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CLINICAL STUDY

Joinpoint analysis of colorectal cancer trend in the Slovakia

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ABSTRACT
OBJECTIVES: The aim of this study is to describe the colorectal cancer trend in the Slovakia between 2002 and 2019.
BACKGROUND: In 2020, the Slovakia ranked second among the 10 countries with the highest incidence of colorectal cancer and the highest number of deaths from colorectal cancer (hereafter also referred to as CRC).
METHODS: To describe the situation of CRC, indicators of incidence and mortality rates stratified by age and sex for the available time period were chosen. A joinpoint regression software was used to identify changes in the trend of development.
RESULTS: During the 18-year follow-up period (2002–2019), the overall trend in colorectal cancer incidence continued to increase with an overall mean annual change of 1.3 %. The incidence of CRC tended to increase from 50 years of age and increased with age. The most pronounced increasing trend was observed in the age group of 75 years and older (AAPC in men 1.9 %, IS +1.4; +2.5 and in women 2.0 %, IS +1.6; +2.4). CRC mortality remained relatively stable for the entire 18-year period. A decreasing trend in mortality was observed in the 25–49 age group with an overall annual percentage decrease of 0.9 % (IS –1.5; –0.3), while an increasing trend was observed in the 75+ age group with an overall annual percentage increase of 1.0 % (IS +0.8; +1.3). The incidence and mortality rates in men were higher than in women.
CONCLUSION: The situation of colorectal cancer trend in the Slovakia has improved compared to the previous period (1971–2001) *(Tab. 4, Fig. 4, Ref. 34)*. Text in PDF *www.elis.sk*
KEY WORDS: colorectal cancer, incidence, mortality, GBD, trend, age, gender.

Introduction

Cancer is the leading cause of death worldwide, accounting for almost 10 million deaths in 2020, almost one in six deaths (1). Besides, cancer patients exhibit poor health outcomes, possibly due to a chronic immunosuppressive state and anticancer therapies, while being more prone to infections such as SARS-CoV-2 infection. Male sex, older age, and active cancer disease or history of cancer are risk factors for COVID-19 infection potentially leading to severe complications, including morbidity and death (2).

Colorectal cancer is the third most common cancer in the world (3). The number of individuals diagnosed with colorectal cancer (CRC) has been on an alarming upward trajectory over the past decade. In some countries, this cancer represents one of the most frequently diagnosed types of neoplasia (4). It had been estimated that in 2020, the incidence and mortality rates of colorectal cancer would increase by more than 1.9 million cases and 930,000 deaths, respectively. The rates were highest in Australia/New Zealand and Europe (40.6 per 100 000, men) and lowest in several regions of Africa and South Asia (4.4 per 100 000, women). More than 80 % of the new cases expected to occur in 2040 are projected to occur in countries with high or very high levels of the Human Development Index (5).

It had been estimated that in 2020, colorectal cancer would account for 12.7 % of all new cancer diagnoses and 12.4 % of all cancer deaths in the EU-27. It is the third most diagnosed cancer in men (after prostate and lung cancer) and the second most diagnosed cancer in women (after breast cancer). It is the second leading cause of cancer death in men (after lung cancer) and the third leading cause of cancer death in women (after breast and lung cancer) (6)

According to data from 2020, Slovakia has long been among the top five countries with the highest incidence rate of colorectal cancer (CRC) worldwide, and the rate continues to rise every year (7). CRC kills nearly 1,700 people in Slovakia every year (8). Every year, 3,000 new cases appear. The paradox lies in the possibility that timely diagnosis of this disease may render it non-fatal (8). For these reasons, an analysis of the trend of CRC in the Slovakia is necessary. It helps us clarify the specific situation regarding colorectal cancer so that we can better orient ourselves in the prevention and treatment of the disease.

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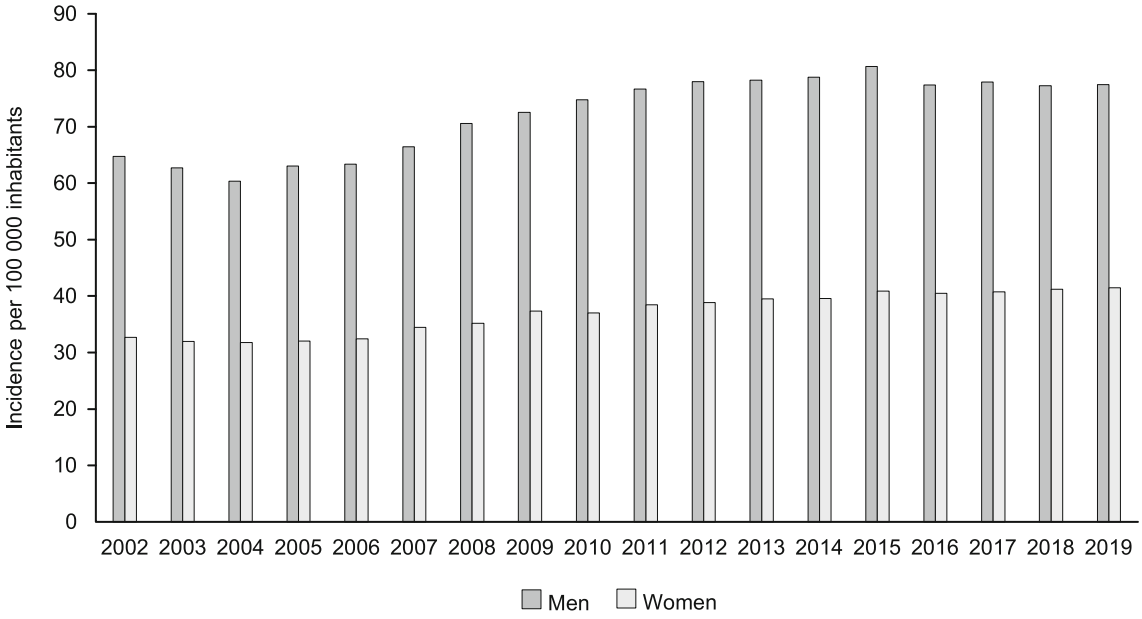

Fig. 1. 2002–2019 incidence of colorectal cancer in the Slovakia by sex.

