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ORIGINAL ARTICLE

Cancer incidence and mortality in Uruguay: 2013-2017

Incidencia y mortalidad de cáncer en Uruguay: 2013-2017

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Abstract

Background:

Uruguay has the highest cancer incidence and mortality rates in Latin America. The National Cancer Registry of Uruguay, which has been in operation since 1992, provides epidemiological information on incidence and mortality at the country level.

Objective:

The objective of this article is to update the incidence and mortality figures by reporting the information for the period 2013-2017.

Methods:

All incident cases of invasive neoplasias except non melanoma of the skin and all cancer deaths occurred in from 2013 to 2017 were analyzed. Age standardized rates were calculated by the direct method, using the world standard population. Complementary, incidence (2002-2017) and mortality (1990-2017) trends were studied for the leading sites.

Results:

Among females, the most common cancers are breast, colon and rectum, lung, cervix and thyroid. The most frequent cancers in males are prostate, lung, colon and rectum, bladder and kidney. Lung, prostate and colorectal cancer are the leading causes of cancer death in males while breast cancer is the first cause of cancer death among females.

Conclusions:

Although cancer mortality has declined monotonously since 1990, cancer control is a challenge for Uruguay, wherein breast, lung and prostate cancer have very high incidence while the country must still make an effort to reduce other cancers that are very common in economically less favored countries.

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The authors have none to declare.

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Resumen

Antecedentes:

Uruguay tiene las mayores tasas de incidencia y mortalidad por cáncer en América Latina. El Registro Nacional de Cáncer de Uruguay, que ha estado en funcionamiento desde 1992 provee información epidemiológica sobre incidencia y mortalidad de todo el país.

Objetivo:

El objetivo de este artículo es actualizar las cifras de incidencia y mortalidad reportando la información para el período 2013-2017.

Métodos:

Se analizaron todos los casos incidentes de neoplasias invasivas excluyendo el cáncer de piel no melanoma y todas las muertes por cáncer del período 2013-2017. Se calcularon las tasas estandarizadas por edad según el método directo, utilizando como estándar la población mundial. En forma complementaria, se estudiaron las tendencias de incidencia (2002-2017) y de mortalidad (1990-2017) para los sitios más frecuentes.

Resultados:

Entre las mujeres, los cánceres más frecuentes son mama, colorrecto, pulmón, cérvix y tiroides. Los cánceres más frecuentes en hombres son próstata, pulmón colorrecto, vejiga y riñón. Los cánceres de pulmón, próstata y colorrecto ocupan los primeros lugares en las muertes por cáncer en hombres, mientras que en mujeres el cáncer de mama ocupa el primer lugar.

Conclusiones:

Si bien la mortalidad por cáncer ha disminuído de manera monótona desde 1990, el control del cáncer es un desafío para Uruguay dónde los cánceres de mama, pulmón y próstata tienen una incidencia muy alta, a la vez que aún se debe hacer un esfuerzo para reducir otros cánceres que son muy comunes en los países económicamente menos favorecidos.

Remark

1) Why was this study conducted?

This study was carried out to update the information about the incidence and mortality from cancer in Uruguay with data from the period 2013 -2017.

2) What were the most relevant results of the study?

Among females, the most common cancers are breast, colon and rectum, lung, cervix and thyroid. The most frequent cancers in males are prostate, lung, colon and rectum, bladder and kidney. Lung, prostate and colorectal cancer are the leading causes of cancer death in males while breast cancer is the first cause of cancer death among females.

3) What do these results contribute?

These results show the increasing burden of cancer in a Latin American country. Since the data come from a population-based cancer registry with national coverage, they contribute to depict the situation in other countries in similar situation.

Introduction

Cancer burden is becoming one of the most relevant problems in less developed countries health spectrum, mainly because cancer dynamics is changing in scale and epidemiological profile [1]. This is a major challenge for most Latin American countries that are assigned low or medium Human Development Index (HDI) since their health systems have less resources to confront a complex and growing threat. The region shows a wide diversity not only in terms of socio-economic status but also regarding cancer epidemiological profiles. This heterogeneity is important between countries and even within countries [2,3].

The relevance that non-communicable diseases have in Uruguayan health profile could be explained mainly because Uruguay has been one of the countries that has experienced earlier in the region the demographic-epidemiological transition, as well as the adoption of western lifestyle [4]. For the reasons stated above, Uruguayan cancer figures may show earlier the transitions that are expected to occur later in other countries of the region.

