

## The burden of premature mortality due to colorectal cancer in Golestan province from 2011 – 2015: a sequential cross-sectional study

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### Abstract

**Background & Aims:** The burden of premature mortality is used to prioritize health problems. The purpose of this study was to estimate the burden of premature mortality due to colorectal cancer in Golestan from 2011 – 2015.

**Materials & Methods:** In this sequential cross-sectional study, based on the province mortality registration data and standard expected years of life lost (SEYLL), the burden of premature mortality was calculated.

**Results:** From 2011 to 2015, a total of 3283 years of the lost years of life was due to the Premature Mortality in Golestan province to colorectal cancer, which occurred 1983 years (60.4%) in the men and 1299 years (39.6%) in the women. The rate of lost years of life for the 5-year period was 1.2 per 1000 people in the men and 1.4 per 1000 people in the women. The results of the study showed that people over 60 years old were at risk of death and losing more potential life expectancy due to premature death due to colorectal cancer.

**Conclusion:** Colorectal cancer seems to be the primary cancer of the province's health system. But definitive judgment requires calculating the burden of disability caused by cancers and ranking them based on the complete calculation of the Disability-Adjusted Life Years (DALY) index.

**Keywords:** Standard expected years of life lost (SEYLL), Burden of premature mortality, Colorectal Cancer, Golestan

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### Introduction

Colorectal (Colon and rectal) cancer (CRC) is caused by the uncontrolled proliferation of colon cells (1). By definition, colon cancer involves major parts of

the large intestine, while rectal cancer affects only the end of the colon. The end of the rectum is attached to the anus. The anus cancer is a completely different condition; thus it is not included in the pathological

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classification of CRC(2). Of the cancers that begin in the colorectal region, the vast majority (over 95%) are classified as adenocarcinomas. They begin in the mucus-making glands lining the colon and rectum. Other less-common cancers of the colorectal region include carcinoid tumors, gastrointestinal stromal tumors, lymphomas, and sarcoma(3).

CRC is the third most common cancer worldwide(4, 5), and the fourth leading cause of cancer-related death in both genders(6). About 9% of total cancer cases (1.4 million cases) and 8% of the total cancer deaths (693,900 cases) were caused by CRC in 2012(4, 7). Developed countries displayed the highest standardized incidence and mortality rates of CRC (29.2 and 11.7 per 100,000, respectively)(7), in other words, CRC is a major public health problem in these countries(5).

About 45% of CRC cases occur and 52% of CRC deaths occur in less developed regions.

In 2012, 3,811 men and 3,352 women were diagnosed with CRC in Iran, making it the fourth and second most commonly diagnosed cancer among Iranian men and women, respectively(8). The incidence of CRC among Iranian people is currently low(9). Due to the aging of the population, the incidence of CRC will increase in future in Iran. According to the GLOBOCAN 2012 estimates, the incidence of CRC will double by 2030 in Iran(8, 9). In Iran, the incidence of CRC is significantly lower in older people and higher in young adults compared to western countries, which can dramatically increase disability-adjusted life years (DALYs) in the future(10).

The DALYs are the sum of the years of life lost (YLLs) due to Premature Mortality and years of life lost due to disability (YLD)(11). Unlike other death measures (rates and numbers of deaths), the YLL give considerable value to deaths of young people, thus emphasizing the concept of premature and preventable death(12).

In Iran, after gastric cancer (19%), leukemia (17%), lung cancer (10%), and liver cancer (8%), the CRC similar to breast cancer had the highest YLL or YLD (6%) in 2003. Results of the previous studies showed that the mean age distribution of CRC is relatively lower which can significantly influence the burden of the disease(10).

In Iran, the incidence of CRC higher in young adults(10) also according to Demographic Cancer Registration Systems reports, the incidence of CRC is higher in Golestan province compared to central and southern provinces (1) and that a limited number of studies have evaluated the SEYLL with the maximum study duration of one year in Iran/ Therefore the present study aimed to evaluate the burden of premature mortality due to CRC in Golestan province, northern Iran between 2011 and 2015.

