Burden of Cancer in Serbia

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Aim To provide a comprehensive assessment of burden of selected cancers in Serbia.

Method We calculated disability adjusted life years (DALY) – the sum of the years of life lost (YLL) from premature mortality and the years lived with disability (YLD) – for cancers of stomach, colon and rectum, lung, breast, and cervical cancer for central Serbia and Vojvodina, Serbia and Montenegro. The obtained values were compared with the corresponding values for European region as estimated by the World Health Organization. The study was conducted between October 2002 and September 2003. The cancer burden was estimated for the year 2000.

Results Observed cancers were responsible for 133 689 DALYs (73 197 for men and 60 482 for women). There were significantly more losses because of premature death than disease disability (95.2% vs 4.8% in men $P<0.001$, and 93.2% vs 6.8% in females, $P<0.001$). The cancer burden was dominated by lung cancer in men and breast cancer in women. The cancer burden was very small before the age of 35.

Conclusion DALYs per 1000 population were higher in Serbia than in the European region for all observed cancers except for stomach cancer. The participation of a burden caused by disability in the total burden of selected cancers was lower in Serbia than in other European countries, with the greatest differences in colorectal, breast, and cervical cancers.

There is growing literature on the use of summary measures of population health, which combine the information on mortality and non-fatal health outcomes (1,2). One of them, called disability-adjusted life years (DALY) was introduced by the World Bank (3) and subsequently used by the World Health Organization and Harvard University for detailed assessment of global burden of disease and injuries (4). Afterwards, many investigators have performed and published studies on burden of diseases and injuries using DALY, which reflect both the years of life lost because of premature death and years lived with disability (5-7).

Morbidity and mortality of cancers have a great impact on population of Serbia. During many decades, malignant neoplasms have occupied the second place as a cause of death, with mortality rates for some cancers showing a slow but steady increase (8,9). In 2000, cancer accounted for 19% of all causes of deaths (21% in men, and 17% in women) in the population of Serbia without Kosovo and Metohia. In 2000, stomach cancer (International Classification of Diseases, version 10 [ICD10], code C16), colorectal cancer (ICD10 codes C18 – C21), lung cancer (ICD10 codes C33 – C34), breast cancer (ICD10 code C50), and cervical cancer (ICD10 code C53) were responsible for 50% of all cancer incidence cases (45% in men and 54% in women) and for 65% of deaths caused by all malignant neoplasms (63% in men, and 66% in women) (10). Lung cancer, colorectal cancer, and stomach cancer were among ten leading causes of deaths in men, whereas breast cancer, colorectal cancer, lung cancer, stomach cancer, and cervical cancer were among twelve leading causes of death in women (11). We chose these cancers to provide a comprehensive assessment of premature mortality and disability attributable to cancers in Serbia by calculating disability adjusted life years (DALY).

Method

The Serbian Burden of Disease Study was carried out by the European Agency for Reconstruction Project Team, using methods largely based on those developed for the Global Burden of Disease study (4). The project commenced in October 2002 and was completed in September 2003. The study was conducted in Central Serbia and Vojvodina, Serbia and Montenegro.

The burden of selected cancers was estimated for the year 2000 by the use of DALY, which combines a measurement of premature mortality and disability (12-15). This indicator is the aggregation of years of life lost (YLL) and years lived with disability (YLD) at the population level and thus reflects the "burden of disease" in a population (DALY = YLL + YLD).

Population data

The population estimates for the calculation of values of needed indicators were based on the census adjustments for 2000, not including the migration component (16). The total number of observed population was 7 551 000. Direct method, with the European population as the standard, was used for standardization (17).

Mortality data

The Regional Offices of Statistics compile information on death certificates. The Serbian Office of Statistics receives these data from each region and provides a unit record file of deaths with diagnosis, death date, age, sex, and place of residence. For the burden of disease estimates, we considered all deaths of people with place of residence in Serbia that occurred anywhere in or out of Serbia and were registered in 2000.

The completeness of Serbian Office of Statistics 2000 mortality database was 98%. In addition to missing data, two other problems with the validity and reliability of cause of death data were present: not assigning a specific code but using "senility" or some other ill-defined code, and assigning the wrong code due to diagnostic fashion or carelessness.

