

# Increasing crude and adjusted mortality rates for colorectal cancer in a developing South American country

A. J. Zarate\*, F. T. Alonso†‡, M. L. Garmendia†§ and F. López-Köstner\*

\*Colorectal Unit, Clínica las Condes, †School of Public Health, Faculty of Medicine, ‡U-Cancer and §Institute of Nutrition and Food Technology, Universidad de Chile, Santiago, Chile

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## Abstract

**Aim** Colorectal cancer (CRC) is a major cause of cancer death worldwide. We examined temporal trends in death rates from colorectal cancer in Chile from 1983 to 2008.

**Method** We analysed the mortality database in Chile from 1983 to 2008. Cases were selected using ICD-9/10 codes. We calculated mortality rates per 100 000 inhabitants according to sex, age group and type of cancer – colon (CC) or rectal (RC). The rates were adjusted by a direct method using the WHO-2000 standard population. Time trends were assessed with Prais–Winsten regression models.

**Results** There were 26 250 deaths from CRC (75.7% for CC). There was a higher frequency of deaths from CC (57.6%) in women than in men, who had a higher frequency of deaths from RC (51.3%). The crude CC mortality rate increased by 116% (from 3.6 to 7.8), while the overall RC rate increased by 71% (from 1.4 to 2.4). After adjusting for age, a significant increase in mortality rate was found for CC (coefficient 0.09, 95% CI 0.08–0.11,  $P < 0.001$ ) and RC (coefficient 0.02, 95% CI

0.009–0.04,  $P = 0.002$ ) in men. In women, this increase was significant for CC (coefficient 0.03, 95% CI 0.005–0.05;  $P = 0.02$ ), but not for RC (coefficient –0.007, 95% CI –0.02 to 0.005,  $P = 0.23$ ).

**Conclusion** The crude mortality rate from CRC has doubled in Chile in this period. After adjustment of mortality rates, it appears that much of this increase is due to the aging population. However, part of this increase could be explained by other factors.

**Keywords** Colorectal neoplasms, mortality, epidemiology

## What is new in this paper?

This is the first study in a developing South American country that analyses long-term mortality trends from colorectal cancer. From 1983 to 2008, the crude mortality rate doubled; this is partially explained by the aging population. The increasing prevalence of risk factors and lack of screening could also explain this trend.

## Introduction

Colorectal cancer (CRC) is one of the main causes of cancer mortality worldwide. Globally, CRC is one of the three main types of new cancer cases. Colorectal cancer is also the commonest type of new digestive cancer.

Incidence rates are higher in men than in women [1]. CRC is the leading cause of death from digestive cancer in women and the third in men worldwide. When analysing developed countries, CRC is the leading cause of death from digestive cancer in both men and women

[1]. In Europe, there is wide variation between countries, ranging from 11 and 32/100 000 deaths per year in men to 7 and 16/100 000 deaths per year in women [2].

European rates of mortality from CRC have decreased steadily since 1980 in women and since 1990 in men. However, the mortality rate has not decreased in all European countries; there has been a substantial decrease in northern European countries, but in some eastern European countries the rate has remained steady or has even increased [2]. In the USA, the mortality rate has remained high since the early 1950s; however, this rate has decreased considerably since the mid-1980s, most likely due to prevention programmes [3].

Over the past few decades, Asian countries like China and Korea have shown an increase in CRC mortality in men [4]; this is in contrast to countries like Vietnam,

Correspondence to: M. L. Garmendia, Institute of Nutrition and Food Technology, Universidad de Chile, El Líbano 5524, Macul, 7830490 Santiago, Chile.  
E-mail: mgarmendia@inta.uchile.cl

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where the death rate for CRC has remained low [5]. In Latin American countries, CRC is one of the three main causes of death from cancer [6].

Chile, a post-transitional developing country, has experienced a shift in its risk factor profile over the last few decades, mainly because of nutritional and lifestyle changes. Changes in the prevalence of risk factors may have affected the incidence of and mortality from CRC in Chile; however, their trends have not been studied on a long-term basis. The aim of this study was to analyse the variations in mortality rates from CRC in Chile over the last quarter of a century.