Materials and Methods

Data were obtained from the Institute of Health Metrics and Evaluation (the Global Burden of Disease Study) over an 18-year period from 2002 to 2019. The situation of CRC is described using age-standardised indicators of disease incidence, incidence and mortality rates by sex and age group. The Join Point Regression software (version 4.5.0.1; Statistical Research and Applications Branch, National Cancer Institute), was used to identify changes in trends in incidence and mortality rates by sex and age (3 age categories selected: 25–49 years, 50–74 years, 75 years or older). Conducting joinpoint analysis of trends in age-adjusted cancer incidence and mortality rates allows the user to improve the accuracy in interpretation of temporal changes and, more importantly, to assess their statistical significance. Briefly, using incidence/mortality rates as inputs, this method identifies the year (s) when the trend change occurred, calculates the annual percentage change (APC) in the rates between the points of trend change, and estimates the average annual percentage change (AAPC) over the entire study period with 95 % confidence intervals.

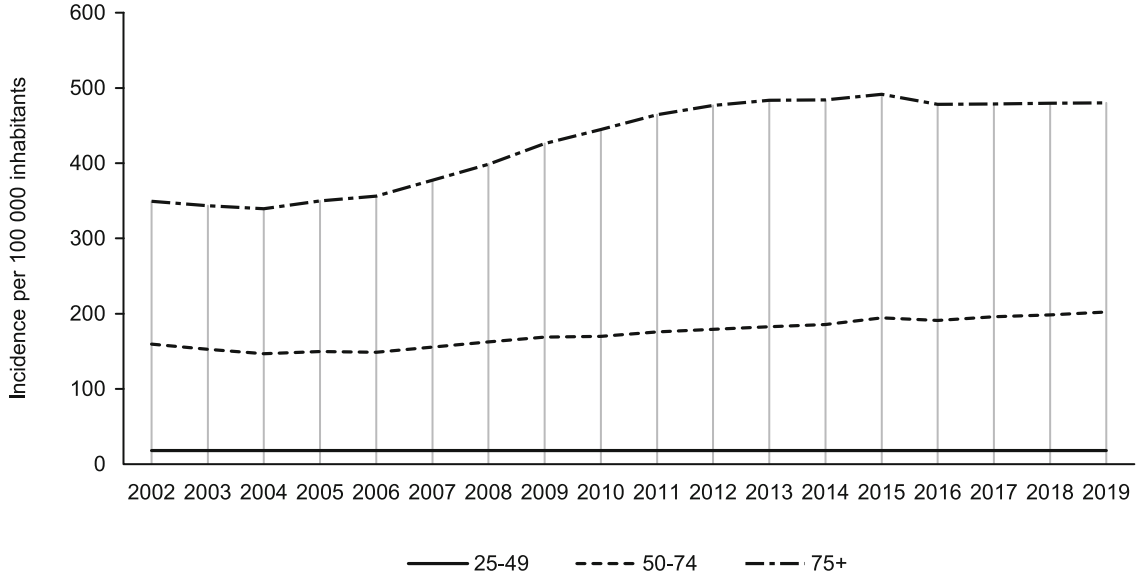

Fig. 2. 2002–2019 incidence of colorectal cancer in the Slovakia by age.

Results

Trends in the incidence of CRC in the Slovakia

Figure 1 shows an increasing trend in the age-standardised incidence rate of CRC for the period of 2002 to 2019 in both sexes. The highest incidence rate of CRC (80.68 per 100,000 population) in men was recorded in 2015 and the lowest in 2004 (60.38 per 100,000 population). In women, the highest CRC incidence rate (41.45 per 100,000 population) was in 2019 and the lowest in 2004 (31.74 per 100,000 population). The incidence of CRC in men is always approximately twice as high as in women.

An increasing trend in incidence rates is observed in all three age groups (25–49, 50–74, 75 and over) (Fig. 2). Incidence rates begin to increase sharply after the age of 50, and thereafter, the progress of the increase rate accelerates with age. The incidence rate was highest in the age group of 75 years or older with a peak in 2015 (491.55 per 100,000 population). The 50–74 age group ranked second with a peak in 2019 (202.24 per 100,000 population). The lowest incidence rate has consistently been observed in the age group of 25–49 years with a maximum in 2019 (14.81 per 100,000 inhabitants).