## Materials and Methods

This was a sequential cross-sectional study. In our study, sampling was not performed, and samples were selected through systematic census method. The overall deaths from CRC for both male and female patients in 2011, 2012, 2013, 2014, and 2015 were 36, 22, 34, 57, and 80 cases, respectively. Also, the overall five-year mortality rate of CRC was reported in 229 cases.

The mortality data in Golestan province was extracted from death certificates by statistics department of health centers, death record files of healthcare centers by physicians through verbal autopsy, history of CRC and existing examination documents, as well as a survey from relatives of deceased cases from forensic medicine, hospitals, and maternity centers.

All the required data were extracted from death record databases of health deputy of Golestan province. The causes of death were categorized based on the International Classification of Diseases-10 (ICD-10) in Excel files.

We extracted the required data without personal name, father's name, and national number of deceased cases from death database of the province. These data similar to any data obtained from surveillance systems are likely to reflect biases. Also, the quality and accuracy assessments of the data is not feasible to collect reference data, and because death data are already recorded and the cause of death is established for each deceased person, the quality and accuracy of death data will depend on how death certificates were completed.

$$YLL = Nc e^{(ra)} / (\beta + r)^2 [e^{-(\beta+r)(L+a)} [-(\beta + r)(L + a) - 1] - e^{-(\beta+r)a} [-(\beta + r)a - 1]]$$

Where,  $N$  is the frequency of death, and  $\beta$  is an age weighting constant equal to 0.04 for different years of life. Also,  $r$  is discounting rate equal to 0.03 for future times (13-16),  $a$  is the age of death, and  $c$  is the correction coefficient for age weighting with a constant value of 1658. Also, the standard life expectancy (standard life table) was calculated based on the Coale and Demeny West Level 26 model life tables. In the present study, the standard life expectancy of the Japanese population (80 years among men and 82.5 years among women) instead of life expectancy at birth in Iran (70 years among men and 75 years among women) (13-16). The results of this study can be compared with other studies by using the standard life expectancy.

The required variables in the Excel Template included age, gender, and cause of death (underlying causes of death and based on death certification). In the present paper, death due to CRC was considered as an underlying cause of death. The YLL was measured using the SEYLL method and expressed as the standardized life expectancy at age of death minus the actual age of death due to CRC. Hence, the total YLLs due to CRC is the sum of SEYLLs per death

in Golestan province between 2011 and 2015.

This increases the probability of measurement bias. In this study, in order to reduce these information defects, the relative deaths of CRC with repeated records, death cases of other provinces of the country who died in Golestan province, and death cases with non-identifying gender or age at death were excluded from data analysis.

The YLLs due to premature mortality was measured by SEYLL method. Calculations were performed based on standards proposed by world health organization using the following expression on Excel Template:

As such, the age- and sex-specific mortality rates of CRC were further estimated in the present work. Comparison of crude death rates of a specific cancer in a specific population at different times regardless of specific age groups may bias the results because the population age composition varies at different time frames. The direct age adjustment was performed to compare mortality rates of CRC between 2011 and 2014. The sum of the total population of Golestan province during 2011 and 2015 was considered as a projected population. The age-specific mortality for this projected population was estimated based on age-specific mortality between 2011 and 2015. Therefore, the confounding effect of age due to population age composition was eliminated.

## Results

The total YLLs due to premature mortality of CRC was 3283 years, with 1983 years (60.4%) among males and 1299 years (39.6%) among females. The highest YLLs due to CRC premature mortality in the whole five year study period was reported among patients aged 45-59 years (Table 1).