## Method

An epidemiological time series study was designed to assess the trends in mortality from colon and rectal cancer in Chile. We analysed the mortality database of the Department of Health Statistics and Information at the Health Ministry of Chile for the years 1983–2008. Information was collected on age, sex, area of residence and cause of death. Causes of death were selected according to codes from the International Classification of Diseases (updated up to 1996 ICD-9 and ICD-10). For colon cancer (CC), the selected codes were 154.0 and 153.0 from ICD-9, and C19 and C18 from ICD-10. Deaths from malignancy of the appendix (codes 153.5 from ICD-9 and C18.1 from ICD-10) were excluded because this cancer has different histopathology and treatment in most cases. For rectal cancer (RC), the selected codes were 154.1 from ICD-9 and C20 from ICD-10.

Chilean death registries cover 100% of the population [7]. Chilean law states that all deaths must be registered in the electronic database of the National Civil Registry. Every death certificate undergoes intense review by the Health Information and Statistics Department of the Health Ministry. Then the cause of death is coded following the International Classification of Diseases protocols. Only medical doctors and police officers are allowed to complete the death certification form (midwives are also allowed, but only for foetal deaths). In the databases used in the present study, medical doctors certified 97% of deaths registered in Chile [8].

Area of residence was classified as urban or rural, according to the residence location. The National Institute of Statistics defines a location as rural if a dwelling area has fewer than 2000 people; 50% of those people work in secondary or tertiary activities. Information regarding area of residence was only available in death databases from 2002 to 2008.

Age, expressed in years, was described using the median and interquartile range (Shapiro–Wilk test).

Deaths were divided into five age groups: under 50, 50–59, 60–69, 70–79 and 80 years and older. Qualitative variables were described in frequencies. Crude death rates per 100 000 inhabitants were calculated. These were subsequently standardized (by age and sex) through a direct method using the World Health Organization 2000 standard population [9]. Age, sex and area of residence relative risks were computed for colon and rectal cancer.

The Prais–Winsten regression model was used to evaluate temporal trends [10]. This model is suitable for the analysis of time series because autocorrelation often exists, meaning that the rate for one year would influence the next. The autocorrelation is corrected in this model and estimated with the Durbin–Watson statistic. Analyses were performed using STATA 11.2 (StataCorp LP, 2009). A *P*-value less than or equal to 0.05 was defined as statistically significant.

## Results

Between the years 1983 and 2008 there were 26 250 deaths from CRC (75.7% for CC). Proportionately more women died from CC (57.6% of deaths), while more men died from RC (51.3% of deaths). The median age at death was higher in women for both CC [75 (interquartile range: 64–82) vs 71 (62–79) years] and RC [71 (60–80) vs 69 (59–77) years]. Crude mortality rates increased by 116% (from 3.6 to 7.8) for CC and by 71% (from 1.4 to 2.4) for RC. Table 1 shows the crude death rates for CC and RC by age group. During the period observed, rates increased with age. The crude mortality rate for CC was higher in women, while the rate for RC was higher in men. Adjusted rates (per 100 000 inhabitants) for the same period were 5.31 and 5.21 for CC in men and women, respectively. The adjusted crude mortality rates for RC were 2.06 and 1.46 in men and women, respectively.

From 2002 to 2008 (Table 2), adjusted rates were higher in urban areas for CC and RC in women and men. Table 3 shows the relative risk of dying from CRC by sex, area of residence and age (women, rural areas and age equal to or less than 50 years were used as a reference). Men died 7% more often from RC and 33% less often from CC. Colon cancer mortality rates increased with increasing age. Urban areas had a risk that was more than 50% higher than rural areas.

