cancer incidence and mortality in Panama 2000 to 2011.

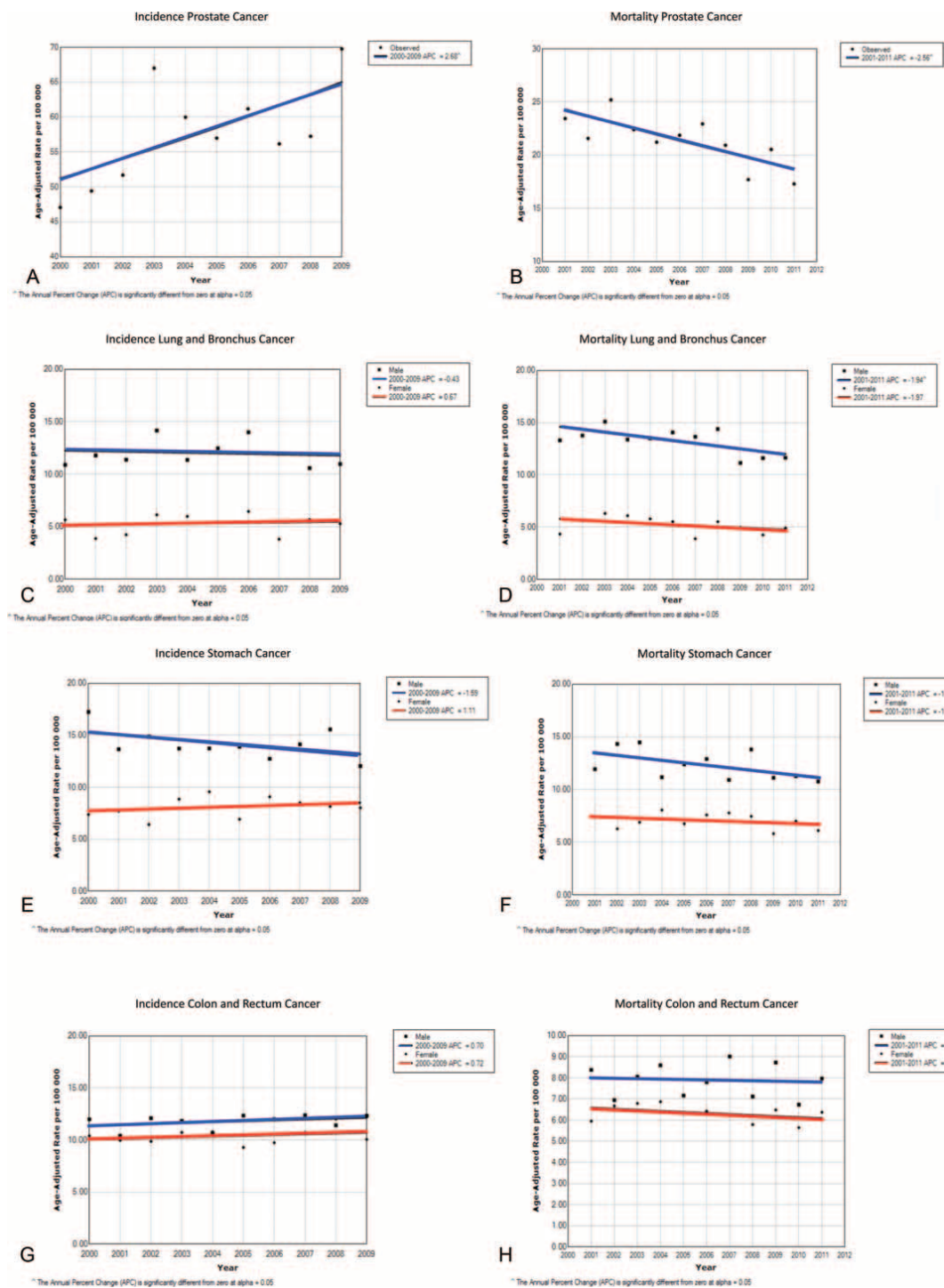


FIGURE 2. Trends in cancer incidence and mortality in Panama.

for lung and bronchus cancer (−1.94% per year). For women, the age-adjusted mortality trend for cervical cancer has decreased significantly (−4.23% per year) (Figure 2, Table 1).

