doi:10.4149/neo_2011_04_283

Do we know the cause of the highest colorectal cancer incidence, the changes in the mortality trends and the clinical stages in the Slovak and Czech Republic, the representatives of the Central European region?

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Received December 27, 2010

Slovak (SR) and Czech (CR) Republics reach up the highest recorded incidence rates of colorectal cancer. In analysis of the development and changes in colorectal cancer incidence in the above-mentioned countries, it was reported the most considerable incidence increase of the disease in males in the SR, then in males in the CR, subsequently in females in the SR and the slowest incidence rate was reported in females in the CR. Colorectal cancer mortality increased most rapidly in males in the SR, then in males in the CR, slower increase was reported in females in the SR and in females in the CR the mortality was in the long term stabilized. In both countries and both sexes clinical stage II is noted most frequently, also the decrease of the disease number in the clinical stage I and in undefined stage, and a slight decrease in other clinical stages. The trends in risk factors of colorectal cancer in the SR and CR would support the hypotheses of the later culmination of incidence and on the higher levels than in other developed countries. The purpose of this study is to analyse the character and changes in development of incidence, mortality and clinical stages of colorectal cancer (1980-2005) and to assess the influence of selected risk factors on the highest disease incidence in above-mentioned two Central European countries.

Key words: colorectal cancer: incidence, mortality, clinical stages, screening, risk factors

Colorectal cancer used to be a rare diagnosis in the beginning of 20th century, however, after commencing economic development in the countries its incidence started to increase steeply. In countries with high incidence rates colorectal cancer is among the most frequent malignancies, whereas in the countries with the low risk it is a rare malignancy which indicates the fact that the majority of colorectal cancers is preventable. In 2008 the estimates of worldwide incidence achieved 663,612 newly diagnosed cases in males and 570,099 in females, which represents 9.7% of the total number 12 667 470 of estimated malignant tumours in both sexes together. Colorectal cancer is placed third in the incidence of all malignancies in males (after lung cancer and prostate cancer except for non-melanoma skin tumours) and second in females (after breast cancer except for non-melanoma skin tumours). In 2008 mortality was estimated on 320,595 cases in males and 288,049 in females, therefore about 8% of all deaths due to malignancies [1].

The purpose of this study is to analyse the incidence of colorectal cancer and resulting mortality and the possible reasons for any differences discovered in two neighbouring countries in the Central Europe (the Slovak and Czech Republic), both of which have national, population-based cancer registries. When the global age-adjusted (WSR) incidence is compared, the Czech Republic (hereafter CR) was a country with the highest incidence in Europe in 2002 [2]. However in the Slovak Republic constantly enhancing disease incidence trend is observed, while in the CR it has a stabilized character, thus in the last analysed year 2005 the SR overtook CR in the standardized disease incidence rates.

This paper compares the results of detected analyses of time progress of colorectal cancer incidence and mortality in the CR and SR, discusses possible causal factors of their highest global incidence and compares the results with selected world countries.

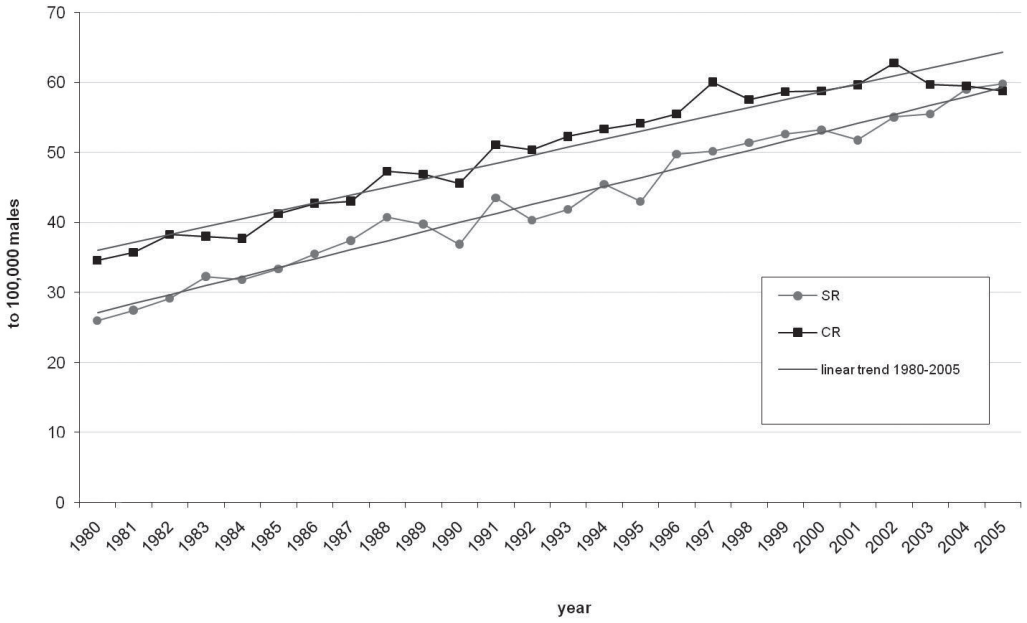

Figure 1. Trends of age-adjusted (WSR) colorectal cancer incidence in males in the Slovak (SR) and Czech (CR) Republic.