Between years 2002 and 2019, an increase in the trend of CRC incidence is observed, with an overall mean annual change of 1.3 % (IS +0.7; +1.8) in both sexes (Tab. 1). However, the overall mean annual change in CRC incidence was higher in women than in men. Specifically, the overall mean annual change in CRC incidence during the study period was 1.1 % (IS +0.5; +1.7) in men and 1.5 % (IS +1.0; +2.0) in women. In both sexes combined, the increase in the CRC incidence trend was most progressive in the period of 2004-2011, with an annual percentage change (APC) of 3.5 % (IS +2.8; +4.2). In men, this trend occurred during the period of 2004–2012 (APC 3.4 %; IS +2.8; +4.1), while in women, it was observed between years 2005 to 2011 (APC 3.3 %; IS +2.3; +4.3). In the subsequent period of 2011–2019, the annual percentage change increased slightly by 0.5 % (IS +0.1; +0.9) when considering both sexes combined. Specifically for women, there was a slightly higher increase in APC, namely by 0.9 % (IS +0.4; +1.3). In contrast, men showed a decrease in APC, albeit not statistically significant.

Table 2 shows that the age-standardised incidence of CRC tended to increase starting with age of 50 years and continued to increase with increasing age. The overall mean annual change in the age group of 50–74 was 1.4 % (IS +0.9; +2.0). However, two cut-off points were identified in this age group in 2004 and 2012, leading to three periods with different trends. An increasing trend in incidence was found between 2004 and 2012, when a 2.8 % annual increase in incidence was observed (IS +2.2; +3.4), while the previous interval between 2002 and 2004 showed a 4.7 % annual decrease in incidence (IS –8.8; –0.5). The rate of increase in the incidence of CRC in the most recent period of years (2012–2019) was significantly lower compared to 1.7 % annual increase (IS +1.1; +2.2) observed in the period of 2004–2012. The same pattern of trend was observed in men (with annual percentage changes of 5.7 %, 2.8 % and 1.3 % or the abovementioned

Tab. 1. Joinpoint analysis of 2002–2019 incidence of colorectal cancer in the Slovakia by sex.

Period	Men		Period	Women		Period	Total (both sexes combined)	
	APC (95 % CI)	AAPC (95 % CI)		APC (95 % CI)	AAPC (95 % CI)		APC (95 % CI)	AAPC (95 % CI)
2002–2019		**1.1* (0.5; 1.7)**	2002–2019		**1.5* (1.0; 2.0)**	2002–2019		**1.3* (0.7; 1.8)**
2002–2004	–3.3 (–7,9; 1,4)		2002–2005	–0.6 (–2.8; 1.7)		2002–2004	–3.2 (–7.1; 0.9)	
2004–2012	**3.4* (2.8; 4.1)**		2005–2011	**3.3* (2.3; 4.3)**		2004–2011	**3.5* (2.8; 4.2)**	
2012–2019	–0.3 (–0.9; 0.2)		2011–2019	**0.9* (0.4; 1.3)**		2011–2019	**0.5* (0.1; 0.9)**	

*Indicates that the Annual Percent Change (APC)/ Average APC is significantly different from zero at the alpha = 0.05 level

Tab. 2. Joinpoint analysis of 2002–2019 incidence of colorectal cancer by sex and age in the Slovakia.

Age group	Period	Men		Period	Women		Period	Total (both sexes combined)	
		APC (95 % CI)	AAPC (95 % CI)		APC (95 % CI)	AAPC (95 % CI)		APC (95 % CI)	AAPC (95 % CI)
25–49	2002–2019		0.4 (–0.9; 1.7)	2002–2019		**0.9* (0.5; 1.2)**	2002–2019		0.6 (–0.2; 1.4)
	2002–2004	–6.3 (–12.7; 0.7)		2002–2011	–0.1 (–0.5; 0.4)		2002–2004	–3.3 (–8.3; 2.0)	
	2004–2008	2.6 (–1.1; 6.4)		2011–2019	**1.9* (1.4; 2.5)**		2004–2017	**0.8* (0.4; 1.1)**	
	2008–2017	0.1 (–0.7; 0.8)					2017–2019	3.6 (–1.5; 8.9)	
	2017–2019	4.5 (–2.4; 12.0)							
50–74	2002–2019		**1.2* (0.5; 1.8)**	2002–2019		**1.6* (1.1; 2.1)**	2002–2019		**1.4* (0.9; 2.0)**
	2002–2004	**–5.7* (–10.4; 0.8)**		2002–2004	–3.0 (–7.3; 1.5)		2002–2004	**–4.7* (–8.8; –0.5)**	
	2004–2012	**2.8* (2.2; 3.5)**		2004–2019	**2.2* (2.1; 2.4)**		2004–2012	**2.8* (2.2; 3.4)**	
	2012–2019	**1.3* (0.7; 2.0)**					2012–2019	**1.7* (1.1; 2.2)**	
75 and more	2002–2019		**1.9* (1.4; 2.5)**	2002–2019		**2.0* (1.6; 2.4)**	2002–2019		**1.9* (1.6; 2.2)**
	2002–2004	–2.1 (–6.4; 2.3)		2002–2005	–0.9 (–2.7; 1.0)		2002–2005	–0.2 (–1.7; 1.3)	
	2004–2012	**5.3* (4.7; 5.8)**		2005–2011	**5.3* (4.5; 6.1)**		2005–2012	**5.1* (4.6; 5.5)**	
	2012–2019	**–0.7* (–1.1; –0.2)**		2011–2019	**0.5* (0.2; 0.9)**		2012–2019	–0.2 (–0.5; 0.1)	

*Indicates that the annual percentage change (APC) / average APC is significantly different from zero at the alpha = 0.05 level

