

Recent Patterns in Stomach Cancer Descriptive Epidemiology in the Slovak Republic with Reference to International Comparisons

Aktuálne charakteristiky deskriptívnej epidemiológie nádorov žalúdka v Slovenskej republike v kontexte medzinárodného porovnania

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Summary

Backgrounds: Even though the incidence and mortality from stomach cancer declined dramatically, it remains the third most frequent cancer worldwide. This study analysed the incidence and resulting mortality, and possible reasons for any differences identified between the Slovak Republic and other countries. **Material and Methods:** Analysis of national data covering the period from 1968 to 2006. Trends have been estimated using linear regression model and are presented with corresponding 95% Confidence Intervals (CI) and p-values with null hypothesis being constant in time. **Results:** In 2006, standardized incidence index for stomach cancer in Slovak males (related to 1968) declined by 0.28, annual percentage change was –3.2% and the average decrease of standardized incidence represented –0.956/100,000 (95% CI –1.059 to –0.853, $p < 0.0001$). The incidence in men had statistically significantly more rapidly declining tendency in the first half of the analyzed period (1968–1986). Decrease in the mortality index was 0.32 with annual percentage change of –2.9% and the mean decrease in standardized mortality of –0.691/100,000 (95% CI –0.750 to –0.632, $p < 0.0001$). In 2006, the standardized incidence index for stomach cancer in Slovak females (related to 1968) declined by 0.23, annual percentage change was –3.7% and the mean decrease in standardized incidence was –0.491/100,000 (95% CI –0.554 to –0.428, $p < 0.0001$), the decline in incidence was more pronounced in the first half of the analyzed period. The mortality index (1968–2006) declined by 0.26, annual percentage change was –3.4% and annual decrement of standardized mortality represented –0.367/100,000 (95% CI –0.407 to –0.326, $p < 0.0001$). Only a non-significant change was identified for the proportions of the individual stomach cancer clinical stages with high proportion of clinical stages III and IV in both sexes. **Conclusion:** Decline in the incidence and mortality appears to be decelerating, intervention in primary prevention is essential.

Key words

stomach cancer – incidence – mortality – clinical stages – risk factors

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Súhrn

Výhodiská: Vývoj incidencie a mortality na nádory žalúdka zaznamenal dramatický pokles, napriek tomu ostáva ochorenie tretím najčastejšie sa vyskytujúcim nádorom v globálnom meradle. Predkladaná štúdia analyzuje incidenciu, mortalitu a možné príčiny prípadných rozdielov dát zistených v Slovenskej republike v porovnaní s ostatnými krajinami a regiónmi sveta. **Materiál a metódy:** Analýza národných údajov prebiehala za roky 1968–2006. Trendy vývoja sa prezentujú s použitím lineárnej regresie s príslušným 95% intervalom spoľahlivosti a štatistickou významnosťou. **Výsledky:** V roku 2006 (prepočítané k roku 1968) predstavoval index poklesu štandardizovanej incidencie nádorov žalúdka u mužov na Slovensku 0,28; ročný priemerný percentuálny pokles bol –3,2 %, ročný priemerný pokles hodnôt štandardizovanej incidencie bol –0,956/100 000 (95% CI –1,059 až –0,853, $p < 0,0001$). Incidencia ochorenia mala u mužov štatisticky významne rýchlejší pokles v prvej polovici analyzovaného obdobia (1968–1986). Index poklesu štandardizovanej mortality v roku 2006 (k roku 1968) predstavoval 0,32; ročný priemerný percentuálny pokles bol –2,9 %; ročný priemerný pokles hodnôt štandardizovanej mortality predstavoval –0,691/100 000 (95% CI –0,750 až –0,632, $p < 0,0001$). V roku 2006 (prepočítané k roku 1968) predstavoval index poklesu štandardizovanej incidencie ochorenia u žien 0,23; ročný priemerný percentuálny pokles bol –3,7 % a ročný priemerný pokles hodnôt štandardizovanej incidencie predstavoval –0,491/100 000 (95% CI –0,554 až –0,428, $p < 0,0001$), incidencia mala podobne ako u mužov výraznejšie klesajúci trend v prvej polovici analyzovaného obdobia (1968–1986). Index poklesu mortality v roku 2006 (k roku 1968) bol 0,26; ročný priemerný percentuálny pokles bol –3,4 % a ročný priemerný pokles hodnôt štandardizovanej mortality predstavoval –0,367/100 000 (95% CI –0,407 až –0,326, $p < 0,0001$). Na Slovensku sa zaznamenali len štatisticky nevýznamné zmeny v zastúpení jednotlivých klinických štádií ochorenia, pričom sa zaznamenali stále vysoké počty nádorov v III. a IV. klinickom štádiu u oboch pohlaví. **Záver:** Pokles incidencie a mortality nádorov žalúdka vykazuje spomaľujúci trend, intervencie v zmysle primárnej prevencie sú aj naďalej nevyhnutné.