Material and methods

The data concerning the incidence of colorectal cancer used in this analysis were obtained from the pre-processed data portals of the National Cancer Registry (hereafter NCR) SR [4] and the NCR CR [5] valid until the end of July 2009 as well as from the standard outcomes and annual reports of the NCR SR and the NCR CR. These registries are national population-based cancer registries with high quality data [6]. Analyses of the overall incidence and mortality take into account the period 1980-2005 in which both countries have validated data. Corresponding national mortality data were obtained from the Statistical Office of the SR and from the NCR CR. The values of incidence and mortality are presented in the form of crude rates in the last statistically closed year 2005. The comparison with other countries is only possible after correction of different age structure in the population. The standardization to the world standard population was performed [7] and the standardized rates (WSR) in the CR and SR have been compared. The trends in incidence and mortality have been extracted using linear regression model separately for each gender and country in time periods 1980-2005 and the trends are presented with corresponding 95% Confidence Intervals (CI) and p-value with null hypothesis being constant with time.

Analysis of clinical stages of the disease was carried out up to the year with the last available data on stages in the SR (year 2003) [4] concerning the differences in particular revisions of TNM which were used in processing of the reports on malignancies.

Results

In 2005 in the SR 2001 colorectal cancers in males were diagnosed, which represents crude incidence rates 76.5/100 000, standardized (WSR) 59.8/100 000 (CI 95% ±2,6841). Estimated average annual increase of WSR colorectal cancer incidence in males in 1980-2005 was 1.286/100 000 (CI 95% =1.193-1.379, $p<0.0001$), disease increase index was 2.3. Increasing character of incidence (Fig. 1) is more significant than in females in the SR. In the same year in females 1392 cases of colorectal cancer were diagnosed (crude incidence rates 50.2/100 000, WSR 28/100 000, CI 95% ±1.5760). Estimated average annual increase of WSR incidence rates in females in 1980-2005 was 0.432/100 000 (CI 95% =0.381-0.484, $p<0.0001$), index of the disease number increase represented 1.61. Incidence in females has constantly and without any significant annual fluctuation increasing character (Fig. 2) which is, however, significantly slower than in males in the SR and CR.

In 2005 in Slovakia 1052 males died of colorectal cancer, which represented crude mortality rates 40.2/100 000 and WSR mortality 30.8/100 000 (CI 95% ±1.9153). Average annual growth of WSR mortality represented in males in 1980-2005 0.655/100 000 (CI 95% =0.554-0.755, $p<0.0001$), index of death number increase was 1.9. Incidence in males grew up almost twice as rapid as mortality, but mortality increased at the same time more rapidly than in Slovak females (Fig. 3). In the same year in females 700 deaths were reported, crude mortality rates 25.2/100 000, WSR 13/100 000 (CI 95% ±1.0475). Estimate of the expected average annual growth