Uruguay has the highest cancer incidence and mortality rates in Latin America: 269.3 and 127.5 cases per 10^5 person-years respectively for all sites combined and both sexes [2,3]. Cancer has been the second cause of death for decades[5] and it is the main cause of premature death [2].

The aim of this study is to describe most recent data on cancer incidence and mortality in a Latin American country, and to contribute for a better understanding of cancer landscape in the region.

Materials and Methods

Population at risk

Uruguay is a South American country with a surface of 176,000 square kilometers, bordering Argentina and Brazil.

The country has a etnically homogeneous (91% self-declared Western European descent) population of 3,286,314 according to the 2011 national census and the projected population for 2017 is 3,493,205 inhabitants [6]. The demographic pyramid corresponds to a stationary phase of the demographic transition and the population is stable in terms of migratory behavior (Figure 1). Life expectancy at birth was for both sexes 77.1 years in 2013 and reached 77.6 years by 2017 [7]. Overall, 95% of the population lives in urban areas and a half lives in its capital, Montevideo and its metropolitan area.

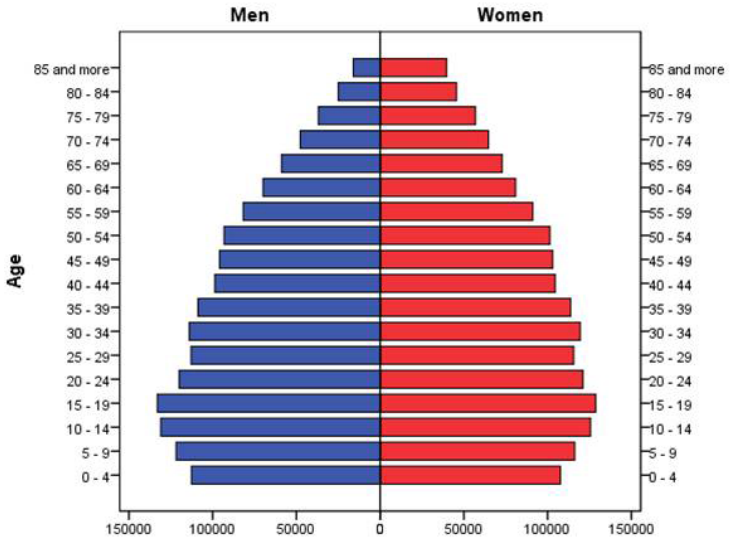

Figure 1. Population structure by age and sex. Uruguay. 2011. Source: Instituto Nacional de Estadística

Currently, Uruguay is classified as a high-income country with a very high HDI [8]. Health care is carried out by private facilities and free public services. The National Integrated Health System provides comprehensive, equitable universal health coverage under a single benefits plan.

The National Cancer Registry of Uruguay

The NCRU records cancer incidence at the national level since 1991 through active case finding. Furthermore, the NCRU accesses all the death certificates of the whole country and records cancer deaths, linked to their corresponding incidence, when it is already registered. Not registered cases notified through a death certificate are traced back to medical records. New cases are checked for duplication, coded according to International Classification of Diseases for Oncology 3ed (ICD-O-3) [9] (ICD-O-1 was used until 2005). IARC rules for multiple primaries are followed. Quality control procedures are performed both manually and automatically through IARC/IACR Check and conversion programs [10] and NCRU software.

Statistical methods

All incident cases of invasive neoplasias collected by the NCRU for years 2013 to 2017and all cancer deaths in the same period were analyzed. Age standardized incidence rates (ASIR) and age standardized mortality rates (ASMR) were calculated. Person-years at risk were estimated using the country's population by linear interpolation and extrapolation of census data from 1996, 2004 and 2011 [6,11,12]. Age standardized rates were calculated by the direct method, using the world standard population [13]. Rates are expressed per 100,000 person-years.

Complementary, incidence (2002-2017) and mortality (1990-2017) trends were studied for the leading sites. The Annual Percent Change (APC) was obtained, representing the average percent increase or decrease in cancer rates per year over each specified period of time. Joinpoint regression models were used to identify change points in mortality trends using publicly accessible software Joinpoint version 4.7 from the Surveillance Research Program of the US National Cancer Institute [14,15]. The maximum number of joinpoints used was the one recommended by the software according to the number of data points analyzed [16]. The terms "increase" or "decrease" were used only when the APC was significantly different from zero (two-sided p <0.05); otherwise, the term "stable" was used.

Results

Global quality indicators

Quality indicators for high incidence locations are shown in Table 1.