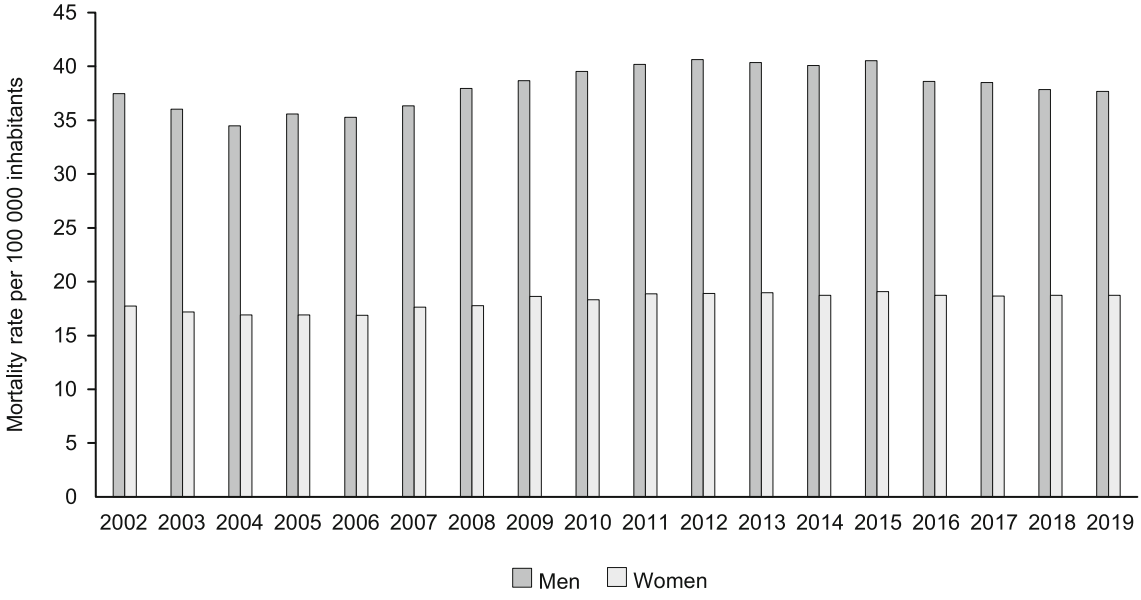

Fig. 3. 2002–2019 mortality from colorectal cancer in the Slovakia by sex.

three consecutive year intervals) but not in women. In women, a 2.2 % annual increase in incidence was observed between 2004 and 2019 (IS +2.1; +2.4). A statistically significant increase in trend was also observed in women in the 25-49 age group (AAPC 0.9 %; IS +0.5; +1.2).

The most pronounced increases in trend were observed in the 75+ age group (AAPC values in men and women were 1.9 %, IS +1.4; +2.5 and 2.0 %, IS +1.6; +2.4, respectively). The most significant annual average increases in the age-standardised incidence rate of CRC was observed between years 2004 and 2012 in women (APC 5.3 %; IS +4.5; +6.1) and in men (APC 5.3 %; IS +4.7; +5.8) in the 75+ age group, and the most significant decrease was observed in the 50–74 age group of men between 2002 and 2004 in men (APC –5.7 %; IS –10.4; +0.8).

Mortality trend from CRC in the Slovakia

Figure 3 shows consistent changes in age-standardised CRC mortality rates for men over the period 2002 to 2019, with smaller changes for women. The highest CRC mortality rate (40.62 per 100,000 population) for men was recorded in 2012 and the lowest

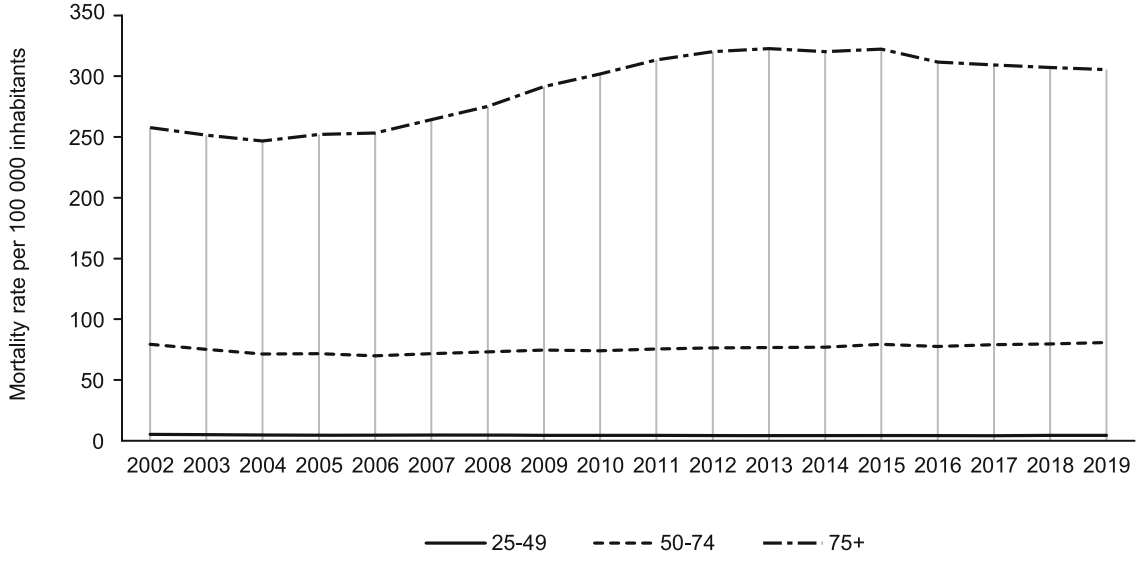

Fig. 4. 2002–2019 mortality from colorectal cancer in the Slovakia by age.