Incidence

There has been a significant decrease in the trend of the age-adjusted incidence of oral and pharynx cancer in men and women (−2.27% per year).

DISCUSSION

Much has changed since Clark in 1915¹⁸ and Tomlinson and Wilson in 1945¹⁹ published the first epidemiologic studies of cancer in Panama focused on people of African descent. Although the National Institute of Census and Statistics and the National Cancer Registry have followed and registered cancer mortality and morbidity for more than 2 decades, there has not been a published study of cancer trends in Panama.

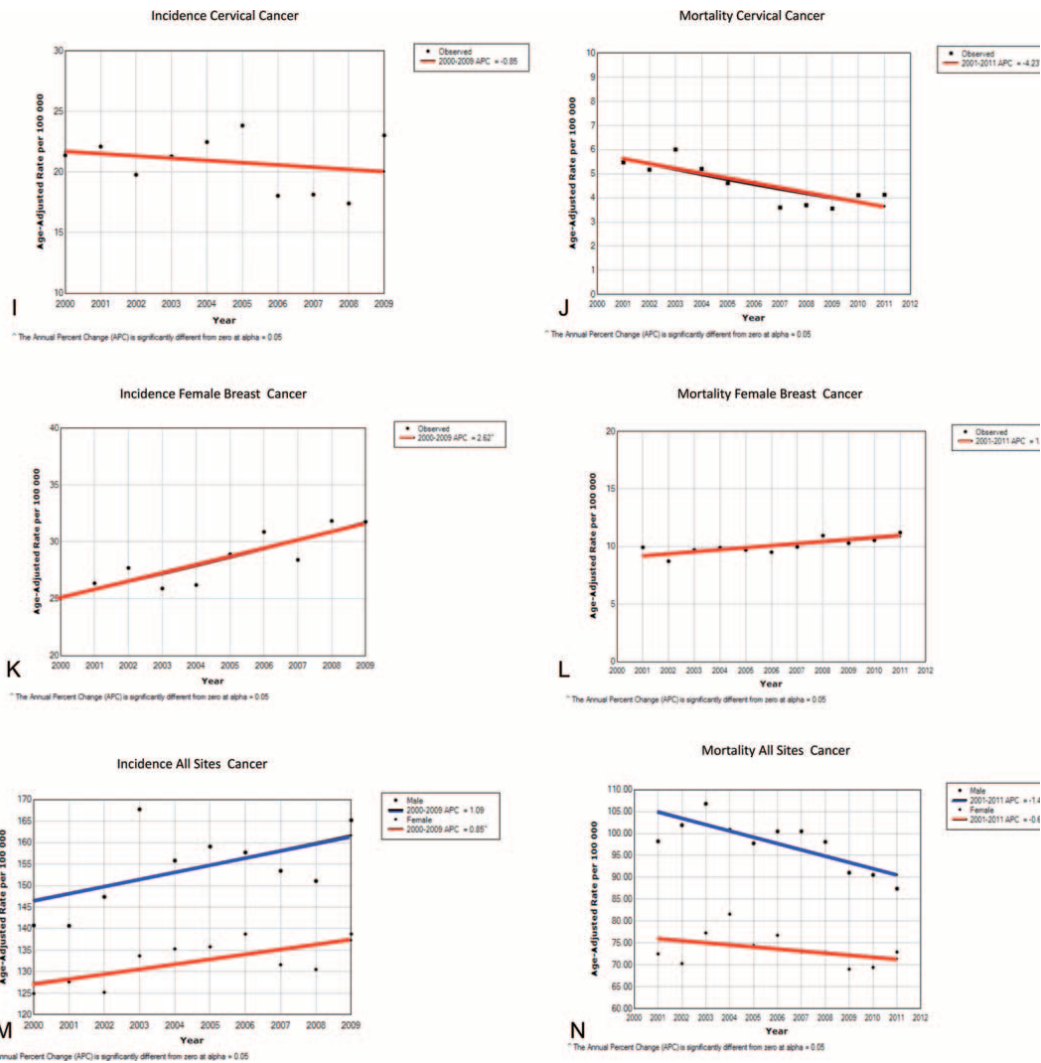


FIGURE 2. Continued.

This is the first epidemiological study of cancer trends in Panama utilizing Joinpoint regression analysis. This study is also the most recent analysis of the incidence and mortality of cancer in the country.