The percentage of cases with morphological verification for all locations remained stable during the 2013-2017 period, being 82% in females and 72% in males. The proportion of cancers for which no information other than death certificate was obtained (DCO) was, for the whole period, 10.9% for females (decreasing over time to 8.2% in 2017) and 13.0% for males (decreasing to 10.6% in 2017). Age was missing in 37 incidence records (all of them DCO). Sex information is present in all registered cases. Figure 2 shows specific incidence and mortality rates by age.

Table 1. Quality indicators for high incidence locations by sex. 2013-2017

	Females		Males	
Site	**DCO%**	**MV%**	**DCO%**	**MV%**
Stomach	15	73.1	13.2	78.3
Colon and rectum	9.4	82.8	7	86.8
Lung	16.4	62.7	18.4	58.5
Breast	3.7	92.3	-	-
Cervix	2.5	94.3	-	-
Prostate	-	-	10.4	79.3
Kidney	7.73	78.2	9.5	78.8
All sites except NMSC	10.9	78.5	13	73.9

NMSC: Non melanoma skin Cancer MV% Percentage of morphological verification DCO% Percentage of cases obtained from death certificate only.

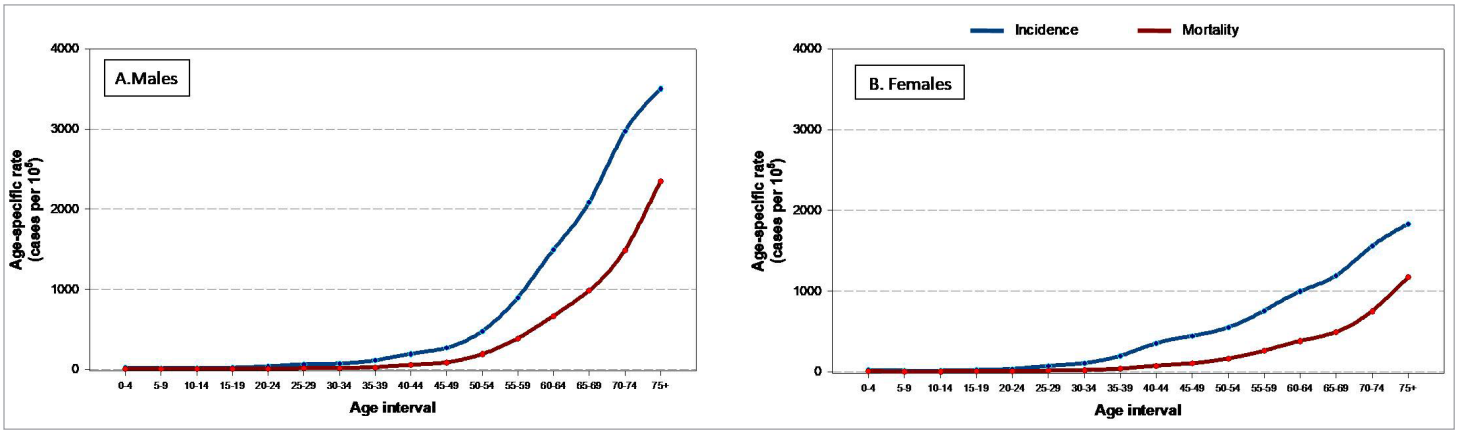

Figure 2. Age specific incidence and mortality rates. Uruguay. A. Males B. Females 2013-2017