Tab. 3. Joinpoint analysis of 2002–2019 colorectal cancer mortality by sex in the Slovakia.

	Period	APC (95 %CI)	AAPC (95 %CI)
Men	2002–2019		0.0 (–0.5; 0.5)
	2002–2004	**–4.2* (–0.8; –0.3)**	
	2004–2012	**2.2* (1.7; 2.8)**	
	2012–2019	**–1.3* (–1.8; –0.7)**	
Women	**2002–2019**		0.4 (–0.1; 0.8)
	2002–2005	–1.6 (–3.5; 0.2)	
	2005–2011	**2.1* (1.2; 2.9)**	
	2011–2019	–0.2 (–0.6; 0.2)	
Total (both gender)	**2002–2019**		0.1 (–0.3; 0.6)
	2002–2004	**–3.8* (–7.0; –0.4)**	
	2004–2012	**1.9* (1.5; 2.4)**	
	2012–2019	**–0.7* (–1.2; –0.3)**	

*Indicates that the annual percentage change (APC) / average APC is significantly different from zero at the alpha = 0.05 level

in 2004 (34.48 per 100,000 population). For women, the highest mortality rate for CRC was observed in 2015 (19.09 per 100,000 population) and the lowest in 2006 (16.86 per 100,000 population). The mortality rate for men is approximately twice that of women.

Figure 4 shows that there is a clear stratification of colorectal cancer mortality between different age groups. An upward trend in mortality is observed in the age group of 75 years or older, which has the highest mortality from CRC. Specifically, the mortality rate in this age group in 2002 was 257.63 per 100,000 population and increased to 305.60 per 100,000 population in 2019. The CRC mortality rate in the 50–74 age group has remained relatively stable from 2002 to 2019, i.e., the increase was slight and not significant. The mortality rate was 79.37 per 100,000 population in 2002 and 80.86 per 100,000 population in 2019. The lowest mortality rate is observed in the age group of 25–49 years. Since the number of deaths is significantly lower compared to the other 2 age groups, its trend is not clearly shown on the graph.

Table 3 shows that age-standardised CRC mortality rates in the Slovakia have remained relatively stable from 2002 to 2019 (i.e., the increase in rates over this time period was slight and not statistically significant at the 95 % confidence level). During the latter period, two cut-off points linked to years 2004 and 2012 were identified, resulting in three subsets of periods with different trends; An increasing trend in mortality was found between years 2004 and 2012. In this period, a 1.9 % annual increase in mortality was observed (IS +1.5; +2.4), while between years 2002 and 2004 as well as between 2012 and 2019, decreasing mortality trends were observed (3.8 % and 0.7 % annual change, respectively). The same trend was observed for men. Specifically, the percentage annual changes in mortality during the above period are –4.2 % (IS –0.8; –0.3); 2.2 % (IS +1.7; +2.8); –1.3 % (IS –1.8; –0.7). For women, there was a 2.1 % annual increase in mortality during years 2005–2011 (IS +1.2; +2.9).

Table 4 shows a declining trend in mortality in the 25–49-year age group, with an overall annual percentage decline of 0.9 % (IS –1.5; –0.3) between years 2002 and 2019. This trend was also observed for women (AAPC –0.8 %; IS –1.1; –0.5). An increasing trend was observed in the age group 75 years or older (AAPC 1.0 %; IS +0.8; +1.3). Two cutoff points were identified, namely in years 2005 and 2012, resulting in three subsets of periods with different trends. Between the years 2005 and 2012, there was an increasing trend in mortality with a 4.0 % annual increase (IS +3.6; +4.5), whereas during the periods 2002–2005 and 2012–2019, a decreasing trend in mortality was observed with annual changes of 1.3 % and 0.9 %, respectively. In this age group, both men and women exhibited increasing trends, namely with AAPC of 1.1 % (IS +0.6; +1.5 and AAPC of 1.1 % (IS +0.8; +1.4), respectively. In the 50–74-year age group, we found one cut-off point, namely in the year 2004, resulting in the division of the latter period into two subsets of periods with different trends, specifically an increasing trend in mortality was found in the period 2004–2019, with an overall average annual change of 0.9 % (IS +0.7; +1.0), whereas in the previous period of 2002–2004 there was a trend towards a decrease in mortality with AAPC of –5.8 % (IS –9.0; +2.4). We identified a

Tab. 4. Joinpoint analysis of 2002–2019 colorectal cancer mortality by sex and age in the Slovakia.