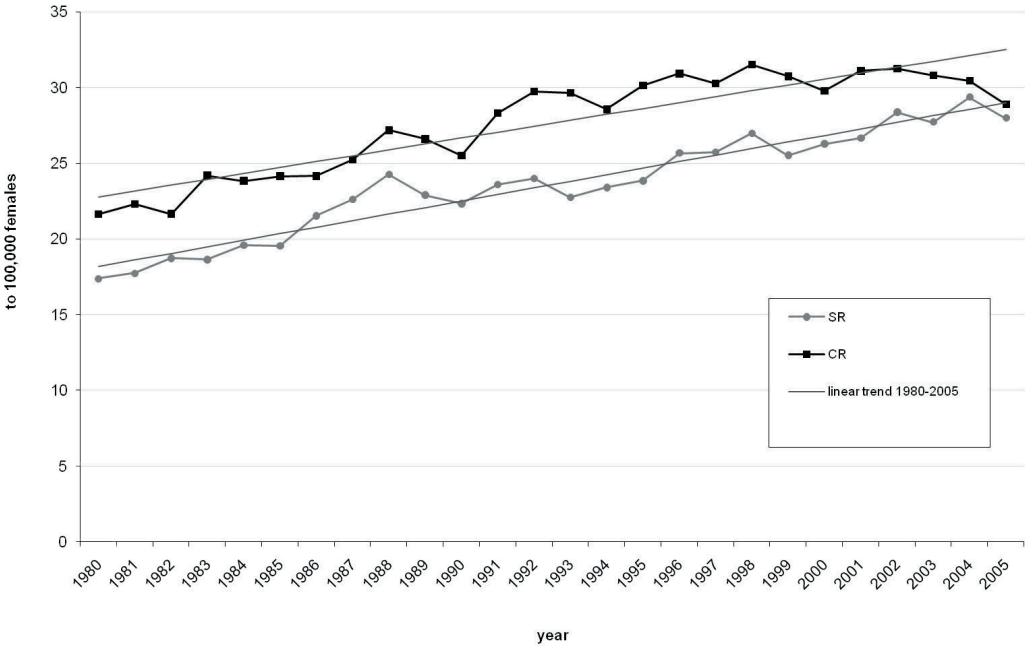

Figure 2. Trends of age-adjusted (WSR) colorectal cancer incidence in females in the Slovak (SR) and Czech (CR) Republic.

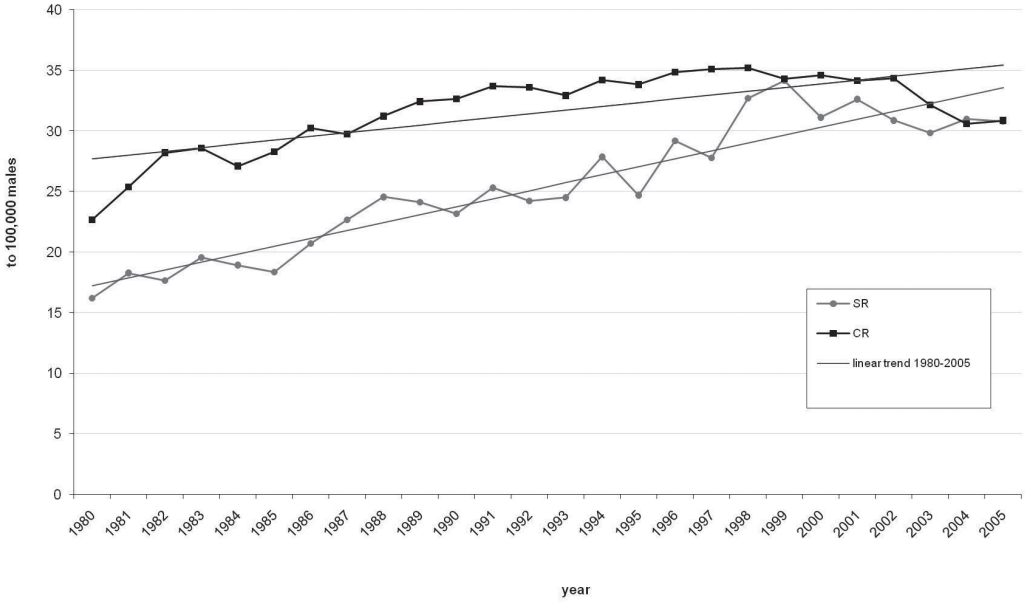

Figure 3. Trends of age-adjusted (WSR) colorectal cancer mortality in males in the Slovak (SR) and Czech (CR) Republic.

of WSR mortality in 1980-2005 was 0.137/100 000 (CI 95% =0.085-0.190, p<0.0001), index of death number increase was 1.17. Mortality grew up significantly slower than the incidence, but concurrently more rapidly than mortality in females in the CR (Fig. 4).

In 2005 in the CR 4798 colorectal cancer cases in males were diagnosed, which represented crude incidence rates 95.9/100 000, WSR 58.8/100 000 (CI 95% ± 1.7195). Average estimated annual growth of incidence in males was in 1980-2005 1.129/100 000 (CI 95% =1.009-1.248, p<0.0001), index of disease number increase was 1.7. Incidence had increasing trend (Fig. 1), which is significantly more rapid than incidence in females both in the CR and SR. In 2005 in the CR 3 279 cases of colorectal cancers in females