According to the Global Burden of Disease methodology, ill-defined causes of deaths were reassigned. The 8.7% of deaths assigned to ill-defined and senility codes (U161) were redistributed proportionally, by sex and age, across the group of communicable, maternal, perinatal, and nutritional conditions among those 0-5 years old, and across the group of non-communicable diseases among those >5 years old. Cancers of unspecified sites (U077), which made 3.4% of all deaths, were redistributed proportionally by age and sex across all specified sites. Finally, 0.1% of deaths with missing age data were redistributed proportionally by sex and cause.

YLL was determined by the average life expectancy at the age of death while discounting future years by 3%. The 3% discount rate, recommended by the International Panel on Cost Effectiveness in Health and Medicine (18), was chosen to allow for international comparisons. YLL were calculated by multiplying age-specific mortality rates by age-specific standard expected for YLL and population numbers. Standard expected YLL were derived from the standard life table West 26 (19) with a life expectancy at birth of 82.5 years for women. Life table West 25 (20) for women was used for men with life expectancy at birth of 80 years.

The Global Burden of Disease Study weighted a year of healthy life lived at young age and older age lower than for other ages, because there is a broad social preference to value a year lived by a young adult more highly than a year lived by a young child or at older ages (4). Although not all investigators agree that young age and older age should be given less weight, in Serbian Burden of Disease Study 2000, we decided to use this approach to be able to compare our results with the results of other studies.

Incidence data

YLD was calculated on the basis of incidence data. The incidence data were obtained from the Cancer Registry of central Serbia for 1999 (10) and from Cancer Registry of Vojvodina for 1998 (21). From data for Central Serbia, only those for Belgrade population were used because they were more reliable than the data for the rest of the region. Global Burden of Disease (22), Dutch study (23) models, and provisional disability weights for cancer stages were used for all cancers. Since Dutch weights do not exist for cervical cancer, we applied weights used in Victoria study (24).

It was accepted that, according to the Global Burden of Disease estimate, 20% of cancers were untreated in the region of the former socialist economies of Europe (4).

For all cancers observed, including breast cancer, we assumed patients who survived five years to be in remission and we took the five-year survival rate as the cure rate. Patients who were cured were assumed to be without disability (22). For patients who died, average time to death was assumed to follow an exponential distribution, so that the mean survival time was estimated by fitting this distribution to available survival data (after 1, 3, and 5 years) by Kaplan-Meier product limit method (24,25). The duration of primary diagnosis, therapy, remission, and preterminal phase of each cancer were discussed with experts. The experts' opinion was also asked for the frequency of small cell and non-small cell lung cancer, both operable and inoperable ones, and for the incidence of breast cancer by size. Since there are no data on survival of cancer patients in Serbia, we used 5-year survival data for Slovenia in the period 1985-1989 (26). Both Serbia and Slovenia had been part of former Yugoslavia before 1991.

Results

The incidence and mortality rates for selected malignant neoplasms in central Serbia and Vojvodina in 2000 (Table 1) were compared for reliability with the same data for Slovenia (27) in 1999 (Table 2). Cancer incidence rates in these

Table 1. Incidence and mortality rates from selected cancers by sex in Serbia, 2000*

	Crude rate (standardized†) per 1000 population			
	incidence‡		mortality	
Cancer site	men	women	men	women
Stomach	0.28 (0.24)	0.14 (0.10)	0.30 (0.25)	0.16 (0.12)
Colorectal	0.57 (0.49)	0.42 (0.32)	0.45 (0.38)	0.31 (0.22)
Lung	1.26 (0.95)	0.29 (0.23)	1.18 (0.99)	0.30 (0.22)
Breast	0.02 (0.02)	1.02 (0.83)	0.01 (0.01)	0.50 (0.40)
Cervical	–	0.33 (0.29)	–	0.16 (0.12)
All cancers	4.70 (4.11)	4.08 (3.24)	3.06 (2.63)	2.15 (1.62)

*Population of Serbia: men – 3 673 529, women – 3 877 326.
†According to European population (17).
‡According to data for Belgrade, 2000 (10), and Vojvodina, 1998 (21).