Kľúčové slová

nádory žalúdka – incidencia – mortalita – klinické štádiá – rizikové faktory

Introduction

Stomach cancer incidence and mortality declined dramatically in the 20th century. Notwithstanding that a remarkable spontaneous global decline has halved the age-standardized incidence in most western countries in the past 30–40 years, this cancer remains the third most frequent one worldwide in both sexes, surpassed only by lung and colorectal cancer (non-melanoma skin cancer excluded) [1,2].

In 2008 the worldwide estimated number of the newly diagnosed stomach cancers in men was 640,031 cases (age-standardized incidence rate (World) – ASR-W was 19.8/100,000) and 348,571 cases in women (ASR-W incidence 9.1/100,000). The expected stomach cancer related death in 2008 was 463,930 cases in men (ASR-W mortality 14.2/100,000) and 273,489 in women (ASR-W mortality 6.9/100,000) [2].

The purpose of this study was to analyse the incidence of stomach cancer and resulting mortality and the possible reasons for any differences discovered in the Slovak Republic (SR) in correlation with neighbouring countries and other world regions. Without an internal analysis of the epidemiological indicators development it is not possible to discover the causes of the unfavourable situation with the relatively high global incidence

related to stomach cancer in both sexes in the SR and time-trend differences and thus condition changes at the level of primary prevention. Thus, there is a desperate need for basic epidemiological data analysis. This study based on epidemiological data analyses for a long period of time (1968–2006) brings highly relevant and new data related to stomach cancer incidence and mortality. In addition, this paper discusses possible factors of these trends and compares national data to appropriate broader international context. We estimated statistically significant decrease in the values of both incidence and mortality in men in the SR, the similar situation with more rapid decrement of mortality was recorded among females. However, decline in incidence and mortality appears to be decelerating.

Materials and Methods

The data concerning the incidence of stomach cancer used in this analysis were obtained from the pre-processed data portal of the National Cancer Registry (NCR) SR [3] (www.nor-sk.org) valid until the end of July 2009 as well as from the standard outcomes and annual reports of the NCR SR [4]. After the termination of the national web portal (www.nor-sk.org) we respond at once with analyses of the calls of the medical pu-

blic for official data suitable for citation. The NCR SR is a population-based cancer registry with high quality data [5]. Analyses of the overall incidence and mortality take into account the period 1968–2006 in which the SR has validated data. The values of incidence and mortality are presented in the form of crude rates in 2006 [4]. The comparison with other countries is only possible after correction of different age structure in the population. The standardisation to the world standard population was performed [6] and the age standardised rates (ASR-W) in the SR with other countries have been compared. The trends in incidence and mortality have been extracted using linear regression model separately for each gender in time periods 1968–2006 and then individually for the periods 1968–1986 (the first half of the period analysed) and 1986–2006 (the second half) and the trends are presented with corresponding 95% confidence intervals (CI) and p-value with null hypothesis being constant with time. The index of the growth of ASR-W incidence was calculated using a linear regression model for the ASR-W data. The output of the linear regression model is a linear regression line. The index of the growth represents a slope of this regression line. The output of the regression for the slope is 95% CI for the index of growth.