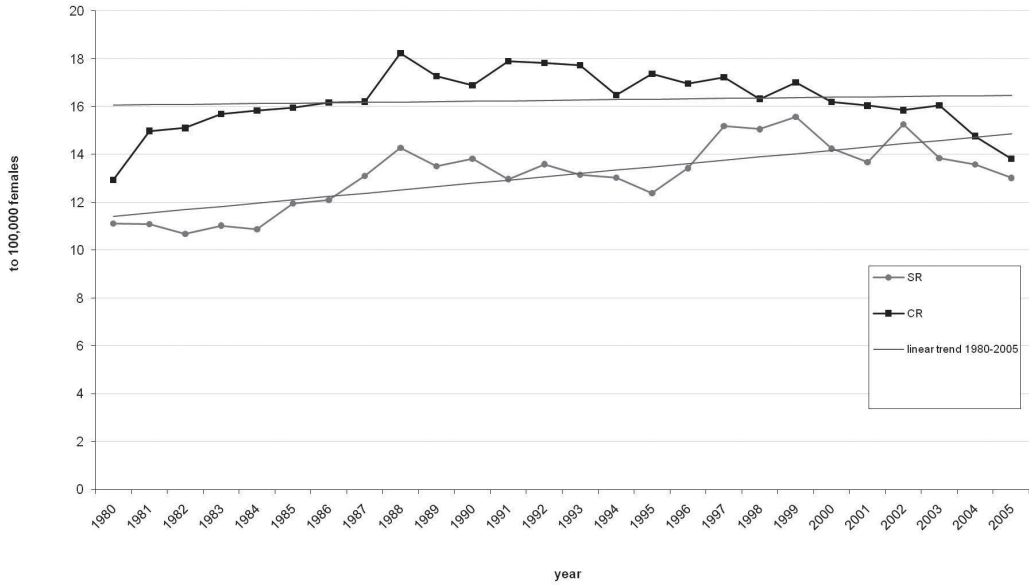

Table 4. Trends of age-adjusted (WSR) colorectal cancer mortality in females in the Slovak (SR) and Czech (CR) Republic.

were diagnosed which represented crude incidence rates 62.5/100 000 and WSR 28.9/100 000 (CI 95% ± 1.0878). In females the average annual incidence increase in 1980-2005 was 0.390/100 000 (CI 95% =0.313-0.466, p<0.0001), index of disease number increase was 1.34. Incidence increase in females (in the CR as well as in the SR) is comparable (Fig. 2), and it is concurrently slower than in males both in the SR and CR.

In the CR in 2005 2 579 males with colorectal cancer died (crude mortality rates 51.6/100 000, WSR 309/100 000, CI 95% ± 1.2402). Average annual increase of WSR mortality in 1980-2005 was 0.309 (CI 95% =0.184-0.433, p<0.0001), index of death number increase was 1.36. Enhancement of death rate was significantly slower than in males in the SR (fig. 3), but concurrently significantly more rapid than in females both in the SR and CR. In females in the same year 1 767 deaths were reported, crude mortality rates 33.7/100 000, WSR 13.8/100 000 (CI 95% ± 1.7142). Average annual increase of WSR mortality in 1980-2005 was 0.016 (CI 95% =-0.053-0.084, p=0.639), index of death number increase was 1.07. Neither decline nor raise of mortality were confirmed (mortality was stabilised) (Fig. 4).

Most frequent clinical stage of the disease at the time of diagnosis in 2003 was in both countries the clinical stage II (SR – 23.2 %, CR – 26 %), nevertheless (in 1980-2003) decrease of the disease number in clinical stage I and in undefined stage were reported overall, as well as the slight increase of the disease number in other clinical stages (Fig. 5, 6). In females in 2003 the disease was diagnosed most frequently in clinical stage II (SR – 25.2 %, CR – 24 %), however in females the decrease of the disease number diagnosed in clinical stage I and undefined stage were reported as well.

Discussion

Age-adjusted incidence rates of colorectal cancer vary markedly among the countries all over the world. Population studies refer to an increasing trend of the disease incidence mostly in developing countries worldwide, while the increase reflects the changes in dietary habits and the lack of physical activity. The highest incidence rates are registered in the countries in Europe, North America and Oceania. Conversely, the lowest rates are in Asia, Africa and South America [8]. In analysis Center et al. [9] significant increase of the disease incidence rate assessed from 1983-1987 to 1998-2002 in 27 from 51 surveyed countries worldwide was reported. In Europe the highest incidence increase in evaluated period was observed in the Slovak Republic, Slovenia and the Czech Republic (more than 45 % in males and 25 % in females), in these countries due to the data collected on a long-term basis the increase has been observed since 1963-1967. Out of 55 evaluated countries the highest incidence was reported in the CR, the SR was placed 4th [9], however the estimates for year 2008 place the CR as the first in a worldwide rank of the colorectal cancer incidence (WSR) 60.7/100 000 in males, while the SR is placed 3rd (after the CR and Hungary) with slightly lower incidence rates (WSR) 60.6/100 000 in males. Situation in females is rather different, in global estimates of the disease incidence in 2008 the CR was placed 13th and SR 14th with the number of cases (WSR) 29.6 (CR) and 29.2 (SR)/100 000. The first three positions belong to New Zealand (37.5/100 000), Israel (36.3/100 000) and Norway (35.2/100 000). In spite of the fact that recently (in 2002-2005) stabilization or slight decline of the disease number both in males and females (after their previous culmination in 2001) has been noticed in the CR,