Table 2. Incidence and mortality rates from selected cancers by sex in Slovenia, 1999*

	Crude rate (standardized†) per 1000 population			
	incidence‡		mortality	
Cancer site	men	women	men	women
Stomach	0.32 (0.35)	0.16 (0.12)	0.25 (0.28)	0.16 (0.11)
Colorectal	0.59 (0.63)	0.42 (0.32)	0.35 (0.38)	0.29 (0.20)
Lung	0.85 (0.86)	0.21 (0.17)	0.78 (0.80)	0.22 (0.16)
Breast	0.01 (0.01)	0.98 (0.83)	0.003 (0.003)	0.39 (0.31)
Cervical	–	0.20 (0.18)	–	0.05 (0.04)
All cancers	4.58 (4.77)	4.15 (3.34)	2.77 (2.95)	2.08 (1.56)

*Population of Slovenia: men – 960 456, women – 1 021 289.
†According to European population (17).
‡According to Cancer Register of Slovenia (27).

two populations were similar, although the frequency of lung cancer and cervical cancer was higher in Serbia, and the frequency of stomach and colorectal cancers was higher in male population of Slovenia. The incidence was almost the same for breast cancer. Mortality rates of stomach and colorectal cancers were similar, but mortality rates for lung, breast, and cervical cancers were higher in Serbia.

Observed cancers were responsible for 73 197 DALYs in men and for 60 482 DALYs in women. There were significantly more YLL than YLD losses for all cancers (95.2% vs 4.8% in men, and 93.2% vs 6.8% in women), showing that the burden of cancer was dominated by mortality rather than long-term disability (Table 3).

Lung cancer accounted for the largest part of the cancer burden in men, followed by colorectal and stomach cancers, whereas the burden of breast cancer was negligible. For women, the burden of breast cancer was the greatest, followed by lung cancer, colorectal cancer, cervical cancer, and stomach cancer (Table 3).

The cancer burden was very small before the age of 35 (Figure 1). The DALY rates per 1000 male population were the highest in the 55-74 age group for lung cancer and in the 65-74 age group for stomach and colorectal cancer. For women, DALY rates were the highest in the 55-74 age group for lung cancer, and in those aged ≥65 years for stomach and colorectal cancers. The burden of breast and cervical cancers was greater in younger age groups, ie, those aged 45-64 years and 45-54 years, respectively.

We compared the incidence, YLD, and DALY per 1000 population, as well as YLD/DALY ratio (%) of selected cancers in Serbia and European region divided in European subregions A, B, and C (Table 4). The incidence of breast

Table 3. Burden of selected cancers by site and sex in Serbia, 2000*

	Measures of population health					
Cancer site	YLD	YLD per 1000	YLL	YLL per 1000	DALY	DALY per 1000
Men:						
stomach cancer	386	0.10	10 416	2.84	10 416	2.94
colorectal cancer	983	0.27	14 542	3.96	15 525	4.23
lung cancer	2136	0.58	44 407	12.09	46 543	12.67
breast cancer	56	0.02	271	0.07	327	0.09
total	3561	0.97	69 636	18.96	73 197	19.93
Women:						
stomach cancer	198	0.05	5487	1.42	5685	1.47
colorectal cancer	802	0.21	9680	2.49	10 482	2.70
lung cancer	518	0.13	12 027	3.10	12 545	3.24
breast cancer	2078	0.54	21 463	5.54	23 541	6.07
cervical cancer	529	0.14	7701	1.99	8230	2.12
total	4125	1.06	56 358	14.54	60 483	15.60

*Abbreviations: YLD – years lived with disability, estimated by use of Global Burden of Disease (GBD) weights (22); YLL – years of life lost; DALY – disability-adjusted life years.

Table 4. Incidence, years lived with disability (YLD)*, disability-adjusted life years (DALY) per 1000 population (all persons), and YLD/DALY ratio from selected cancers in Serbia and European region

	Region†				
Cancer site	Serbia	European	European A	European B	European C
Stomach cancer:					
incidence	0.16‡	0.25	–	–	–
YLD	0.06‡	0.06	0.06	0.04	0.09
DALY	1.84‡	1.83	1.15	1.48	3.29
YLD/DALY (%)	3.0	3.0	5.0	3.0	3.0
Colorectal cancer:					
incidence	0.39‡	0.43	–	–	–
YLD	0.20‡	0.27	0.50	0.12	0.20
DALY	2.85‡	2.14	2.63	1.30	2.49
YLD/DALY (%)	7.0	13.0	19.0	9.0	8.0
Lung cancer:					
incidence	0.62‡	0.46	–	–	–
YLD	0.29‡	0.12	0.14	0.08	0.11
DALY	6.66‡	3.75	4.04	2.76	4.49
YLD/DALY (%)	4.0	3.0	3.0	3.0	2.0
Breast cancer:					
incidence	0.45‡	0.42	–	–	–
YLD	0.25‡	0.36	0.50	0.18	0.27
DALY	2.76‡	2.14	2.46	1.36	2.29
YLD/DALY (%)	9.0	17.0	20.0	13.0	12.0
Cervical cancer:					
incidence	0.15‡	0.06	–	–	–
YLD	0.06‡	0.05	0.03	0.05	0.06
DALY	0.98‡	0.46	0.26	0.67	0.69
YLD/DALY (%)	6.0	11.0	12.0	7.0	9.0