**Table 1:** The Number of years of life lost (YLLs) due to Premature Mortality of colorectal cancer for sex and age groups in Golestan province between 2011 and 2015

year	0-4 years			5-14 years			15-29 years			30-44 years			45-59 years			60-69 years			70-79 years			+80 years			Total			
	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T	
2011	0	0	0	0	0	0	0	0	27	27	72	0	72	80	209	289	42	30	72	16	36	52	19	11	30	229	313	542
2012	0	0	0	0	0	0	0	0	27	27	24	25	49	36	22	58	126	33	158	8	0	18	7	7	14	211	114	325
2013	0	0	0	0	0	0	27	0	27	95	0	95	187	57	244	57	28	85	35	21	56	0	21	21	401	127	528	
2014	0	0	0	0	0	0	108	0	108	47	50	97	155	63	218	94	150	243	84	18	102	25	21	46	512	302	814	
2015	60	0	60	0	0	0	0	0	146	47	193	111	101	212	148	206	354	122	57	179	44	32	76	630	443	1074		
Total	60	0	60	0	0	0	134	54	188	384	122	506	569	453	1022	466	447	912	275	132	406	95	93	187	1983	1299	3283	

M: Men, W: Women, T:Total

Also, the highest YLL rate due to premature mortality of CRC was observed: among 80 years and higher (2.1 per 1000) in 2011, 60-69 years (2.3 per 1000)

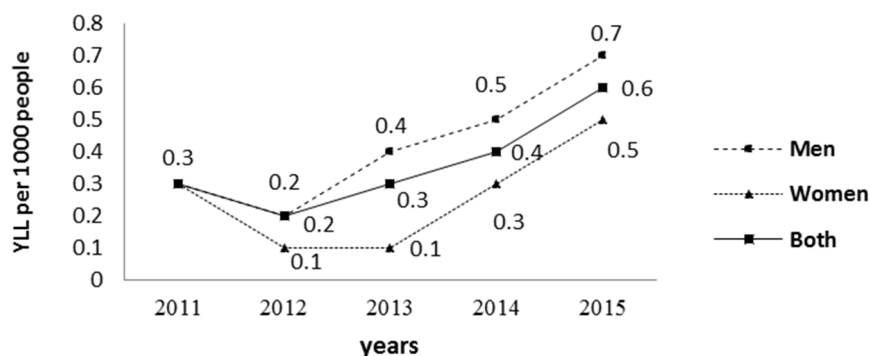
in 2012, 70-79 years (1.5 per 1000) in 2013, 60-69 years (3.2 per 1000) in 2014, and 70-79 years (4.7 per 1000) in 2015 (Table 2).

**Table 2:** The rate of lost years of life (per 1000 people) due to Premature Mortality of colorectal cancer for sex and age groups in Golestan province between 2011 and 2015

year	0-4 years			5-14 years			15-29 years			30-44 years			45-59 years			60-69 years			70-79 years			+80 years			Total		
	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T
2011	0	0	0	0	0.1	0	0	0.1	0	0.4	0	0.2	0.8	2	1.4	1.4	0.9	1.2	0.8	2.1	1.4	2.6	1.6	2.1	0.3	0.4	0.3
2012	0	0	0	0	0.1	0	0	0.1	0	0.1	0.1	0.1	0.3	0.2	0.3	3.9	0.9	2.3	0.9	0	0.5	0.8	0.9	0.8	0.2	0.1	0.2
2013	0	0	0	0.1	0	0	0.1	0	0	0.4	0	0.2	1.6	0.5	1.1	1.7	0.7	1.2	1.8	1.1	1.5	0	2.6	1.2	0.4	0.1	0.3
2014	0	0	0	0.4	0	0.2	0.4	0	0.2	0.2	0.2	0.2	1.3	0.5	0.9	2.6	3.8	3.2	4.4	1	2.7	2.4	2.4	2.4	0.5	0.3	0.4
2015	0.6	0	0.3	0	0	0	0	0	0	0.6	0.2	0.4	0.9	0.8	0.9	4	5.1	4.6	6.3	3	4.7	4.2	3.6	3.9	0.7	0.5	0.6

M: Men, W: Women, T:Total

The YLLs rate due to premature mortality of CRC between 2011 and 2015 showed a decreasing trend between 2011 and 2012 among both men and women, with a gradual increase in trends from 2012 to 2015 (Figure 1).