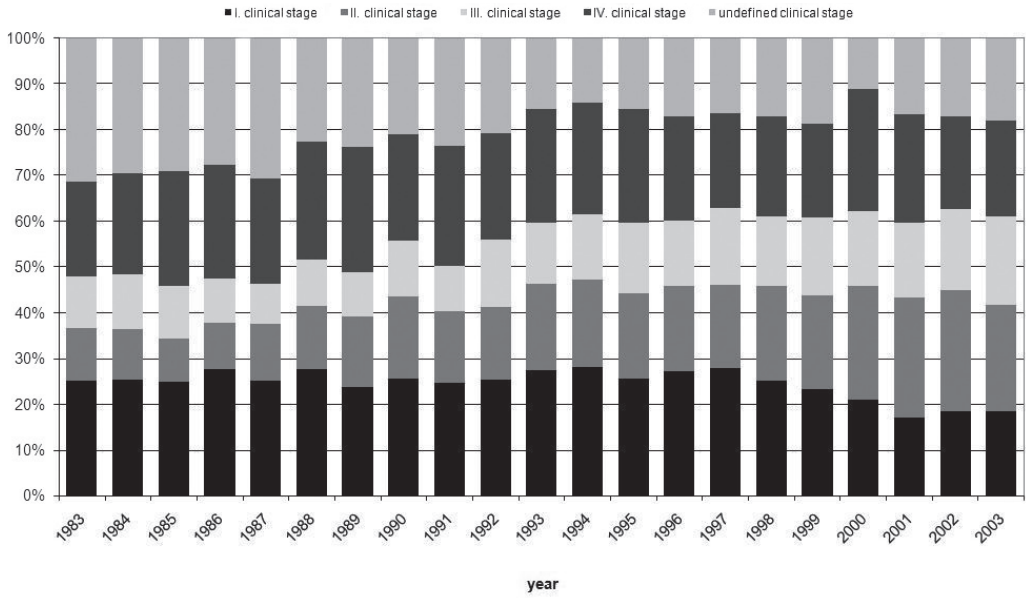

Figure 5. Clinical stages of colorectal cancer in males in the Slovak Republic.

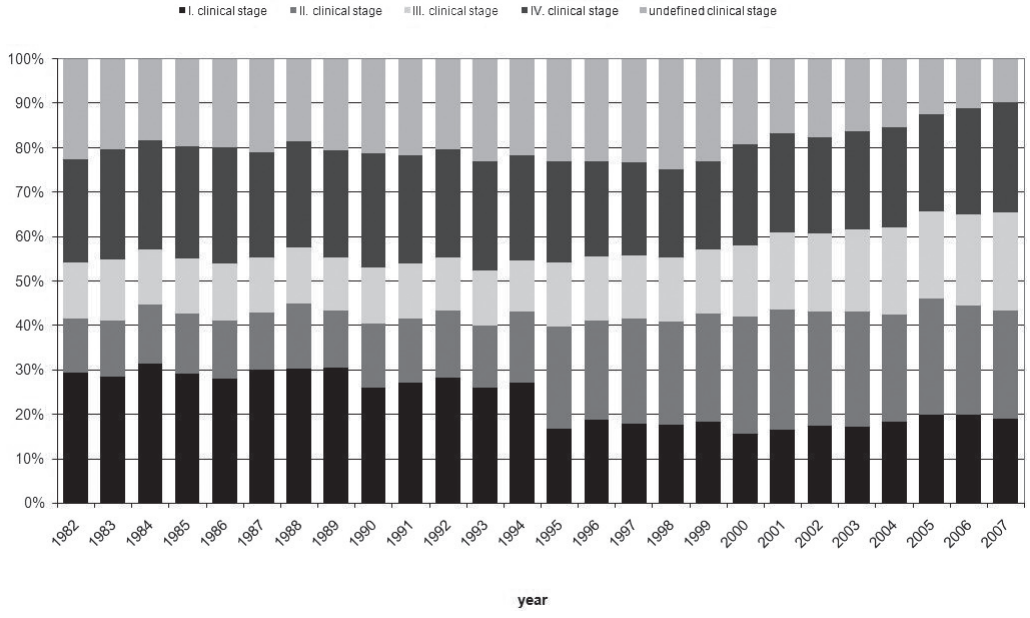

Figure 6. Clinical stages of colorectal cancer in males in the Czech Republic.

in the SR this trend has not been confirmed yet (despite the opportune screening carried out since 2002) and the disease incidence has rising tendency. Probable cause of increasing incidence in the SR might be poor participation on preventive examination reaching 15% over 5 years (from planned screening introduction in 2000). Comparing the development of time trends in the disease incidence in the CR and SR more rapid increase of standardized disease incidence from 1980 (to 2005) has been observed both in males and females in the SR, which places the SR – in case of the last year 2005 in males – in the incidence rates before the CR [3, 10, 11]. Incidence of colorectal cancer in males exceeded in the CR and SR the highest rates of the incidence culmination in developed countries such as New Zealand, USA and Australia, which in the previous period showed the highest rates of overall incidence [8]. Are we able to explain which factors might influence the

high incidence rates and also mortality in the region of the Central Europe, particularly in the SR and CR?