The analysis was performed using XLSTAT (www.xlstat.com) software. The analyses of the clinical stages are based upon the period 1978–2003, which is a period for which the SR had, within the framework of the web portal www.nor-sk.org [3], data that was accessible and open to public about the stages of disease. At the same time, it took into account changes in the coding system of NCR SR, that occurred only once in the period analyzed 1978–2003 (in 2000 with the transition from TNM-3rd ed. to TNM-4th ed.).

Results

In the year 2006 in the SR 539 cases of stomach cancer in men were diagnosed, this represented the crude incidence rate 20.6/100,000 of men and standardized (ASR-W) incidence 15.5/100,000 (95% CI ± 1.350). In 2006 the stomach cancer participated with 4.1% in total cancer occurrence in men population and therefore it represents the 5th place, following colorectal cancer, lung cancer, prostate and bladder cancer (non-melanoma skin cancers excluded). The index of the decrease of the ASR-W incidence, related to year 1968, represented 0.28; from ASR-W incidence value 55.6/100,000 (95% CI ± 3.001) in the year 1968 to the current 15.5/100,000; annual percentage incidence decline was –3.2%. The estimated average annual decrease of incidence in men regarding the entire period 1968–2006 represented –0.956/100,000 (95% CI –1.059 to –0.853, $p < 0.0001$). Stomach cancer incidence in men had statistically significant a more rapidly declining tendency in the first half of the period analyzed (1968–1986), in this period the mean annual decrease of the ASR-W incidence represented –1.547/100,000 (95% CI –1.793 to –1.301, $p < 0.0001$). In the time period of 1986–2006 slowing down of the annual decrease of ASR-W incidence was observed, the decrease was –0.516/100,000 (95% CI –0.570 to –0.461, $p < 0.0001$) (Fig. 1).

In 2006 in the SR 447 men died of stomach cancer, which represented the crude mortality 17.1/100,000 and ASR-W 12.5/100,000 (95% CI ± 1.193). Index of the decrease of ASR-W mortality was 0.32; from the ASR-W morta-

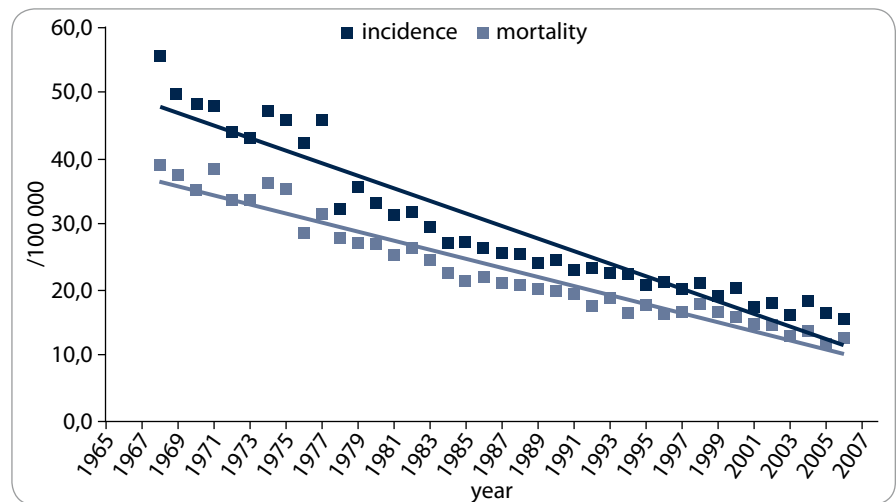


Fig. 1. Trends of the standardized (to the World standard population) stomach cancer incidence and mortality in males in the Slovak Republic.

lity values 39/100,000 (95% CI ± 1.633) in 1968 to the current 12.5/100,000; annual percentage mortality decline was –2.9%. In the overall analyzed period 1968–2006 in linear expression had the mortality less expressive decreasing tendency (compared to incidence), mean annual decrease represented –0.691/100,000 (95% CI –0.750 to –0.632, $p < 0.0001$). The character of the ASR-W mortality curve had similar characteristics as incidence, statistically significant more pronounced decrease of mortality was observed in the first half of the period analysed (1968–1986), –1.003/100,000 (95% CI –1.149 to –1.858, $p < 0.0001$), in 1986–2006 the annual change was –0.449/100,000 (95% CI

–0.510 to –0.387, $p < 0.0001$). Mortality was lowering down more slowly than incidence (Fig. 1).