Table 2. Cancer incidence by location and sex. Uruguay. 2013-2017

Location	ICD-10 codes	Females			Males		
		n	CR	ASIR	n	CR	ASIR
Oral cavity and pharynx	C00-C14	397	4.60	2.50	1,127	14.23	10.20
Esophagus	C15	405	4.69	2.12	783	9.89	6.26
Stomach	C16	1,008	11.67	5.72	1,591	20.09	13.10
Small bowel	C17	127	1.47	0.88	132	1.72	1.23
Colon and rectum	C18-C20	4,462	51.66	26.22	4,677	59.05	37.73
Annus	C21	221	2.56	1.38	132	1.67	1.21
Liver	C22	190	2.20	1.11	473	5.97	4.08
Gallbladder and bile ducts	C23-C24	674	7.80	3.70	445	5.62	3.33
Pancreas	C25	1,606	18.60	8.35	1,408	17.78	11.28
Nose,ear and paranasal sinus	C30-31	27	0.31	0.19	63	0.80	0.54
Larynx	C32	105	1.22	0.69	624	7.88	5.50
Lung and trachea	C33-C34	2,003	23.19	13.58	5,461	68.94	45.91
Other thoracic organs	C38-C39	31	0.36	0.17	48	0.61	0.45
Bones and joints	C40-C41	60	0.69	0.61	98	1.24	1.12
Melanoma*	C43	658	7.62	4.83	701	8.85	6.06
Mesothelioma	C45	23	0.27	0.14	37	0.47	0.30
Kaposi Sarcoma	C46	19	0.22	0.16	51	0.64	0.54
Sarcomas	C47-C49	270	3.13	2.08	269	3.40	2.55
Breast	C50	9,666	111.92	73.63	81	1.02	0.67
Vulva	C51	219	2.54	1.21	-	-	-
Vagina	C52	85	0.98	0.52	-	-	-
Cervix uteri	C53	1,555	18.00	14.26	-	-	-
Corpus uteri	C54	1,178	13.64	8.31	-	-	-
Uterus NOS	C55	218	2.52	1.25	-	-	-
Ovary	C56	1,121	12.98	8.46	-	-	-
Other female genital organs including placenta	C57-C58	95	1.10	0.52	-	-	-
Penis and other male genital organs	C60, C63	-	-	-	173	2.18	1.44
Prostate	C61	-	-	-	7,331	92.55	59.36
Testis	C62				666	8.41	1.44
Kidney and renal pelvis	C64-C65	1,087	12.59	7.86	2,033	25.67	18.09
Bladder, ureter and urethra	C66-C68	692	8.01	3.77	2,210	27.90	17.40
Eyes	C69	12	0.14	0.15	30	0.38	0.30
Central nervous system	C70-C72	549	6.36	4.22	625	7.89	6.24
Thyroid	C73	1,413	16.36	13.85	303	3.83	3.25
Hodgkin lymphoma	C81	200	2.32	2.16	236	2.98	2.71
Non-Hodgkin lymphoma	C82-85,C96	1,154	13.36	7.90	1,269	16.02	11.53
Myeloma	C90	379	4.39	2.21	419	5.29	3.47
Leukemia	C91-C95	652	7.55	5.24	775	9.78	7.37
Other hematologic diseases	C96	367	4.25	2.18	362	4.57	2.88
Ill defined and unknown	C76,C80	1,111	12.86	5.14	1,123	14.18	8.26
All sites except non melanoma of skin	C00-C96	34,222	396.25	238.49	35,914	453.40	303.71

* Includes 604 cutaneous cases and 54 extracutaneous in females and 657 cutaneous and 44 extracutaneous in males, CR Crude rate per 100.000 persons per year, ASIR Age Standardized Incidence Rate (Segi world population) per 100.000 person-year

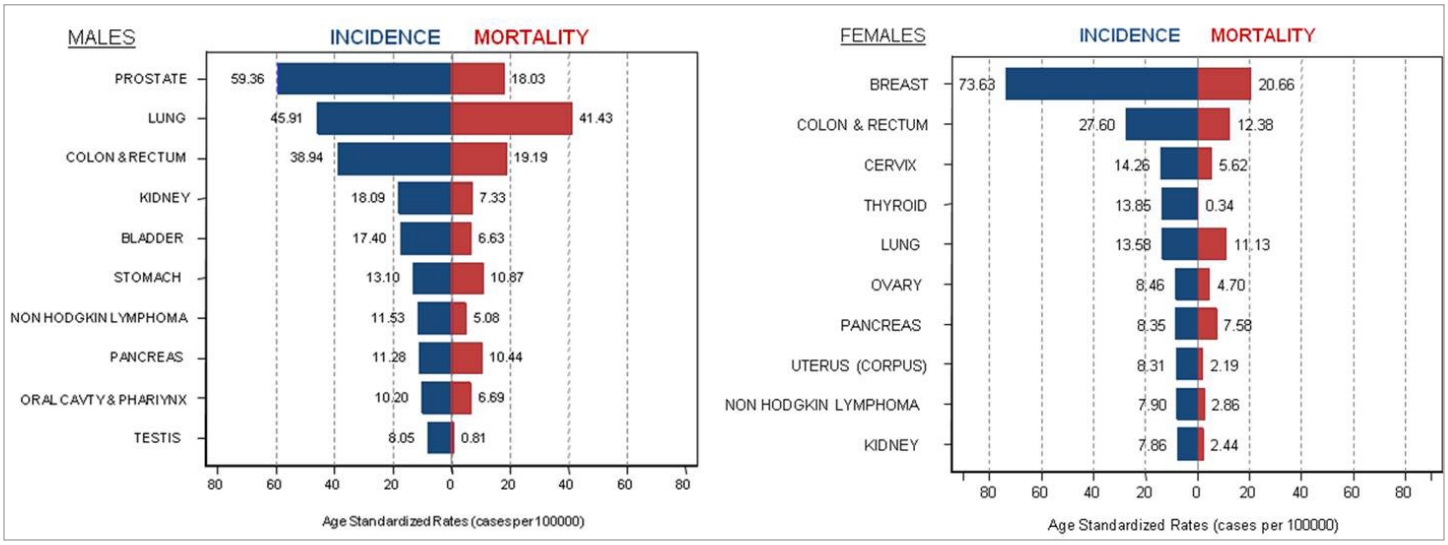

Figure 3. Incidence and mortality age standardized rates for the leading sites by sex. Uruguay. 2013-2017