Temporal increase and culmination of the disease incidence is observed in the countries with well organized screening, as all the screening tests including occult bleeding and colonoscopy detect also previously non-diagnosed cases. Opportunistic and population screening enhance the probability of the detection and successive opportunity of adenomatous polyps removal, as well as the identification of the early disease stages with more favourable prognosis [12]. Colonoscopy, as a screening method, can participate in a subsequent decline in disease incidence under the influence of precancerous polyps removal [9]. Overall screening impact on the incidence (and subsequently mortality) rate is difficult to explicate. Long-term screening programmes ongoing in the last two decades in USA participate significantly on the incidence and mortality reduction. Short-term screenings carried out in the majority of European countries, including the CR and SR, recently have probably less impact on mortality, whereas disease incidence according to analyses [12] in the last decade was slightly increasing mostly in males in Austria, Slovenia, Spain and the CR, while in other countries in males and in almost all European countries in females (excepting Spain) it had decreasing tendency (the SR has not been included to analyses [12]). Worldwide differences in colorectal cancer incidence might be influenced by the differences in prevalence of the risk factors and intensity of screening programmes application. Well known and suspected risk factors including obesity, insufficient physical activity, smoking, heavy consumption of alcohol and diet rich in red and smoked meat, as well as inadequate consumption of fruit and vegetable are linked to the development of economy and Western lifestyle in the countries [9], which is probably more striking in the CR comparing with the SR, and can support the theory of the higher overall disease incidence in the CR. In post-communist countries of the Central and Eastern Europe the increase of the colorectal cancer incidence is influenced according to Knai [13] mostly by the raising obesity prevalence. However, according to the WHO Country-wide Integrated Non-communicable Disease Intervention Programme (CINDI) [14] the decrease of the obesity/overweight prevalence occurred in Slovakia (values reached minus 5.3% in men and minus 1.3% in women in 1998-2003). Since the earlier national data in the SR are not available, the possible impact of obesity/overweight decrease in the last years on the development of incidence and mortality of colorectal cancer might be noticeable within the next decade. Data in time changes in obesity/overweight prevalence in the CR are not available. According to the results of CINDI project [14] prevalence of smoking in the SR, as one of the risk factors of the disease, was significantly decreased in males (by -6.5%), in females it was non-significant decline by -0.8%. According to Tyczynski (15) activities focusing on the reduction of tobacco smoking prevalence had already been introduced in countries of Central and Eastern Europe (the SR and CR included) by 1980s or even later. The prevalence of male-smokers was in the SR in 1990s about 55 % and in 2000 about 44 %, in the CR in 1990s it was about 43 % and in 2000 about 36%. Similar situation was recorded also in female-smokers, the prevalence in the SR in 1990s was about 29 %, in 2000 about 15%, in the CR in 1990s it was about 31 % and in 2000 about 22%. However, tobacco use among young people continues to rise as the industry aggressively promotes its products to potential new customers. The highest increase in prevalence of young male-smokers was recorded in the SR and CR (together with Slovenia and Lithuania), in young female-smokers the situation was even worse, the prevalence had increased in all the countries studied (15). Concerning the SR, these results are supported also by the national project of the Statistical Office of the Slovak Republic [16], according to which particularly from 2002 in Slovakia the number of regular and occasional smokers decreases and the number of non-smokers increases (up to 62% in adult population in the last assessed year). These trends would in case of the SR and CR support the hypotheses [9] that the later decrease of smoking prevalence in the Central European countries indicates later culmination of colorectal cancer incidence and on the higher levels than in e.g. USA [9]. Differences in the incidence levels between males and females (not only) in the SR and CR and particularly slowlier increase of the disease incidence in females can reflect slowlier adaptation to certain risk behaviour related to the disease. For example smoking prevalence in females is delayed worldwide compared with males and culminates on lower levels [17]. Moreover, mechanisms of increased risk globally connected to increase of obesity prevalence are in case of colorectal cancer affected mostly by abdominal fat, which men usually accummulate more than women, in which the increase of subcutaneous fat is more frequent [18]. The question of the influence of obesity/overweight and smoking on the development of colorectal cancer incidence in two countries (the SR and CR) with the highest levels of incidence worldwide remains unanswered.