Age group	Period	Men		Period	Women		Period	Total (both sexes combined)	
		APC (95 %CI)	AAPC (95 %CI)		APC (95 %CI)	AAPC (95 %CI)		APC (95 %CI)	AAPC (95 %CI)
25–49	2002–2019		–1.0 (–2.2; 0.2)	2002–2019		**–0.8* (–1.1; –0.5)**	2002–2019		**–0.9* (–1.5; –0.3)**
	2002–2004	**–7.3* (–13.1; –1.2)**		2002–2012	**–2.0* (–2.3; –1.6)**		2002–2004	–5.0 (–9.1; –0.7)	
	2004–2008	0.3 (–3.0; 3.7)		2012–2019	**0.9* (0.2; 1.6)**		2004–2016	**–1.0* (–1.3; –0.7)**	
	2008–2017	**–1.3* (–2.1; –0.6)**					2016–2019	2.2 (–0.2; 4.7)	
	2017–2019	4.4 (–2.6; 11.9)							
50–74	2002–2019		–0.1 (–0.6; 0.4)	2002–2019		**0.2* (–0.1; 0.5)**	2002–2019		0.1 (–0.3; 0.5)
	2002–2004	**–6.4* (–10.6; –2.0)**		2002–2005	**–3.2* (–4.9; –1.4)**		2002–2004	**–5.8* (–9.0; –2.4)**	
	2004–2019	**0.8* (0.6; 1.0)**		2005–2019	**0.9* (0.8; 1.1)**		2004–2019	**0.9* (0.7; 1.0)**	
75 and more	2002–2019		**1.1* (0.6; 1.5)**	2002–2019		**1.1* (0.8; 1.4)**	2002–2019		**1.0* (0.8; 1.3)**
	2002–2006	0.3 (–1.1; 1.7)		2002–2005	–1.4 (–2.9; 0.2)		2002–2005	**–1.3* (–2.5; –0.0)**	
	2006–2012	**4.7* (3.8; 5.7)**		2005–2012	**3.8* (3.3; 4.4)**		2005–2012	**4.0* (3.6; 4.5)**	
	2012–2019	**–1.5* (–2.1; –1.0)**		2012–2019	**–0.5* (– 0.9; –0.1)**		2012–2019	**–0.9* (–1.2; –0.6)**	

*Indicates that the annual percentage change (APC) / average APC is significantly different from zero at the alpha = 0.05 level

similar cut-off point in both men (in year 2004) and women (in year 2005). The most pronounced annual mean increase in age-standardized CRC mortality was observed in the age group 75+ years in both men and women, specifically in the period of 2006–2012 in men (APC 4.7 %; IS +3.8; +5.7) and in 2005–2012 in women (APC 3.8 %; IS +3.3; +4.4), while the most significant trend declines in men were observed in the age group of 25–49 years in the period of 2002–2004 (APC –7.3 %; IS –13.1; –1.2) while in women the most pronounced decline took place in the period of 2002–2005 (APC –3.2 %; IS –4.9; –1.4) in the 50–74 age group.

Discussion

Main finding

Between years 2002 and 2019, the overall trend in colorectal cancer incidence continued to increase, with an overall average annual change of 1.3 %. The trend of CRC incidence tended to gain momentum at the age 50 years and the increase further accelerated with age. The most pronounced increasing trend was observed in the age group of 75 years or older (AAPC of 1.9 % in men (IS +1.4; +2.5) and AAPC of 2.0 % in women (IS +1.6; +2.4). CRC mortality remained relatively stable over the 18-year follow-up period. A decreasing trend in mortality was observed in the 25–49-year age group with an overall annual percentage decrease of 0.9 % (IS –1.5; –0.3), while an increasing trend was observed in the 75+ age group with an overall annual percentage increase of 1.0 % (IS +0.8; +1.3). The incidence and mortality rates in men were higher than in women.

Interpretation of findings

In this work, we selected a time period of 18 years for the analysis, specifically from the initiation of the screening programme in Slovakia in 2002 until 2019. It is worth noting that the pilot period associated with the implementation of a central organised invitation screening programme using immunochemical TOKS started on 1st of January 2019. The time interval from 2002 to 2019 was chosen for two main reasons. The first reason is that we can provide an overview of colorectal cancer trends in Slovakia that follow the previously reported NOR (National Oncology Registry) period from 1971–2001. The second reason is that it can help us better review the impact of introducing the colorectal cancer screening programme on the trend of colorectal cancer in the Slovakia.

The results of our work indicate that the incidence and mortality rates in men are higher than in women. This conclusion is not fully explained and is probably the result of a combination of greater awareness of screening in women, sex-specific exposure to risk factors, and the protective effects of both endogenous and exogenous hormones. This result is similar to the general situation in the world. The age-standardised (world) prevalence of CRC per 100,000 people in 2018 for both sexes combined is 19.7, 23.6 specifically for men and 16.3 for women (9). This is consistent with the results of Siegel et al. who report in their study that in 2017 in the U.S., the incidence and mortality rates for men are 30 % and 40 %, respectively (10). This is also in line with the findings of the author Somnath Pal in 2018, where the overall incidence of new cases was higher in men than in women (42.1 vs 32.3). The mortality rate in men was higher than in women (16 vs 11.4) (11).