There were 374 newly diagnosed cases of stomach cancer in women in the year 2006 in the SR, this represented crude incidence rate 13.5/100,000 and ASR-W 7.1/100,000 (95% CI ± 0.785). In 2006 the stomach cancer reached 3% of all cancers and gained the 7th place in women's malignancies scale (non-melanoma skin cancer excluded). The incidence has continuously decreasing tendency (similarly to men) since year 1968, while the index of decrement of the ASR-W incidence represented 0.23; of ASR-W incidence value 30.5/100,000 (95% CI ± 2.029) in 1968 to 7.1/100,000 in

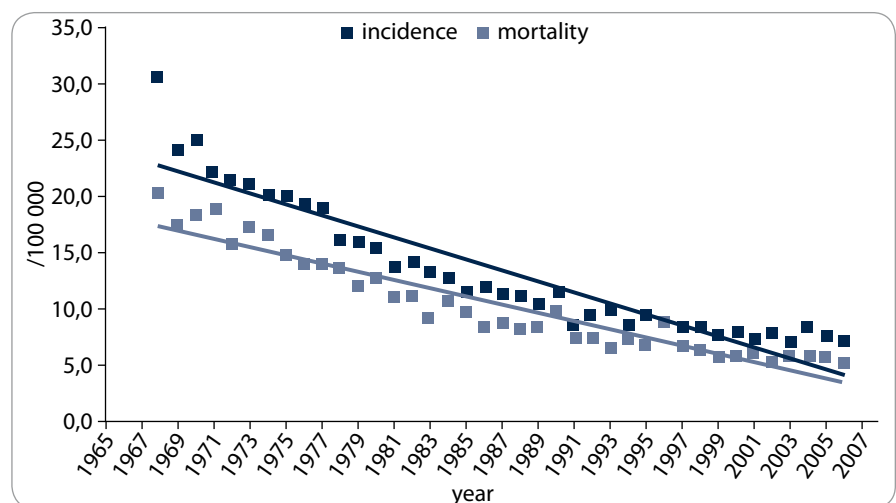


Fig. 2. Trends of the standardized (to the World standard population) stomach cancer incidence and mortality in females in the Slovak Republic.