Colon and rectal cancer mortality is according to the WHO data highest in both sexes in the countries of North America, West and Central Europe including the Slovak and Czech Republic, but also for example in New Zealand. The lowest mortality rates are in Latin America and certain regions of Africa and Asia. In the study of Fernandez [19] on colorectal cancer mortality in chosen 21 countries in Europe favourable development of mortality was reported in terms of its stabilization or decline in both sexes and in the majority of analysed countries from 1990th (e.g. in Austria, Finland, Ireland, Netherlands, Norway, Sweden, Switzerland, UK, France and Italy), in several countries even earlier (Belgium, Germany and Denmark). However increasing mortality trend was preserved to the analysed year 2001 in some East European countries, e.g. Bulgaria, Poland and Romania and in the Mediterranean countries (Greece, Portugal, Spain). Mortality rates were highest in the Czech and Slovak Republic and in Hungary, but their slight decrease was also reported in the last years [19]. Mortality decrease, however, was not significant

to 2000 in Spain and in the majority of European countries including Slovakia, with the exception of the CR. In analysis of standardized mortality time trends in 1980-2005 in the CR and SR its more significant increase in males and females was found out in the SR in comparison with the CR, which results in approximation of mortality rates in the SR to those in the CR (particularly in males) in spite of the fact that the mortality development in the CR was from 1980 on substantially higher levels than in the SR. On the other side in the CR in both sexes and in the SR mostly in females the decline of mortality rates in the last assessed years was reported, most likely as the impact of early disease diagnosis using screening tests and improvement of the disease treatment (with successively better survival) [12, 19].

In analysis of overall development of colorectal cancer clinical stages in the CR and SR (in 1980-2003) significant decrease of disease numbers in clinical stage I was discovered and the increase of the disease number in clinical stage II. Simultaneously disease number slightly increases in clinical stage III and non-significantly decreases in clinical stage IV in both countries and both sexes. Eventual cause of unregistered increase of disease number in clinical stage I and II (at the expense of stage III and IV) was the low participation of the population on preventive examinations and national programmes running on short-time basis so far, in the SR without legislative opportunity of checking the feed-back of the precise number of screened population and results of preventive examinations.

When recording, the TNM classification 3rd revision was used longest [20] (in the SR in 1980-1999, CR 1982-1994). In analysis of clinical stages development solely during the period when 3rd edition of TNM classification was used, gradual decrease of undetected stages rate and increase of clinical stages II and III rate were reported. Stages I and IV maintain their levels. This development is reported both in males and females. In the CR during the use of 3rd edition of TNM classification no significant change occurred (in neither sex). Changeover from 3rd edition of TNM classification to 5th edition (used in 2000-2003) [21] in the SR (4th edition was not used in coding system) might participate in more significant decline of the clinical stage I rate at the expense of stage II rate, more detailed analyses are not possible with regard to the short time in which the mentioned TNM edition is used. At the same time opportune screening of colorectal cancer was introduced in the SR. Changeover to 4th edition of TNM classification [22] in the CR (used in 1995-2000) might participate in significant increase of stage II rate at the expense of stage I rate and slight increase of stage III rate at the expense of stage IV rate decrease. Using of 5th edition of TNM classification [21] (in 2001-2004) in the CR meant decrease of undetected stages rate which was manifested particularly in (slight) increase of the stage III rate. At the same time disease screening was introduced in CR.

Principal means which can lead to the improvement of patients´survival are at present the facilities of secondary prevention which can reveal and effectively help treat some precancerous lesions, as well as to diagnose proper malignancies in the early stage. Screening programme based on occult bleeding detection and subsequent colonoscopy was introduced in Slovakia in 2002 and in the CR in 2000. Since then it is a short time to evaluate the impact, although possible incidence culmination and slight mortality decrease in the last years in the CR [23, 24] is being detected. In the SR the incidence culmination has not been confirmed so far in neither studied group, which might be influenced by constantly insufficient return of screened persons and also by later establishment of national screening programme. Primary prevention is based on recommendations of proper diet with a hight rate of fiber food, in increase of physical activity, decrease of fat intake, eventually also in chemoprophylaxis, since hereditary and familial diseases are not directly influenced.

References

[1] FERLAY J, SHIN HR, BRAY F, FORMAN D, MATHERS C et al. GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon, France: IARC; 2010. Available from: http://globocan.iarc.fr

[2] CURADO MP, EDWARDS B, SHIN HR, STORM H, FERLAY J et al. Cancer Incidence in Five Continents, Vol. IX, IARC Scientific Publ. No. 160, Lyon, IARC 2007.

[3] SAFAEI-DIBA, C, PLESKO I, OBSITNIKOVA A et al. Cancer incidence in the Slovak Republic 2005. Bratislava, NHIC, 2009, 173 p. ISBN 978-80-89292-15-8.