Figure 1 shows the trend in crude and age-adjusted mortality rates for CRC in both men and women; in general there was an increase in rates. The largest increase was observed for CC in men (coefficient = 0.079), i.e. each year 0.079 more people died per 100 000 habitants than the previous year. Thus, there were 5.6 more deaths

**Table 1** Crude mortality rates for colorectal cancer by age group and sex: Chile 1983–2008 (rates per 100 000 inhabitants).

Age group	Colon cancer		Rectal cancer		Total	
	Men	Women	Men	Women	Men	Women
< 50 years	0.42	0.51	0.25	0.24	0.67	0.75
50–59 years	6.66	7.37	3.17	2.53	9.83	9.90
60–69 years	22.04	19.53	9.09	5.80	31.13	25.33
70–79 years	55.38	50.07	19.58	12.41	74.96	62.48
80 years or more	117.04	126.97	35.27	27.62	152.31	154.59
Total	4.56	6.06	1.77	1.65	6.34	7.71

**Table 2** Adjusted mortality rates for colorectal cancer by area and sex: Chile 2002–2008 (rates per 100 000 inhabitants).

Area	Colon cancer		Rectal cancer		Total	
	Men	Women	Men	Women	Men	Women
Urban	6.57	5.84	2.53	1.60	9.10	7.44
Rural	3.71	3.98	1.54	1.13	5.25	5.11
Total	6.04	5.61	2.35	1.54	8.39	7.96

**Table 3** Relative risk of death from colorectal cancer by sex and age group: Chile 1983–2008.

	Colon	Rectum
Sex		
Women (ref.)	1	1
Men	0.75	1.07
Age group		
< 50 years (ref.)	1	1
50–59 years	15.09	6.13
60–69 years	44.70	16.01
70–79 years	113.39	34.40
80 years or more	262.38	67.62
Area*		
Rural (ref.)	1	1
Urban	1.61	1.55

\*Only available from 2002 to 2008.

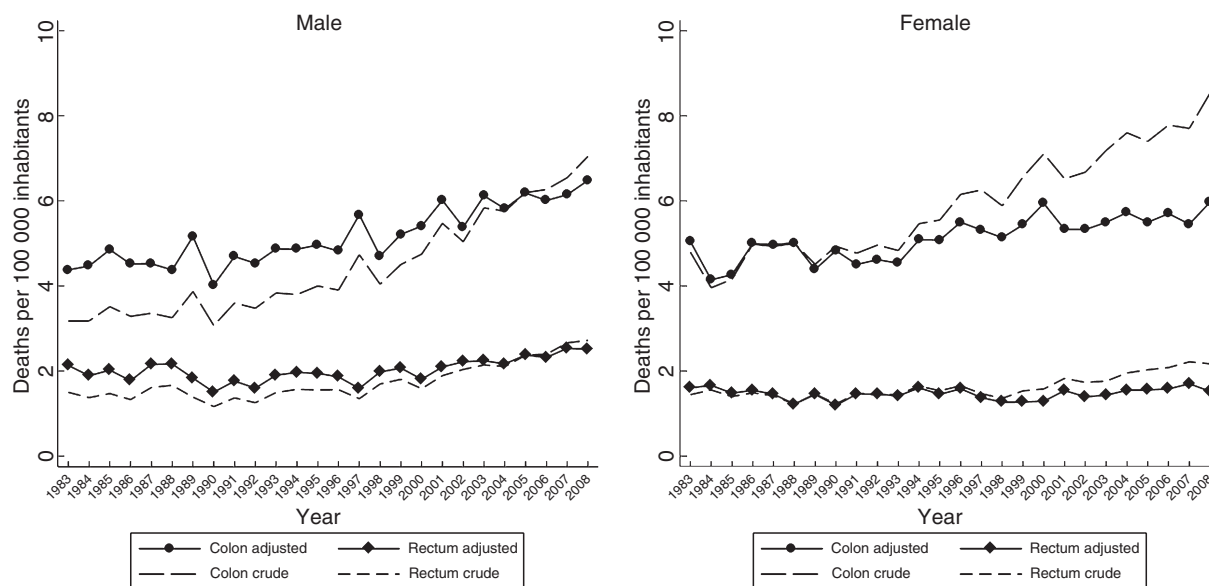
per 100 000 from CC for each additional year. In women, there were 3.8 more deaths per 100 000 from CC for each additional year. In the case of RC, there was only a significant increase in men, representing 1.3 more deaths per 100 000 annually (Table 4).