Table 3. Trends in cancer incidence (2002-2017) and mortality (1990-2017). Annual percent change obtained from Joinpoint regression models. Uruguay 2002-2017. Selected sites.

	Incidence					
	Females			Males		
	Period	APC	95% CI	Period	APC	95% CI
Esophagus	2002-2017	-3.12*	-4.47;-1.74	2002-2017	-4.16*	-5.48;-2.83
Stomach	2002-2017	-1.48*	-2.38;-0.57	2002-2017	-1.48*	-2.36;-0.59
Colon and rectum	2002-2017	0.03	-0.55;0.62	2002-2017	0,57	-0.21;1.37
Pancreas	2002-2006	-4.95	-12.02;2.69	2002-2017	0.85*	0.03;1.67
	2006-2017	2.60*	1.02;4.2			
Lung	2002-2017	3,15*	2.39;3.91	2002-2017	-1,36*	-1.87;-0.84
Thyroid	2002-2014	9.23*	6.64;11.88	2002-2017	6.16*	3.98;8.39
	2014-2017	-5.69	-19.68;10.73			
Melanoma	2002-2017	2.40*	0.81;4.02	2002-2004	18.90*	2.01;38.57
				2004-2017	1.38*	0.72;2.04
Breast	2002-2017	-0.28	-0.70;0.15		N/C	
Cervix	2002-2017	-2.31*	-2.91;-1.70		N/A	
Prostate		N/A		2002-2004	13,41	-6.1;36.98
		N/A		2004-2017	-0,64	-1.53;0.27
Testis		N/A		2002-2017	3.24*	2.32;4.18
Kidney	1990-2017	0.83*	0.08;1.58	2002-2017	2.61*	1.84;3.37
Bladder	1990-2017	-0.15	-0.86;0.57	2002-2017	-0.16	-1.03;0.73
All sites except NMSC	1990-2017	-0.50*	-0.60;-0.40	2002-2017	-0.29	-0.72;0.14
	Mortality					
	Females			Males		
	Period	APC	95% CI	Period	APC	95% CI
Esophagus	1990-2017	-2.05*	-2.58;-1.52	1990-2017	-2.67*	-3.10;-2.23
Stomach	1990-2017	-1.69*	-2.10;-1.27	1990-2017	-1.58*	-1.98;-1.19
Colon and rectum	1990-2017	-0,52*	-0.77;-0.27	1990-2017	0,33*	0.07;0.58
Pancreas	1990-2017	1.44*	1.07;1.81	1990-2017	1.09*	0.74;1.44
Lung	1990-2017	3,49*	3.07;3.92	1990-2017	-1,21*	-1.38;-1.04
Thyroid	1990-2017	-1.91*	-3.51;-0.28	1990-2017	0.15	-1.11;1.43
Melanoma	1990-2017	1.94*	1.01;2.87	1990-2017	1.63*	0.57;2.70
Breast	1990-2017	-1.04*	-1.28;-0.80		N/C	
Cervix	1990-1998	3,35	-0.41;7.25		N/A	
	1998-2017	-1,23*	-2.16;-0.30			
Prostate	1990-2004	0,95*	0.29;1.61	1990-2004	0.95*	0.29;1.61
	2004-2017	-2,14*	-2.83;-1.44	2004-2017	-2.14*	-2.83;-1.44
Testis	1990-2017	-0.71	-1.88;0.47	1990-2017	-0.71	-1.88;0.47
Kidney	1990-2017	1.33*	0.82;1.84	1990-2017	1.33*	0.82;1.84
Bladder	1990-2017	-0.63*	-0.98;-0.27	1990-2017	-0.63*	-0.98;-0.27
All sites	1990-2017	-0,71*	-0.79;-0.64	1990-2017	-0,71*	

APC Annual percent change, CI95% : confidence interval, NMSC Non melanoma of the skin
*Significantly different from 0, N/A Not applicable, N/C Not computed