Although the overall mortality rates have remained low when compared to global cancer rates,²⁰ they are similar to the ones reported by other countries in the Americas.¹¹ The incidence rates are also lower than the overall world rates,²¹ but also similar to the ones seen in economically developing countries.²²

In Panama, as in most of the countries of the world, the overall cancer age-adjusted mortality trend has been decreasing during the last decade.^{11,21,22} This decline has been driven mostly by reduction in the mortality of tobacco-related malignancies, such as lung and bronchus, oral cavity and pharynx, and stomach cancers. It has also been driven by reductions in mortality from cervical and prostate cancers. An exception to these trends has been the increase of the mortality from breast cancer, which follows the trend seen in lesser-developed nations undergoing an economic transition.²²

In general, cancer incidence trends in Panama have remained unchanged when compared to the increasing trends noted and projected for less developed countries.²³ Exceptions are the increased incidence trends seen for prostate and breast

cancers, which probably have resulted in part from the population screening campaigns that began more than a decade ago.

Selected Cancers

Prostate

Prostate cancer is the 2nd most frequently diagnosed cancer and the 6th cause of death in men worldwide.^{20,21} In Panama, the incidence rates are comparable to the ones seen in developing nations.²¹ The mortality rates are similar to the ones seen in Caribbean nations with populations predominantly of African descent,^{21,23,24} which in part could be explained by the genetic susceptibility of this group.^{8,25,26} In the past 10 years the mortality trend of prostate cancer in Panama has shown a decrease similar to the one seen in developed countries.^{21,27} This finding sets Panama apart from the stable or increasing mortality trends (Figure 2) seen in other countries of Latin America.²⁸⁻³⁰ This paradoxical decrease seen in mortality due to prostate cancer in the face of an increase in its incidence may be due to improvements in diagnosis, earlier detection through screening and better management options.

Breast

Countries facing the burden of breast cancer have implemented national strategies to raise awareness about this cancer.³¹ Because of the high incidence and mortality rates of breast cancer (Figure 1), Panama has instituted national strategies of breast cancer awareness and cancer screening campaigns that include both the public and private health sectors. In spite of these initiatives, female breast cancer has continued to show an increasing trend in mortality (Figure 2), comparable to other countries of Latin America, which also are trying to prevent mortality from this disease through awareness and screening campaigns.³²

In contrast, developed countries show decreasing trends in mortality from breast cancer.^{33,34} A recent study by Webb et al³⁵ reports that approximately 3-quarters of the mortality due to breast cancer occurred in women who had not undergone screening with mammography. Nevertheless, other reports indicate that screening campaigns have no impact on mortality,³³ and that additional factors should be considered. Other factors that could explain the observed increases in mortality trends include late breast cancer diagnosis, which reduces treatment survival rates and inadequate treatment in rural areas.³⁶

Several studies suggest that there is a difference in incidence between Hispanics in their country of origin from those who have migrated to developed countries.² A great deal of this phenomenon has been attributed to lifestyle changes.^{37,38} The nutritional changes that are occurring in developing countries,^{39,40} predispose the development of obesity that may be having an impact on breast cancer incidence rates. The Panamanian population has experienced a marked increase in obesity and this is particularly evident among females.⁴¹ Other factors, such as reproductive behavior and lifestyle modifications, could also be contributing factors to the increase in breast cancer incidence in Panama.³⁸

Lung and Bronchus

Lung and bronchus cancer has been shown to be strongly linked to tobacco consumption.⁴² In the past decade, Panama has experienced a significant decrease in tobacco-related cancer mortality rates, including those for oral cavity and pharynx, and lung and bronchus, especially in men. This trend probably is driven by the marked decrease of tobacco consumption evidenced in the past 2 decades. By the year 2007, the overall prevalence of tobacco consumption was 9.4% and 17.7% for men and 3.9% for women,⁴³ but by the year 2010 it had decreased to 6.4%, 14.1%, and 3.1%, respectively.⁴⁴ The difference in the mortality trends in men, when compared to the stable trend seen in women, could be related to the earlier peaking and subsequent decrease in the prevalence of tobacco consumption seen in males as compared to females (Figure 2).^{45,46}

In Panama, the mortality rate for lung and bronchus cancer is similar to the one seen in the world's less-developed regions and also those of Central America.^{8,20,21,30} However, the trend of the age-adjusted mortality for lung and bronchus cancer in Panama has followed a pattern similar to the one seen in developed countries such as Canada, the USA, and major countries in Europe,^{47–49} setting Panama apart from other countries in Latin America where mortality trends for cancer of the lung and bronchus are increasing.⁵⁰ The vigorous antitobacco campaigns and legislation of the last decades⁵¹ have probably contributed to a reduction in the mortality of this form of cancer and other tobacco-related cancers in Panama.