*Years lived with disability, estimated by use of Global Burden of Disease (GBD) weights (22).
†European region (22): European region A (very low child, very low adult mortality) – Andorra, Austria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxemburg, Malta, Monaco, Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland, United Kingdom; European region B (low child, low adult mortality): B1 – Albania, Bosnia and Herzegovina, Bulgaria, Georgia, Poland, Romania, Slovakia, The Former Yugoslav Republic of Macedonia, Turkey, Serbia and Montenegro; B2 – Armenia, Azerbaijan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan; European region C (low child, high adult mortality) – Belarus, Estonia, Hungary, Kazakhstan, Latvia, Lithuania, Republic of Moldavia, Russian Federation, Ukraine.
‡Standardized according to European population (17).

cancer in Serbia was almost the same as that in the European region. The incidence of stomach and colorectal cancers was lower and the incidence of lung and cervical cancers was higher in Serbia. The most pronounced difference was found in the incidence of cervical cancer, which was 2.5 times higher in Serbia than in the European region. DALY per 1000 population in Serbia was higher than in the European region for all observed cancers, except for stomach cancer. The differences between Serbia and the European region in participation of YLD and YLL in the total burden (DALY) were presented through YLD/DALY ratio. The proportion of YLD in DALY for stomach and lung cancers in Serbia was similar to that estimated for the European region. For colorectal, breast, and cervical cancer, the proportion of YLD in DALY was smaller even in comparison to European B and European C regions.

The burden of the same cancers was also estimated by Dutch weights used for calculation of

Table 5. The burden of cancers by site in the population of Serbia and selected countries, 2000

		YLD* per 1000			DALY† per 1000		YLD/DALY (%)‡			
Cancer site	YLD	crude	standardized§	DALY	crude	standardized§	Serbia	Victoria	New Zealand	The Netherlands
Stomach	1246	0.17	0.14	17 149	2.27	1.92	7.0	10.0	not available	not available
Colorectal	2945	0.39	0.32	27 167	3.60	2.97	11.0	20.0	18.0	not available
Lung	4192	0.55	0.52	60 626	8.03	7.89	7.0	9.0	7.0	6.5
Breast	5086	0.67	0.59	26 820	3.55	3.10	19.0	28.0	26.0	27.0
Cervical	1121	0.15	0.14	8822	1.17	1.06	13.0	19.0	not available	not available

*YLD – years lived with disability; Dutch weights used for estimation of YLD (23,24).
†DALY – disability-adjusted life years.
‡Victoria (24), New Zealand (28), the Netherlands (29,30).
§Standardized according to European population (17).

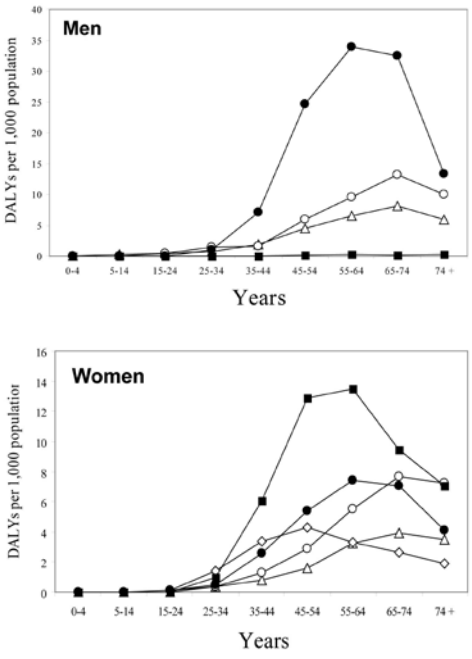

Figure 1. The burden of cancer by site, sex and age in Serbia, 2000. Triangles – stomach cancer; open circles – colorectal cancer; rhombs – cervical cancer; squares – breast cancer; closed circles – lung cancer.

YLD (Table 5). Since Dutch weights were much higher, the values of YLD and DALY were also higher than those obtained by Global Burden of Disease study weights. The same was true for YLD/DALY ratios. Participation of YLD in DALY for lung cancer in Serbia was similar to that found in Victoria study (24), but YLD/DALY ratio for stomach, colorectal, breast, and cervical cancers in Serbia was lower.