Table 4. Cancer mortality by location and sex. Uruguay. 2013-2017

Location	ICD-10 codes	Females			Males		
		n	CR	ASMR	n	CR	ASMR
Oral cavity and pharynx	C00-C14	236	2.73	1.25	764	9.65	6.69
Esophagus	C15	361	4.18	1.72	726	9.17	5.67
Stomach	C16	816	9.45	4.38	1373	17.33	10.87
Small bowel	C17	66	0.76	0.39	88	1.11	0.73
Colon and rectum	C18-C20	2467	28.56	11.79	2557	33.14	19.19
Annus	C21	107	1.24	0.59	68	0.86	0.58
Liver	C22	170	1.97	0.94	407	5.14	3.38
Gallbladder and bile ducts	C23-C24	617	7.14	3.27	406	5.13	2.96
Pancreas	C25	1514	17.53	7.58	1316	16.61	10.44
Nose,ear and paranasal sinus	C30-31	21	0.24	0.11	43	0.54	0.34
Larynx	C32	42	0.49	0.24	419	5.29	3.40
Lung and trachea	C33-C34	1712	19.82	11.13	5001	63.14	41.43
Bones and joints	C40-C41	30	0.35	0.25	53	0.67	0.61
Melanoma	C43	191	2.21	1.12	242	3.06	1.89
Mesothelioma	C45	20	0.23	0.12	39	0.49	0.29
Kaposi Sarcoma	C46	4	0.05	0.02	5	0.06	0.03
Sarcomas	C47-C49, C38.0	149	1.73	0.96	157	1.98	1.39
Breast	C50	3393	39.29	20.66	34	0.43	0.27
Vulva	C51	95	1.10	0.42	-	-	-
Vagina	C52	54	0.63	0.29	-	-	-
Cervix uteri	C53	704	8.15	6.62	-	-	-
Corpus uteri	C54	402	4.65	2.19	-	-	-
Uterus NOS	C55	161	1,86	0,76	-	-	-
Ovary	C56	742	8.59	4.70	-	-	-
Other female genital organs including placenta)	C57-C58	78	0.88	0.35	-	-	-
Penis and other male genital organs	C60, C63	-	-	-	65	0.82	0.45
Prostate	C61	-	-	-	2868	36.21	18.03
Testis	C62	-	-	-	72	0.91	0.81
Kidney and renal pelvis	C64-C65	442	5.12	2.44	925	11.68	7.33
Bladder, ureter and urethra	C66-C68	307	3.55	1.27	964	12.17	6.63
Eyes	C69	6	0.07	0.07	10	0.13	0.08
Central nervous system	C70-C72	470	5.44	3.24	548	6.92	5.16
Thyroid	C73	69	0.80	0.34	43	0.54	0.32
Hodgkin lymphoma	C81	47	0.54	0.39	53	0.67	0.54
Non-Hodgkin lymphoma	C82-85,C96	542	6.28	2.86	640	8.08	5.08
Myeloma	C90	303	3.51	1.46	319	4.03	2.43
Leucemia	C91-C95	481	5.57	2.79	535	6.75	4.24
Other hematologic diseases	C96	211	2.44	0.84	209	2.64	1.49
Ill defined and unknown	C76,C80	1024	11.86	4.57	1026	12.95	7.39
All sites except non melanoma of skin	C00-C96	18235	211.14	102.08	22147	279.60	170.99

CR Crude rate per 100,000 persons per year, ASMR Age standardized Mortality Rate (Segi world population) per 100,000 person-year

Incidence

The NCRU registered 84,765 cases of cancer diagnosed in the period 2013-2017, from which 14,629 were non melanoma of the skin (NMSC). Of the remaining 70,136 cases, 48.8% were females. Mean age was 65 years for females and 67 for males. Only471 (0.7%) of the cases occurred in population younger than 15 years old. The ASIR per 100,000 person year for all sites (excluding NMSC) was 238.5 for females and 303.7 for males. (The number of cases and specific rates for age groups by sex are presented as supplementary materials.)

Among females, the most common cancers were breast (28.2%), colon and rectum (13.0%), lung (5.9%), cervix (4.5%) and thyroid (4.1%). The most frequent cancers in males were prostate (20.4%), lung (15.2), colon and rectum (13.0%), bladder (6.2%) and kidney (5.7%), accounting for 60.0 % of the cases. (Table 2, Figure 3)

Globally, incidence was stable from 2002 to 2017 for both sexes when NMSC are excluded. In males, while stomach, esophagus and lung cancer decreased, kidney, pancreas, thyroid, and testicular cancer increased, as well as melanoma. The break registered in 2004 in melanoma trends is probably an artifact due to data collection improvement. For females, decreasing trends were observed in cervix, stomach, and esophagus, while lung, kidney, pancreas (since 2006) and thyroid showed marked increases until 2014, although incidence stabilized in most recent years. (Table 3).