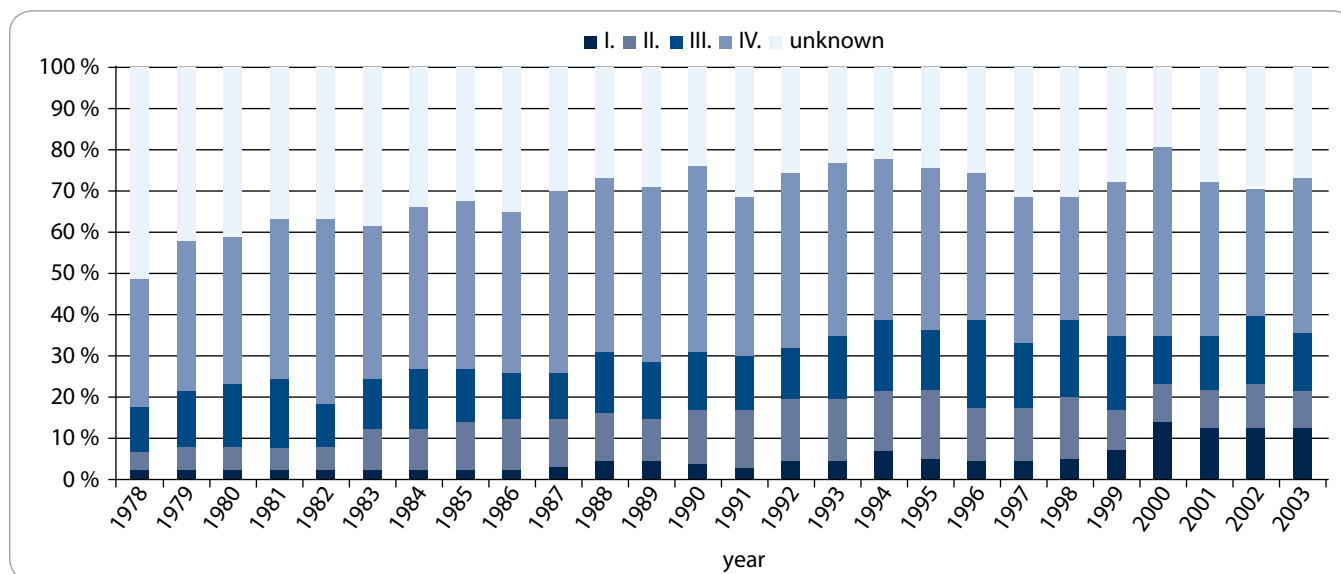


Fig. 3. Clinical stages of stomach cancer in males in the Slovak Republic.

2006; annual percentage incidence decline was -3.7% . The estimated mean annual decrease of the incidence in 1968–2006 was $-0.491/100,000$ (95% CI -0.554 to -0.428 , $p < 0.0001$), in the period time of 1968–1986 it was $-0.869/100,000$ (95% CI -0.991 to -0.747 , $p < 0.0001$), in 1986–2006 the estimated annual decrease was $-0.217/100,000$ (95% CI -0.268 to -0.167 , $p < 0.0001$). Decline of incidence was more pronounced in the first half of the analysed period (Fig. 2).

298 women in the SR died of the stomach cancer in 2006, which represents

crude mortality $10.7/100,000$ and ASR-W $5.3/100,000$ (95% CI ± 0.657). The index of decrement of death count related to the year 1968 represented 0.26 of the ASR-W mortality value $20.1/100,000$ in 1968 (95% CI ± 1.648) to $5.3/100,000$ in 2006; annual percentage mortality decline was -3.4% . Stomach cancer mortality had similarly to incidence continuously decreasing character in the whole analyzed period 1968–2006, the estimated mean annual decrement of ASR-W mortality represented $-0.367/100,000$ (95% CI -0.407 to -0.326 , $p < 0.0001$).

Mortality among women declined more slowly than did incidence, however the difference between the decline in incidence and mortality among women in comparison with men was less pronounced. Like incidence, the decline of mortality was more pronounced in the period 1968–1986 ($-0.606/100,000$; 95% CI -0.675 to -0.537 , $p < 0.0001$) compared to the period time of 1986–2006 ($-0.181/100,000$; 95% CI -0.232 to -0.129 , $p < 0.0001$) (Fig. 2).