**Figure 1:** The rate of lost years of life (per 1000 people) due to Premature Mortality of colorectal cancer for sex in Golestan province between 2011 and 2015

The highest premature mortality due to CRC was observed among patients aged 80 years and higher between 2011 and 2015, as 42.6 per 100,000 in 2011, 18.1 per 100,000 in 2012, 22.8 per 100,000 in 2013, 46.9 per 100,000 in 2014, and 76.9 per 100,000 in 2015 followed by 70-79 years as 16.1 per 100,000 in 2011,

60-69 years as 16.3 per 100,000 in 2012, and 70-79 years as 16 per 100,000 in 2013, 32 per 100,000 in 2014, and 52.3 per 100,000 in 2015. The premature mortality of CRC between 2011 and 2012 decreases among women, and increases between 2012 and 2015 among both men and women (table 3).

**Table 3:** the mortality rates (per 1000 people) due to Premature Mortality of colorectal cancer for sex and age groups in Golestan province between 2011 and 2015

year	0-4 years			5-14 years			15-29 years			30-44 years			45-59 years			60-69 years			70-79 years			+80 years			Total		
	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T	M	W	T
2011	0	0	0	0	0	0	0.3	0.2	0	1.5	0	0.7	3.8	0.3	7.1	10.1	6.8	8	10.1	20.2	16.1	54	27	42.6	1.8	2.2	2
2012	0	0	0	0	0	0	0.3	0.2	0	0.5	0.5	0.5	1.8	0.9	1.3	28.1	5.6	16.3	10.3	0	5.4	23	12.7	18.1	1.8	0.7	1.2
2013	0	0	0	0	0	0	1.3	0	0.2	1.8	0	0.9	8.6	2.6	5.6	11.9	5.3	8.4	20.7	11	16	0	48.5	22.8	2.5	1.2	1.8
2014	0	0	0	0	0	0	1.4	0	0.7	0.9	0.9	0.9	6.6	2.5	4.6	19.6	25.2	22.5	52.3	10.9	32	49	44.5	46.9	3.8	2.2	3
2015	1.2	0	1.1	0	0	0	0	0	0	2.5	0.9	1.7	4.8	4.1	4.5	29.7	32.1	31	71.9	32	52.3	86.1	66.3	76.9	5	3.4	4.2

*M: Men, W: Women, T: Total, Mortality Rates Using Direct Age & Sex Adjustment*

### Discussion

In the present study, we estimated the age- and sex-specific mortality as well as the overall CRC mortality using direct age adjustment to eliminate the confounding effect of age resulting from different population age composition.

Results of this study showed that 60.4% of the YLLs due to premature mortality of CRC occurred in male and 39.6% occurred in female patients. Mahmoudlo et al. reported the YLLs due to premature mortality of CRC as 57% and 43% among male and female patients, respectively(10). Also, a study by Richard et al. reported the YLLs due to premature mortality of CRC as 58% and 42% among male and female patients, respectively (17).

Moreover, about 60% of DALYs due to premature mortality and disability was observed among male patients (18). The results of the present study showed that the highest YLLs due to CRC premature mortality was reported among patients aged 45-59 years in both

genders, which was consistent with the study of Mahmoudlou (10).

The mean age of death was almost constant in both genders from 2011 – 2015 but the rate of YLL (per 1000 people) due CRC showed an increasing trend between 2011 and 2015, which may be due to the increased incidence rate of CRC and subsequently CRC mortality. As such, the life standards have improved over the past thirty years and consequently the life expectancy in Iran increased significantly. Moreover, the lifestyles have dramatically changed in terms of physical activity and dietary habits rich in meat and fat and low in fiber similar to common diets in western countries (2). The higher rate of YLL (per 1000 people) due to CRC may have resulted from the improved electronic death registration system. As shown in Table 3, the rates of mortality due to CRC increased during the study period, whereas the mean age of death showed no significant difference in both men and women. Therefore, the increased burden of CRC premature mortality can be

attributed to increased mortality rates, and the reduced average age of death was not associated with the increased burden of CRC premature mortality.