Mortality

During the period of study, 40,382 deaths from cancer were reported. Cancer mortality rate was higher in males than in females (ASMR 171 and 102 respectively). Tumors of breast (18.5%), colon and rectum (13.5%) and lung (9.4%) were the most frequent among females accounting for 42% of all cancer deaths while lung (22.5%), prostate (13.0%) and colorectum (11.6%) were the most frequent in males.

Globally, mortality declined monotonously since 1990 for both sexes. This was mainly driven in males by a steady decrease in lung, stomach and since 2004 also prostate cancer mortality. For females, a worrisome increase in lung cancer mortality (3.5% per year) is the most important finding. Decreasing trends were observed in breast and colon and rectum. For cervical cancer, after a stable phase in the 90´s, trends declined from 1998 on. Mortality trends for the leading sites are shown in Table 4.

Discussion

Female breast cancer

Breast cancer is, according to IARC estimates [2], the most common cancer diagnosed among females (excluded NMSC) in 160 out of 185 countries. Regarding mortality, although breast cancer holds the first place in cancer deaths for females in the majority of countries, it is surpassed by cervical cancer in almost a quarter of the nations (those with lesser degree of development) and by lung cancer in several of the most developed countries [2].

In Uruguay breast cancer is by far the most common malignancy diagnosed in females and the first cause of female cancer death. As previously reported, incidence remains stable since the early 2000s [17]. Mortality trends show a significant decrease of more than 1% per year from 1990 to 2017 (Table 3).

For the period 2013-2017; 9666 females were diagnosed with invasive breast cancer (ASIR 73.63) and 3393 died due to the disease (ASIR 20.66).

Although a formal screening program for breast cancer is not yet implemented, nationwide guidelines for early breast cancer detection [18], broad access to mammogram and some support measures such as a paid day off at work to perform the test costless for females between the age 50 and 69 are granted for every female in the country. On the other hand, access to surgery and oncological treatments (included radiation, chemotherapy and her2 blockade when required) are provided by the public and the private health systems.

Almost 70% of the cases for which stage information is available, were diagnosed on early stage (TNM I or II). [19]

Prostate cancer

In Uruguay, prostate cancer is the most frequently diagnosed cancer among males and ranks third in mortality, given the potentially long survival of those patients. Incidence rates are stable since 2004. A nonsignificant increase in incidence rates prior to that period may mainly be attributable to improvements in cases uptake. A sustained decrease in mortality from prostate cancer is observed from 2004, which could reflect better disease control and availability of more effective treatments.

Lung cancer

In Uruguay, lung cancer is the second most frequent type of cancer in males and the first cause of death from cancer in this sex. While the incidence in males has decreased along the last decades [20], it has dramatically increased among females. The aforementioned fact is probably a consequence of the delay of smoking habit acquisition in females compared to males[21].. Among females, lung cancer is currently the fifth most common cancer (after breast, colorectal, cervix

and thyroid cancer) and has been the third leading cause of cancer mortality for some years [17]. A previous analysis of lung cancer incidence trends in Uruguay has shown cohort effects in both sexes and indicate that lung cancer incidence rates in Uruguayan males are expected to continue to decline, while in females they are expected to further rise until around 2035 [21,22].

In 2004, Uruguay ratified the WHO Framework Convention on Tobacco Control (FCTC). Henceforth, an unprecedented series of stringent tobacco control measures were implemented: Latin America's first ban on smoking in enclosed public places, the world's largest pictorial warnings (80% of the front and back of cigarette packs), the first ban on differentiated branding, alongside a series of tobacco excise tax hikes [23].

Colorectal cancer

According to IARC estimates, in 2020, 1,931,590 cases of colorectal cancer were diagnosed worldwide and 935,173 people died because of this malignancy [2]. It is a disease strongly correlated to Human Development Index [24].

In Uruguay, between 2013 and 2017, 1,828 new cases were diagnosed in average per year (both sexes) and 1,005 people died.

For males it represents the third most frequent neoplasm and for females the second for both, incidence and mortality.

As previously reported [17], in the present update colo-rectal cancer incidence remained stable for both sexes. In a recent age group analysis, we found sharp increasing trends for males and females aged 40 to 49 (APC 3.1 and 2.6 respectively) [25]. Those findings are aligned with the observed increasing trend in colorectal cancer incidence among young adults in other high incidence settings [26,27].