[4] ONDRUSOVA, M, PLESKO, I, SAFAEI-DIBA, C, OBSITNIKOVA A, STEFANAKOVA, D et al. Comprehensive analysis of incidence and mortality of malignant tumours in the Slovak Republic (online). Bratislava, National Cancer Registry of the Slovak Republic, NHIC, 2007, http://www.nor-sk.org/.

[5] DUSEK L, MUZÍK J, KUBASEK M, KOPTIKOVA J, ZALOUDIK J et al. Epidemiology of malignant tumors in the Czech Republic [online]. Brno, Masaryk University, [2005], Available from WWW: http://www.svod.cz. Version 7.0 [2007], ISSN 1802 – 8861.

[6] AARELEID T. Central and Eastern Europe, p. 19-20. In: Whelan S L. IARC Newsletter No. 33 – Dec. 2003. www.iarc.com.fr

[7] BRAY F, GUILLOUX A, SANKILA R, PARKIN DM. Practical implications of imposing a new world standard population. Cancer Causes Control, 2002; 13:175–182. doi:10.1023/A:1014344519276

[8] CENTER M, JEMAL A, SMITH R, WARD E. Worldwide variations in Colorectal Cancer. CA Cancer J Clin., 2009a; 59: 366–378. doi:10.3322/caac.20038

[9] CENTER M, JEMAL A, WARD E. International trends in colorectal cancer incidence rates. Cancer Epidemiol. Biomarkers Prev 2009b; 18: 1688–1694. doi:10.1158/1055-9965.EPI-09-0090

[10] VYZULA R. Colorectal cancer – the world leader in incidence, important healt-care problem in the Czech Republic. Colorectal Cancer 2009, Pharmacotherapy 2009; 5: 5–20 (in Czech).

[11] DUSEK L, HOCH J, MUZIK J, PAVLÍK T. Epidemiology and treatment of colorectal carcinoma – Czech population data. Rozhl Chir 2009; 88: 295–302.
[12] BOSETTI C, LEVI F, ROSATO V, BERTUCCIO P, LUCCHINI F et al. Recent trends in colorectal cancer mortality in Europe. Int J Cancer 2010, Sep 7. [Epub ahead of print]
[13] KNAI C, SUHRCKE M, LOBSTEIN T. Obesity in Eastern Europe: an overview of its health and economic implications. Econ Hum Biol 2007; 5: 392–408. doi:10.1016/j.ehb.2007.08.002
[14] AVDICOVA M, HRUBA F. Trends in the chronical non-infectious diseases occurrence in the Slovak Republic in 1993-2008. Text-book from the 35th Stodola Days of Health Education, 2009 (in Slovak).
[15] TYZSYNSKI JE, BRAY F, AARELEID T, DALMAS M, KURTINAITIS J et al. Lung cancer mortality patterns in selected Eastern and Southern European countries. Int J Cancer 2004; 109: 598–610. doi:10.1002/ijc.20019
[16] STATISTICAL OFFICE OF THE SLOVAK REPUBLIC. Extension of drug using in the Slovak Republic. Statistical Office of the Slovak Republic, 2006, 113 p. (in Slovak)
[17] MACKAY J, AMOS A. Women and tobacco. Respirology 2003; 8: 123–130. doi:10.1046/j.1440-1843.2003.00464.x
[18] PISCHON T, BOEING H, HOFFMANN K, BERGMANN M, SCHULZE MB et al. General and abdominal adiposity and risk of death in Europe. N Engl J Med 2008; 359: 2105–2120. doi:10.1056/NEJMoa0801891
[19] FERNÁNDEZ E, LA VECCHIA C, GONZÁLEZ JR, LUCCHINI F, NEGRI E et al. Converging patterns of colorectal cancer mortality in Europe. Eur J Cancer 2005; 41: 430–7. doi:10.1016/j.ejca.2004.11.014
[20] HARMER MH et al. TNM classification of malignant tumors, 3rd ed. Geneva, UICC 1978.
[21] SOBIN LH, WITTEKIND C. TNM classification of malignant tumors. 5th ed. New York, Wiley-Liss, Inc. 1997.
[22] HERMANEK P, SOBIN LH. TNM classification of malignant tumors. 4th ed. Geneva, UICC 1987.
[23] PLESKO I, SEVERI G, BOYLE P, ONDRUSOVA M, TOMASEK L et al. Dominant position of colorectal cancer in Slovakia: The old-new problem for cancer control. Neoplasma 2008; 55: 10–15.
[24] ZAVORAL M, SUCHANEK S, ZAVADA F, DUSEK L, MUZIK J et al. Colorectal Cancer screening in Europe. World J Gastroenterol 2009; 15: 5907–5915. doi:10.3748/wjg.15.5907