It is important to note that down staging of colorectal cancer by cancer screening program reduces the CRC-related mortality by 30% worldwide(19, 20). It can be concluded that cancer screening programs can effectively reduce the burden of disease as secondary prevention of cancer is of great importance. Similar to our findings, Pourhoseingholi et al. found that the burden of premature mortality of CRC showed an increasing trend in years of study (9), which was supported by a study on the global burden of diseases (1).

In our study, the burden of CRC premature mortality was higher in men than in women. Therefore, men are more at risk of losing the potential YLLs due to CRC premature mortality. Two variables in the rate of YLL can be affected: 1- the age of death, 2- the mortality rate. The lower the age of death and the higher the death rate, the more YLL will be (13) (14). In our study, the age of death in both sexes was almost constant, but mortality rates were higher for men than women during the years of study. Also, the share of YLL (%) in men is 60.4%. The greater share of YLL for men than women in our study is related to high prevalence and ultimately high mortality in men than women. Other studies have shown that the prevalence of this cancer is higher in men than in women (21). It demonstrated that mortality in men is 25% higher than that of women (22, 23). Richard (17) and Mahmoudlo's studies also had these results (10). In our study, mortality was 21.4% higher in men than in women which is consistent with the results of the previous studies.

The present study reveals that the rate of YLLs due to premature mortality of CRC is higher in men (2.1 per 1000) than in women (1.4 per 1000) during a 5-year period. Mahmoudlou et al. reported the rate of YLLs due to premature mortality of CRC as 67.7 per 100,000 in

men and 58.7 per 100,000 in women(10). Richard et al. also reported the rate of YLLs due to premature mortality of CRC as 2.2 per 1000, and 1.9 per 1000 among men and women, respectively (17).

Results also suggest that the rate of mortality and the burden of CRC premature mortality is higher at older age groups. Hence, individuals at old ages (over 60 years) are at higher risk of CRC death and more significant YLLs due to premature mortality of CRC, which was in compliance with Pourhoseingholo et al. (24). In summary, the risk of CRC increases by age, that is the majority of patients were 60 years and older at the time of diagnosis(2). Which results in an increase in the death rate.

In conclusion, the mortality rates of CRC showed an increasing trend in all age groups. Pourhoseingholo et al. proposed an increasing mortality trend of CRC over the past years in Iran, whereas this trend is declining in European countries. However, the incidence of CRC has remained low compared to most western countries (24).

This difference may have resulted from a greater proportion of youth population as well as a lower prevalence of CRC among elderly in Iran. Moreover, lower rates of CRC mortality may be due to the lack of screening programs and early diagnosis of the disease in Iran and the limitations of this study. As such, the data collected through mortality registration system of the province may be inaccurate and uncertain leading to increased measurement bias in the final results.

In Golestan province, in cooperation with the department of information and statistics, information about active diagnostic and therapeutic centers of the whole province was collected and all centers were identified. The main sources of data collection for Golestan population-based cancer registry program include pathology centers, hospitals, and death records. Other sources of data, including cancer expert clinics, radiotherapy and chemotherapy centers, radiology centers, illicit drug control units, etc. were also selected

as data collection sources (25). Therefore, the calculation of years lost due to disability (YLD) of cancers, such as CRC, and calculation of the Disability-Adjusted Life Year (DALY) would be feasible.

### Conclusion

According to the findings of the present paper, the burden of premature death due to CRC showed an increasing trend in Golestan province between 2011 and 2015. It can be concluded that colorectal cancer should have a high priority in the health system. However, the burden of disability due to CRC and classification of the disease through the calculation of DALYs should be taken into account for more accurate results.

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