Incidence

The results of this work on colorectal cancer in the Slovakia provided a conclusion of CRC incidence of 56.45 cases per 100,000 inhabitants in 2019. This result is much higher than the European average. The incidence of colorectal cancer in Europe is 28.8–32.1 cases per 100,000 inhabitants (12). This result may reflect the current situation. In a new study, researchers from the International Agency for Research on Cancer (IARC) provide estimates of the incidence and mortality of colorectal cancer in 185 countries in 2020 and predictions of the future burden in 2040. Europe was one of the regions with the highest incidence of CRC (13).The data on colorectal cancer indicate a high prevalence in Central and Eastern Europe. Countries such as Hungary, Slovakia, and Croatia are leading (14). In addition to this, the results of the work also showed an increasing trend in the incidence rate of CRC over the period 2002 to 2019 in both sexes. This result is in line with the results of Øystein Høydahl et al who researched the period of 1980–2016 in central Norway. The incidence of CRC increased from 43/100,000 person-years in 1980–1984 to 84/100,000 person-years in 2012–2016 (15). In general, the increasing trend of colorectal cancer incidence throughout the 2002–2019 period had a decreasing trend in the growth rate with an overall average annual change of 1.3 % (IS +0.7; +1.8) compared to the previous period. According to the National Cancer Registry (NCR), which recorded the development of colorectal cancer (CRC) incidence and mortality in men and women in Slovakia (1971–2001), every 10 years. the incidence of CRC increased by 10 % in men and by approximately 6 % in women (16). This result can be explained by the effectiveness of the colorectal cancer screening programme in Slovakia. Compared to no screening, the biennial faecal immunochemical test (FIT) would detect 29,600 CRC cases while annual FIT would detect 37,800 CRC cases. Mortality due to CRC showed benefits for both strategies with 17.38 % reduction in biennial FIT and 24.67 % reduction in annual FIT approach (17). However, the overall trend of the incidence of CRC in both men and women has continued to increase over the last two decades. This may be because the 50 % participation in screening level has not yet been reached (15 % participation during the first phase increased to just over 30 %), which is essential if a sustained decline in incidence and mortality at the population level is to be achieved (16). In addition, one of the possible reasons for the reduction in the effectiveness of the screening program could be the cost and public risk concerns. Among series of clinical examinations, colonoscopy has been proposed as a gold standard to determine the prognosis of adenoma of the colon and CRC in many countries. However, with respect to the previous studies, the technique entails substantial risk and/or cost. Thus, there is a growing interest in investigating novel markers for the detection of asymptomatic early-stage CRC that are both efficient or cost-effective, for example intestinal bacteria *S. bovis* and *F. nucleatum* have been highlighted as novel tools for early-stage CRC diagnosis (18).

The results of this work also show that the incidence rates have been steadily increasing since 2004, but during the period of 2011–2019, the upward trend has slowed down, almost coming to a standstill. This result can be explained by the impact of the established colorectal cancer screening programme in Slovakia. The exact cause of CRC has not yet been identified although genome-wide association may play a role in its development. One study emphasizes the possibility of existence of a high risk of CRC development in patients with TT genotype of rs7903146 (19). Hereditary CRC syndromes account for approximately 5–10 % of all CRC cases, with a lifetime risk of CRC that approaches 50–80 % in the absence of endoscopic or surgical treatment (20). However, the treatment of CRC is very complex, and if not treated early, the chance of successful treatment is compromised. Therefore, regular screening for colorectal cancer can be considered as one of the optimal measures against CRC. The screening programme was launched in Slovakia in 2002 (13), this was the first time the patients had access to CRC screening through GPs. Cases of latent cancers were caught early, which led to an increase in the number of CRC cases. The standstill in the rise in incidence in the later period can be partly explained by the fact that a larger number of latent cases was detected. although a shift to greater awareness of the disease among people and the ability to prevent it promptly may have served as contributing factors.

The incidence of colorectal cancer is higher in men than in women, but the overall mean annual change in the incidence of CRC in women (AAPC 1.5 %; IS +1.0; +2.0) was greater than in men (AAPC 1.1 %; IS +0.5; +1.7). This heightens the need of questioning the trend in the incidence of CRC in women in the Slovakia.

A statistically significant increase in trend was also observed for women in the age group of 25–49 years (AAPC 0.9 %; IS +0.5; +1.2). More specifically, a 1.9 % annual increase in the incidence has been observed in the most recent period 2011–2019 (IS +1.4; +2.5). This result is in line with the trend of colorectal cancer incidence in younger age groups observed in recent years and confirmed by the results of research conducted by Vuik et al, who collected and analysed data on 143.7 million people aged 20–49 years from 20 European countries (1990–2016). Of this number, 187,918 (0.13 %) were diagnosed with CRC. On average, the 2004–2016 prevalence of CRC increased by 7.9 % per year in people aged 20 to 29 years. The 2005–2016 increase in the 30–39-year age group was 4.9 % per year, and the 2004–2016 increase in the 40–49 age group was 1.6 % per year. This result is consistent with that of Sifaki-Pistolla et al who conducted research on Crete (Greece) from 1992–2021. The average age-specific incidence rate (ASpIR/100,000/year) yielded a 29.6 % increase from 2001 to 2011 in the age group 20–34 years, and a further increase is expected during the period of 2022–2030 (projected change of 42.8 %) (21). In addition to this, according to research by Vuik et al, in England (1999, 2009, 2019 and 2020), in the younger adult population aged <40 years, the incidence rates have increased sevenfold over three decades, with a disproportionate increase in women compared to men (22). Similar, this result is consistent with that of Wong et al who conducted research in 2021 in 39 countries in relation to age, sex, and anatomic location (colon vs rectum). Twelve of 36 countries (all from Asia and Europe) yielded an increase in colon cancer incidence among women. The incidence of rectal cancer in women decreased in 8 countries. Rectal cancer incidence increased among women younger than 50 years, while it decreased in women older than 50 years. In countries such as Costa Rica, Slovenia, Japan, Slovakia, Canada, and the United States, the overall incidence increased, but their elder population had either a stable or decreased incidence (23).

The results of this work also showed that incidence rates began to increase sharply after the age of 50, and thereafter, their progression accelerated with age. This result is consistent with those by Siegel et al from the USA (1995–2016), who report that the incidence rates escalate rapidly with age. Up to the age of 50 years, they approximately double each 5-year accruement in age and thereafter, they increase by approximately 30 % in subsequent age groups 55 years and older (24). The incidence rate in our study was highest in the age group of 75 years or older. Cancer statistics from 2022 say that the incidence is strongly associated with age, with the highest incidence in the elderly. In the UK in 2016–2018, on average, more than 4 in 10 new cases (43 %) were recorded each year in people aged 75 or older (25). These results suggest that future decisions should continue to be considered to screen people aged 76 to 85 years. According to research by Chan et al in the US (findings published in JAMA Oncology on 20 May 2021)., colorectal cancer screening also appears to benefit people over 75 years of age. His team found that the risk of dying from colorectal cancer was reduced by more than one third in people over 75 who underwent colonoscopy or sigmoidoscopy, compared to people in the same age group who did not undergo any of these screening tests (26).