Discussion

The total burden of lung, stomach, colorectal, breast, and cervical cancers in Serbia in 2000 amounted to 133 689 DALYs. There were significantly more losses on account of premature death than disease-related disability. The participation of a burden caused by disease-related disability in the total burden of selected cancers was lower in Serbia than in other European countries, with the greatest differences being found for colorectal, breast, and cervical cancers.

Although we considered our mortality data reliable, percentage of deaths assigned to ill-defined codes was not small. However, we could expect that among ill-defined causes of deaths, cardiovascular diseases were more frequent than malignant diseases.

On the basis of comparison with cancer incidence in Slovenia (27), we assumed that data from the Cancer Register for Belgrade and for Vojvodina were reliable enough to estimate cancer incidence in Serbia. Slovenia was chosen for comparison for several reasons. Serbia and Slovenia had been part of former Yugoslavia before 1991, the health service in Slovenia was closely related to that in Serbia, and Cancer Registry in Slovenia was one of the oldest services of this type in Europe (26). With some exceptions, incidence rates of observed cancers were similar in these two populations. Higher incidence rates of lung and cervical cancers in Serbia were expected, because smoking rate is one of the highest in Europe and screening for cervical cancer has not been established yet.

Method used for estimation of DALY was largely based on the one developed for the Global Burden of Disease study (4). After discussion with experts for selected cancers, the Global Burden of Disease model and provisional disability weights for cancer stages were used (22). The estimation of YLD by Dutch disease model and disability weights (23) was also performed to allow for comparison with other population data analyzed by the same method. As expected, however, we obtained similar information from these two models, at least when the burden of cancer is concerned. Only the participation of YLD in DALY was higher when Dutch weights were applied. In Australian Burden of Disease study (5), the two sets of weights were used concurrently because there was a high correlation between them for 54 conditions, indicating that the two sets of weights valued the same conditions similarly. Although it is possible to create own disease model and to estimate own disability weights, in

our opinion, the same disease model and disability weights should be used in all studies to make comparison between populations possible. Since we had no reliable data about treated and non-treated cases, we accepted that, according to the Global Burden of Disease estimate, 20% of the cancer cases were untreated (4).

We used 5-year survival data for Slovenia from 1985 to 1989 (26) because it was more appropriate than to use data on some other neighboring country or Europe as a whole. The reason was that in Serbia we could not expect positive changes in survival during the preceding 10 years, ie, in the period 1991-2000. The civil strife in 1991, which led to the war and the break-up of the former Yugoslavia, United Nation's economic sanctions imposed on Serbia and Montenegro, and the ensuing economic crisis had a highly adverse effect on the population health and the quality of health care (31).

We may conclude that DALYs, used as the summary measure of population health in the present study, can be considered a good estimate of cancer burden in Serbia. The differences in cancer burden and especially the differences in YLD/DALY ratio between Serbia and European region, and between Serbia and Victoria, New Zealand, and the Netherlands, could be explained by higher incidence and/or higher fatality of almost all observed cancers in Serbia. Early diagnosis and early and adequate therapy of lung cancer and to a less extent of stomach cancer do not influence significantly their prognosis. That is why YLD/DALY ratio for these cancers is similar both in the developed and in the developing countries. On the other hand, early diagnosis and therapy of cervical, breast, and colorectal cancers have considerable influence on their outcome. Consequently, the participation of YLD in DALY is lower in countries like Serbia, in which regular screening for these cancers has not been organized yet, than in countries in which early detection was established years ago. It should be also mentioned that YLD/DALY ratio can be affected by age distribution of the diseased – the participation of YLL in DALY is greater when fatal disease occurs in younger age groups.

The most important advantage from a policy perspective of the approach taken in this study is that estimates of burden of cancers are expressed in terms of a summary health-outcome measure, which combines mortality and morbidity. These estimates should guide future health strategies and interventions and would allow for monitoring of the improvements in health and the performance of the health care system. However, there are views that burden of disease assessment should be supplemented with positive measures of health expectancy or health adjusted life expectancy (HALE). According to Tobias (28), these two families of summary measures of population health could be measured in such a way to make them not only conceptually, but also quantitatively complementary. In any case, the estimate of disability adjusted life years for selected cancers should be repeated after several years in order to assess the effects of preventive strategies, which are in the process of implementation.

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