## Discussion

This study shows that CRC mortality has increased significantly over the last 25 years, and the crude CRC mortality rate has increased by over 100%. This analysis reflects a long period of study in a developing South

American country. The CRC mortality increase is mainly attributed to an increase in CC mortality. After adjusting for age, this increase is preserved and is significant for CC in both sexes and for RC in men.

The Chilean mortality rate places Chile among countries with a rate higher than 10/100 000 inhabitants. Chile has the third highest mortality rate in the region and is surpassed by only Argentina and Uruguay [11–13]. A study that analysed major cities in Brazil revealed high variability in mortality rates among localities, with higher mortality rates found south and south-east Brazil. In addition, the same study showed a higher mortality rate in men than in women [14]. In Colombia, CRC is among the five top causes of cancer death. A study involving death rates between the years 1981 and 1996 showed that the leading causes of death in the 1980s from gastrointestinal tract cancer were stomach, liver, colorectal and gallbladder cancer. An analysis of mortality trends revealed that only CRC had increased during the 1990s [15]. The increase in mortality from CRC in Chile over the last 26 years was similar to that described in Brazil [16], Colombia [15], Argentina [17] and Ecuador [18]. Another study also showed that CRC mortality had increased in this region [19]. The increasing mortality trend of CRC is also observed in eastern European countries such as Romania and Russia [18]. These countries also have risk factors that are found in developing countries. In Chile, the increase in mortality may have several explanations, including an aging population. However, after rate adjustment, a significant increasing trend was sustained, though it was smaller in magnitude.



**Figure 1** Trends of colorectal cancer mortality rates: Chile 1983–2008.

**Table 4** Trends of adjusted colorectal cancer mortality rates by sex and type of cancer: Chile 1983–2008 (Prais–Winsten regression model, age-adjusted rates).

	Coefficients	95% CI	P-value
Colon			
Men	0.079	(0.064; 0.095)	< 0.001
Women	0.052	(0.035; 0.069)	< 0.001
Rectum			
Men	0.019	(0.001; 0.037)	0.044
Women	0.001	(-0.009; 0.011)	0.815

Therefore, there must be other factors that explain the increasing trend of mortality rates found in this study. We hypothesized that an increased incidence, higher prevalence of traditional risk factors for developing CRC, and lack of programmes for prevention and early detection of CRC may affect survival. There is no national cancer registry in Chile; hence there is a lack of information regarding cancer incidence. We could not verify the impact of a supposedly increased incidence on mortality.

Regarding risk factors for developing CRC, Chile is embedded in a group of underdeveloped or developing countries that are in the process of demographic, epidemiological and nutritional transition [19], which may be an effect of ‘westernization’. This includes increase in food availability, low fibre intake and a sedentary lifestyle. This, in addition to a marked increase in the numbers of obese people [20] and a high consumption of cigarettes [21], both of which are risk factors for developing CRC [22], means Chile is at risk for an increase in CRC cases.

Urban areas had a higher risk in our study, supporting the idea that westernization probably has a marked effect on CRC rates. Of note, both diet and obesity can be modified through individual and population-based public health strategies. Programmes for early detection and treatment of precancerous lesions (polyps) and cancers at an earlier stage have proven to be effective in improving overall survival and reducing mortality rates [3,23]. These programmes have not been systematically implemented nationwide in Chile and may be another explanation for the steady increase in CRC mortality rates reported in the present study.

In conclusion, the crude death rate for CRC has doubled in Chile during 1983–2008. After rate adjustment, it appears that much of this increase is due to an aging population; however, this increase could also be explained by other factors that were not identified in this study and should be considered for the prevention and control of this disease.

## Conflict of Interests

The authors declare that they have no disclosures.

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