Mortality

Our results showed that the age-standardised mortality rate for CRC in the Slovakia remained relatively stable from 2002 to 2019. This result is consistent with that of Moura et al, who conducted research in Brazil between years 1996 and 2015. For both sexes, mortality was stable (27). In our work, mortality tends to decrease with an annual change of 0.9 % between years 2012 and 2019 (IS –1.2; –0.3). This result is somewhat similar to the general trend in Europe. According to the results of the author Driss Ait Ouakrim's research in Europe, from 1989 to 2011 there was a smaller or no decrease in colorectal cancer mortality in most Central European countries (28). This is a positive result. This is due to the positive impact of the colorectal cancer screening programme in Slovakia.

In our study, a decreasing trend in mortality was observed in the 25–49-year age group with an overall annual percentage decrease of 0.9 % (IS –1.5; –0.3). This is in line with the results of Vuik et al, who conducted research in Europe between years1990 and 2016. CRC mortality did not change significantly among young adults but decreased by 1.1 % per year between years1990 and 2016, and by 2.4 % per year between years1990 and 2009 for those aged 30–39 or 40–49 years (29). This is a desirable result. Although there has been an increase in the incidence of colorectal cancer in these age groups, the mortality rate is still on a downward trend. However, in our work, we found an increasing trend

in mortality among women in the age group of 25–49 years in the period of 2012–2019. The rise of incidence within this age group gives us an alarming signal for strengthening the prevention. It highlights the need for increased attention toward women, as well as emphasises the importance of proactive detection and treatment of underlying causes.

The results of the study showed that in the initial period of the study (2002–2004), the mortality rate for colorectal cancer in the age group of 50–74 years decreased dramatically with an annual change of 5.8 %. However, during the time frame of the subsequent long-term follow-up period of 2004–2019 the trend gained an upward trajectory. This result is particularly surprising because screening, which can both prevent the development of cancer and detect the disease early when there is a chance of successful treatment, is recommended for patients over 50 years of age and was introduced in Slovakia in 2002.

Our results also showed an increasing trend in the age group of 75 years or older (AAPC 1.0 %, IS +0.8; +1.3). This result is also similar to the research results of Orive et al, where among the patients' sociodemographic characteristics, being older and male were related to higher mortality (30). It is also consistent with the result of Mondschein et al who focused on the years 2009 to 2018 in their research in Chile. In their study, the survival was shorter in people over 70 years of age, but with no significant differences in the younger age groups (31). This can also be explained by the fact that people in this age group often suffer from poor health (polymorbidity) and deficient mobility which forces them to stay mainly at home and diminishes their access to information on the availability of screening programmes as compared to younger age groups. Cognitive decline is not inevitable in older adults as some individulas within the normal range may show signs of decline at 60 years of age (23) Therefore, when the disease is detected in late stages, along with the health conditions that accompany old age, it leads to a higher probability of death. When cancer metastasises to distant parts of the body, the 5-year survival rate is 15 % (32). According to the results of research by Bos et al, in the Netherlands between years 2008 and 2013, the excess mortality per year increased with age (17.3 % for colon cancer patients or 12.9 % for rectal cancer patients <85 years) (33). According to GLOBOCAN 2018 data, this result is not consistent with the results of Prashanth Rawla et al. Mortality rates have declined overall, with the most significant decline seen in the 75+ age group (9).

In addition, a downward trend was observed in the most recent period of 2012–2019 with a 0.9 % annual change. This partly reflects the positive impact of the Slovakian CRC screening programme. When the colorectal cancer screening programme was introduced into the population, latent cases were detected at an early stage. Screening is also beneficial for the introduction of early disease treatment, which reduces the mortality rate of colorectal cancer in the population. In addition to this, changes in mortality over time may be due to a variety of factors including demographic characteristics, lifestyle, disease awareness, screening, and access to effective treatment. However, in general, temporal changes in mortality are difficult to interpret because they are influenced by trends over time in incidence and survival. Incidence rates may be a more appropriate indicator of trends in disease incidence. The incidence of CRC is not affected by changes in treatment and survival, although it has been shown to be affected by improved diagnostic techniques and screening programmes (34).

Implications, strengths, and limitations

The results of this work show an overall trend in colorectal cancer incidence and mortality (by sex, age groups). In this work, the incidence and mortality rates were standardised by age. There are also limitations to our study. Due to the unavailability of the data, there is a relatively large gap between the age groups included in the analysis of the work, making it difficult to show accurate disease trends between age groups.

Instructions for future research

Based on our findings, we recommend that future research focuses on evaluating the effectiveness of the introduction of a CRC screening programme and investigating the situation of colorectal cancer in Slovakia.

Conclusions

The situation of colorectal cancer in Slovakia has improved compared to the previous period (1971–2001). However, the incidence rate for colorectal cancer is still on an upward trend, but this upward trend undergoes constant change. The mortality rate for CRC remained relatively stable from 2002 to 2019. However, preventive measures require a gradually intensified effort to maintain the results achieved and to continuously improve the situation.

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