In the SR just a non-significant change in the percentage of stomach cancer cli-

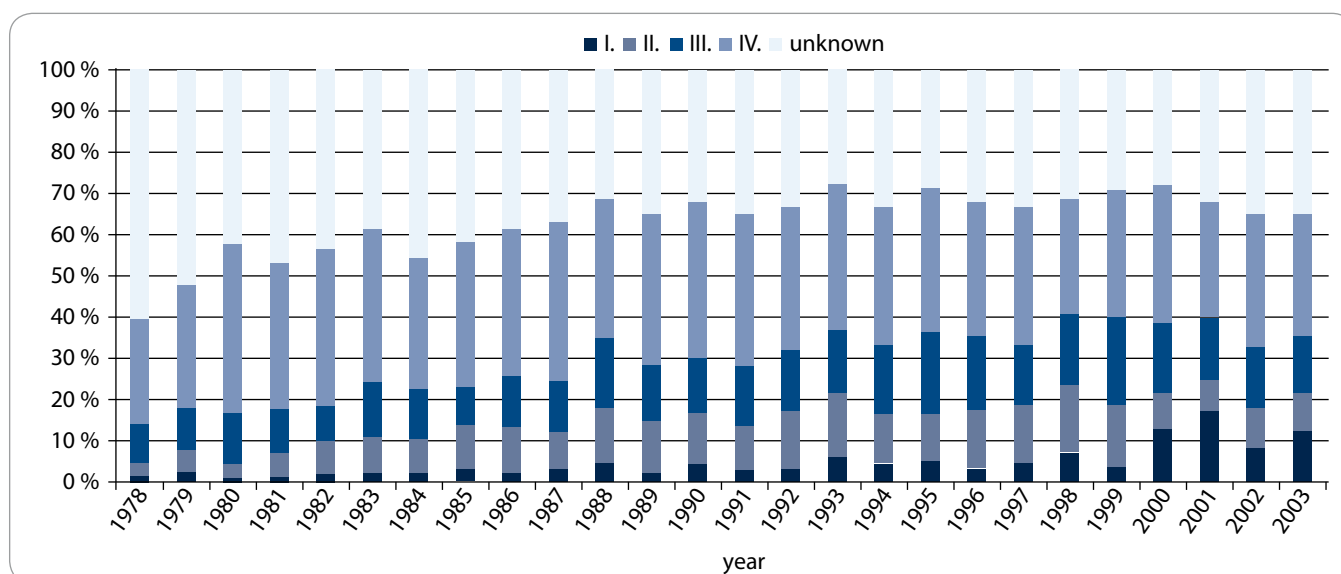


Fig. 4. Clinical stages of stomach cancer in females in the Slovak Republic.

nical stages has been recorded during the period 1978–2003. The number of cases diagnosed in the clinical stage I increased sharply after 2000 in both males and females, however, in that time the TNM coding system was changed. The only significant change in both sexes was decrease which occurred in the number of cases in the unspecified clinical stage. The number of cases in the clinical stages III and IV was relatively stable and on high level in both sexes (Fig. 3, 4).

Discussion

Stomach cancer accounts for almost 8% of all cancers worldwide. Due to the aging of the world's population and the steep age gradient in incidence among the elderly, stomach cancer continues to claim an increasing number of victims [1,2]. The incidence of stomach cancer varies greatly across populations (Fig. 5). The highest estimated values of ASR-W incidence of stomach cancer for the year 2008 in males are in Korea (62.2/100,000), Mongolia (48.2/100,000) and Japan (46.8/100,000), where screening is ongoing. The lowest ASR-W incidence in males was estimated to be in Botswana (0.6/100,000) and Namibia, Malawi and the Gambia (each 1.8/100,000). From the European countries, the highest ASR-W incidence in males was estimated in Belarus (34.2/100,000) followed by Russian Federation and Albania. The SR was placed 16th with estimated ASR-W incidence of 15.3/100,000, followed by Hungary (14.9/100,000) and other, mainly western countries (e.g. Spain, the Czech Republic and Austria etc.) The lowest ASR-W incidence were estimated in Sweden (4.6/100,000), followed by Cyprus and Iceland [2]. With few exceptions, the incidence among women is approximately half of that among men, regardless of geographical area, culture and religion. Worldwide, the highest incidence rate for 2008 was estimated to be in Guatemala (25.9/100,000) and Korea (24.6/100,000), the lowest in Botswana (0.2/100,000) and Namibia (0.6/100,000). From the European countries, the highest incidence was estimated in Albania (17.6/100,000) and the lowest in