Mortality, on the other hand presents divergent trends, slightly increasing for males (APC 0.3%) and decreasing for females (APC -0.5%).

Several known risk factors, such as obesity, high intake of red meat, low dietary fiber consumption and a sedentary lifestyle are highly prevalent among the population [28]. Although early diagnosis and screening programs have been active for several years [29], more recently National Guidelines were launched to unify criteria, improve adherence and efficacy. [30].

Cervix uteri cancer

Cervical Cancer is highly correlated with poverty and inequality. Uruguay is internationally situated in the third quintile and presents the second lowest incidence and mortality rates in South America, after Chile [2].

It is the third more frequently diagnosed cancer in Uruguayan females, only surpassed by breast and colorectum and it holds the fifth place in mortality.

Unlike most of tumors that affect elder people, more than half of the females diagnosed with cervical cancer are younger than 50.

Age-standardized incidence rates in Uruguay decline 2.31% per year. Meanwhile mortality rates declined along the 21st century 1.23% per year [31].

A Cervical Cancer Prevention Program based on PAP smear testing is active since 1994; but only in 2006 it was expanded nationwide. Several strategies (analogous to those describe earlier for breast cancer) are also implemented to enable access to screening tests were implemented[32].

Since 2009, the human papilloma virus (HPV) quadrivalent vaccine is available in the country. In 2013 it became free of charge and was administered under medical prescription to girls aged 11 to 12. In 2019 began the vaccination of boys in the same age group. Currently, two doses of the quadrivalent vaccine are administered six months apart within regular vaccination program [33,34].

Stomach cancer

Stomach cancer incidence has decreased both in men and women, similarly to what happened in the rest of the world, mainly in developed countries, since the middle of the 20th century. Initially, this decrease was attributable to changes in food preservation, while the current variations are mainly attributed to early treatment of *Helycobacter pylori* infections [35,36]. However, this cancer still ranks high in incidence and mortality among Uruguayan males and more prevention efforts are to be driven.

Kidney

An alarming increase in kidney cancer has been observed worldwide, particularly in North America, Europe, and some Asian countries [37]. This increase has been partially attributed to overdiagnosis [38]. However, an important fraction of the risk (25% according to European studies) is attributable to obesity and overweight, which have increased almost worldwide. In Uruguay, age-standardized kidney cancer incidence rates show significant and sustained growth, both in males (increase of 2.6% per year) and in females (3.0% per year),

Thyroid

Striking increases in Thyroid cancer incidence rates, especially in women, have been reported worldwide in the last decades. Those increases are mostly driven by small papillary carcinomas diagnosis. Nevertheless, mortality rates remain worldwide low and stable. The aforementioned findings raised the attention on the potential effect of overdiagnosis and has lead in most recent years to a setback in aggressive detection practices. Consequently, a slowing down and even stabilization in incidence trends in several countries was described in most recent years [39,40].

In Uruguay thyroid cancer incidence displays the sharpest increase in males from 2002 to 2017 (APC: +6.16). In females, after a long period of growing incidence rates (APC: +9.23) they seem to stabilize for the last three years (2015-2017). Such a dramatic change in trends, must be followed up. Although an artifactual effect, due to the short period analyzed, cannot be completely ruled out, the similar behavior observed in other regions might be indicating the initiation of a true shift in trends.

Limitations and strengths

The major strength of this study is that it presents good quality data at a country level. Indeed, the National Cancer Registry of Uruguay (NCRU) covers the whole population of the country (ca. 3.5 million) and has published its data in the last two volumes of CI5 (X and XI) ranking in A level regarding quality data indicators [41,42]. The registry has been operational for almost three decades and is continuously improving its processes. Nevertheless, certain indicators as the proportion of DCO cases ought to be improved for specific sites.

Conclusions

Uruguay has a mixed epidemiological profile regarding cancer: incidence rates (all sites combined both sexes) are close to average values of very high HDI countries, but some cancers like cervix in women and stomach and esophagus in men still rank high. Breast, prostate, lung, and colorectal cancer take account of approximately half of the incident cases.

There are several challenges regarding cancer control in Uruguay: in females, breast cancer mortality rates rank in the first quintile around the world according to Globocan 2020 estimates, cervical cancer still shows high rates and lung cancer incidence and mortality

increase in average more than 3% per year. In males: unless lung cancer incidence and mortality rates have declined it is still the first cause of cancer death, prostate cancer mortality is one of the higher in the region and colorectal cancer incidence and mortality rates are among the highest around the world.

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