Colon and Rectum

Panama's incidence and mortality rates are similar to the ones reported by other countries in Latin America.^{8,52,53} However, in contrast to countries in this region where incidence rates of colon and rectal cancer are higher in males than in females, in Panama there is no difference in mortality rates between males and females.²¹

Colorectal cancer incidence rates have continued to increase in countries undergoing economic transition.⁵² In contrast to the upward mortality trend seen in Latin America,^{30,54} Panama has maintained a stable trend as the ones seen in many developed countries.^{53,54} However, this trend could change in the future as a result of dietary changes and the increasing rates of obesity now affecting the Panamanian population.^{41,55–59} Nevertheless, if effective screening programs were to be implemented, as the ones that now exist for breast and cervical cancer, this could result in a decrease in mortality like observed in developed countries.^{21,47,54}

Cervical

As in breast cancer, national programs have been implemented for the awareness and early detection of cervical cancer. These interventions could be the cause of the marked decrease in the mortality trend (Figure 2) observed during the study period.⁶⁰ The Latin American countries that have had a comparable decrease in cervical cancer mortality are Chile and Uruguay,⁶¹ while the rest of the countries in the region have seen increases in mortality trends.⁸

Incidence rates, however, have remained among the highest of female cancers in Panama. The high levels of prevalence of the human papilloma virus and associated risk factors probably are contributing to these high incidence rates and support the need for intervention at an early age.⁶² The recent implementation in Panama of the HPV vaccine as a nationwide strategy could decrease further cervical cancer incidence in future years.⁶³ Other potential factors associated with the development of cervical cancer were not assessed in this study.

Stomach

Stomach cancer is among the top 5 cancers in Panama in incidence for both males and females. This study did not find significant changes in the incidence and mortality trends in the last decade. Although there are reports that among Hispanics in North America there is a higher risk for developing stomach cancer, the overall incidence trend has been decreasing. In Latin America, the incidence rates vary.² Infection with *helicobacter pylori*, which is a risk factor, has been shown to be common among Latinos and more so among those with a low socioeconomic status and this is also probably true in Panama.^{64,65} Additional factors to be considered are high consumption of alcohol, especially if contaminated by carcinogens found in illegally distilled alcohol, and also the deleterious effect of tobacco use.

Limitations

The limitations of this study include the deficient registration of death certificates and an underestimation of cancer mortality in the indigenous regions where approximately 7% of the total population of the country reside. There is also an underestimation of the cancer incidence data in the indigenous regions that could be as high as 20%. Another limitation was the relatively short study period for the trend analysis, but this

period spanned the most robust data available at the time of the study. A longer study period may reveal other statistically significant trends in cancer incidence and mortality. Finally, the higher mortality than incidence rates for lung cancer seen in males could have been due to misdiagnosis, frequently attributing the symptoms and signs to an infectious disease like tuberculosis because of deficient diagnostic facilities, thus delaying the true diagnosis of cancer to time of death.

CONCLUSION

This study is the first analysis of cancer trends at a national level in Panama using Joinpoint regression analysis. In addition to providing a valuable data baseline on current cancer incidence and mortality, the study reveals contrasting trends in cancer rates over the past 10 years. Although Panama is considered a developing nation, our data demonstrate that some cancer mortality trends, like the ones seen for cervical and lung cancer, are similar to the ones seen in developed countries. These trends could be the result of effective public health measures. In contrast, other trends, such as ones seen in breast cancer, follow patterns similar to countries undergoing a transition to a developed economy with its associated lifestyle, nutrition, and body weight changes.

Longer periods of observation will make these trends more robust and will help to evaluate and develop, in a dynamic way, better public health interventions which are essential in the fight to reduce the incidence and mortality of this disease.

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