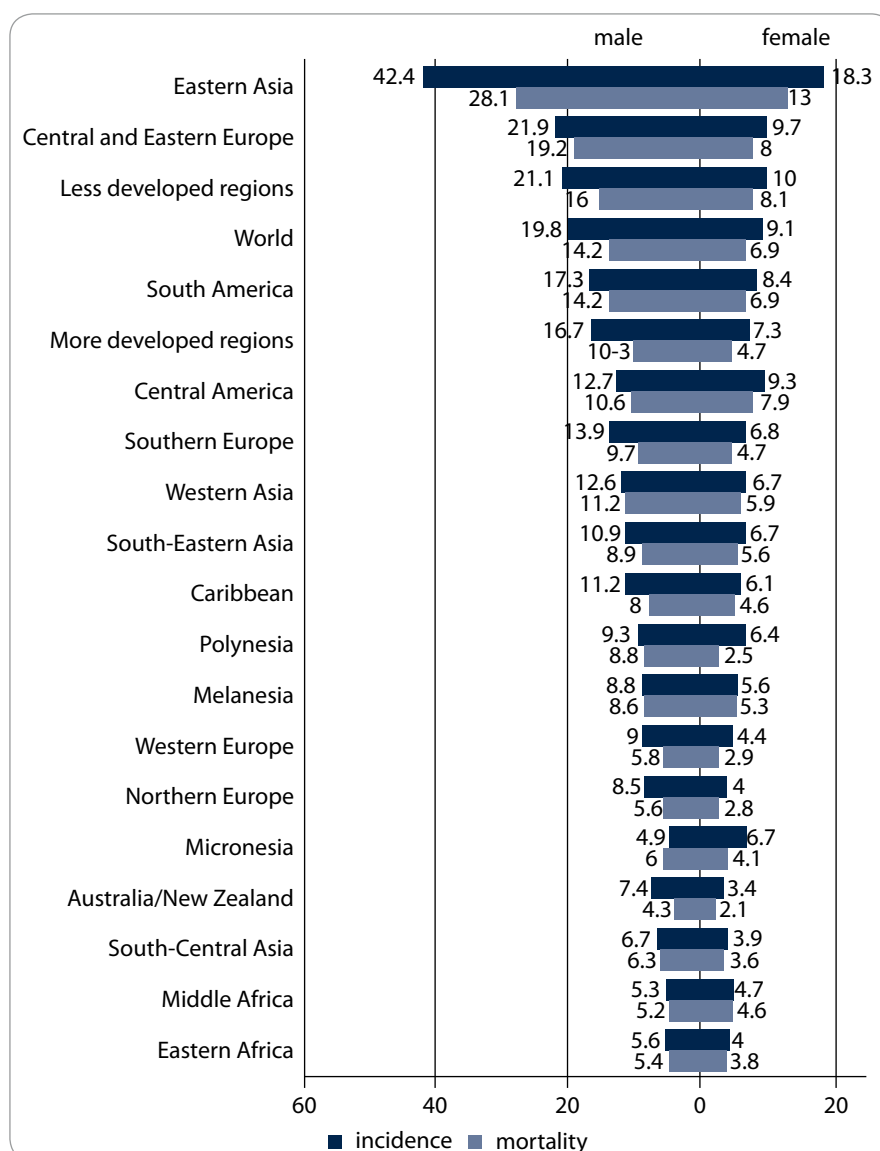


Fig. 5. Recent patterns in stomach cancer incidence and mortality according to the World-regions, published by the IARC WHO.

Iceland (2.5/100,000). The SR was placed 15th with estimated ASR-W incidence of 7.1/100,000 [2].

Except in Japan, stomach cancer is rarely seen before age of 50. The age-distribution patterns are similar in most countries, and the 2 : 1 male/female ratio persists throughout all age groups in all countries [1,7,8].

Stomach cancer includes adenocarcinomas of the fundus, corpus and distal stomach, whose incidence has long been falling. However, adenocarcinomas of cardia are influenced by reflux disease and have been rising in Europe and North America over the last two de-

cades. The incidence of other rarer histological types of stomach cancer has not been declining [9].

The SR has been placed among countries with higher incidence of stomach cancer in both sexes from the European region, however, worldwide highest incidence rates has been recorded in most of the Eastern European countries. Regional variations in part reflect differences in dietary pattern and the prevalence of *Helicobacter pylori* infection. Stomach cancer rates have been decreased substantially in the SR as well as in most parts of Europe, in part due to factors related to the increase use and availability

of refrigeration including the increase availability of fresh fruits and vegetables, and a decreased reliance on salted and preserved foods. Other major determinants for the favorable trends are reductions in chronic *Helicobacter pylori* infection (which is still very high especially in developing countries and among older cohorts, e.g. in the Czech Republic were the estimates of *Helicobacter pylori* prevalence in population 50–70% [10], data from the SR are not available) and smoking [9,11]. The higher level of the rates of stomach cancer incidence in the SR might continued to be caused by high appeal of several deleterious factors, primarily the effect of diets with a significant component of salt and N-nitroso compounds and the more frequent occurrence of *Helicobacter pylori*, particularly in comparison with several more westernized countries [12]. Likewise, in contrast to the West, the higher level of incidence may also be influenced by the historic later widespread accessibility to more suitable ways of preparing and keeping food – the freezer. However, in the SR, (with the exception of the prevalence of smoking), official data which might help to explain the higher value of incidence are not available.

The reasons for the generalized decline in stomach cancer rates are complex and not completely understood. Most of the global decline in stomach cancer mortality (recorded also in the SR) can be attributed to the reduction in incidence [8,13], since the prognosis of the disease, due to high representation of advanced clinical stages, remains poor. A role of improved diagnosis and treatment is also possible, although difficult to quantify on national mortality rates [13]. The falls in stomach cancer mortality were observed both in high-mortality areas (not only Russian Federation and other eastern and central European countries, the SR included, but also in Portugal and Italy) and in low-mortality ones (not only most northern Europe, but also France and Greece), in-

dicating that the downward trends are likely to persist in the future [9,14]. From 1990–1994 to 2000–2004, stomach cancer mortality in the European Union declined by 30% in both sexes [13]. The highest value of the ASR-W mortality was reached in the worldwide estimates for 2008 in males in Mongolia (36.9/100,000) and China (30.1/100,000), the lowest in Botswana (0.6/100,000). From Europe, the highest mortality rates in males are estimated to be in Belarus (30.1/100,000), the lowest in Iceland (4.1/100,000). The SR was in the 19th place among European countries, with ASR-W mortality levels of 11.2/100,000 [2]. Situation in the mortality rates in females is similar to those in males, with the highest global estimates in Guatemala (22.1/100,000) and the lowest in Botswana (0.2/100,000). The SR was placed 17th with estimated ASR-W mortality of 5.2/100,000; the highest mortality in Europe was estimated to be in Albania (15.1/100,000), the lowest in Cyprus (1.8/100,000) [2]. In many countries, the SR included, the decline in incidence and mortality appears to be decelerating, with smaller reduction apparent for the younger age groups [8].

Incidence rates have been observed to decrease in all clinical stages. Although the overall trend is positive and the incidence rate of stomach cancer has steadily decreased, the recently diagnosed variety of clinical stages recorded not only in the SR, but also e.g. in the Czech Republic [15] is unsatisfactory [13]. In the SR more than 30% of the newly diagnosed cases in males are in the clinical stage IV and also one third of cases are diagnosed under circumstances, which do not allow an objective determination of the stage. Because of high representation of advanced clinical stages, most deaths of patients with stomach cancer occur within the first couple of months to year following diagnosis.

Conclusion

Effort to improve treatment have had limited success. In contrast, considerable

knowledge about potentially causal factors has been gathered and primary prevention no longer appears to be an unattainable goal. Dietary factors, particularly the intake of antioxidant-rich fruits and vegetables, are likely to be important. It has been estimated that the global burden of stomach cancer could be reduced by up to 50%, if there were dietary modification that led to a high intake of fresh fruit and vegetables. *Helicobacter pylori*, the strongest and most important risk factor, is likely to become the first target in future prevention strategies.

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