

ORIGINAL ARTICLE

Cancer burden of breast and gynecological cancers in Bulgaria: epidemiology and clinical aspects

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Summary

Purpose: In Bulgaria, there are over 3700 cases diagnosed with breast cancer annually and over 3300 with gynecological cancers. The purpose of this study was to estimate the burden of breast and gynecological cancers in Bulgaria, analyzing trends of incidence, mortality and survival for the past two decades.

Methods: Data from the Bulgarian National Cancer Registry for women diagnosed with cancer of breast (C50, ICD10), cervix uteri (C53), corpus uteri (C54) and ovary (C56) during 1993 – 2009 were analyzed. Age-standardized incidence and mortality rates (ASR) per 100,000 persons were calculated using the world standard population. Average annual percent changes (AAPC) for 1993-2009 were estimated by Joinpoint regression. The observed survival was analyzed with the Life Table method for two periods: 1993-1997 and 2005-2009.

Results: Incidence rates of the most frequent cancers among Bulgarian women are increasing – from 1.7% to 2.6% annually. Mortality rates are decreasing significantly for breast (-0.8% annually) and increasing for corpus uteri cancers (4.9% annually). Survival for all sites increased from 3 to 8% over the study period. We observed greater proportion of cases diagnosed in stage I in 2009 than in 1993, for the 4 sites.

Conclusion: These results indicate some differences in trends in incidence and mortality of the reviewed sites compared with other European countries, highlighting the need for more strict adherence to integrated treatment standards and the necessity of introduction of population screening programs.

Key words: breast, cancer, cancer burden, epidemiology, gynecological cancers

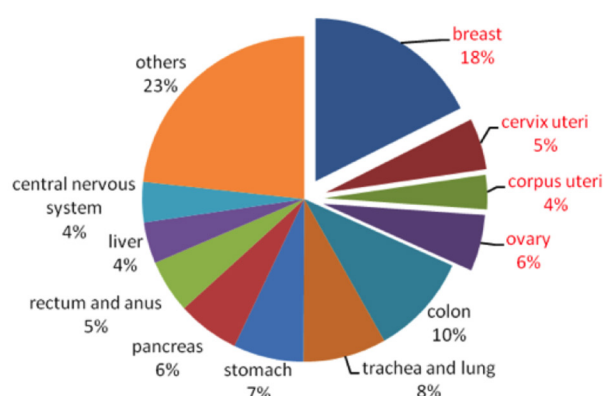
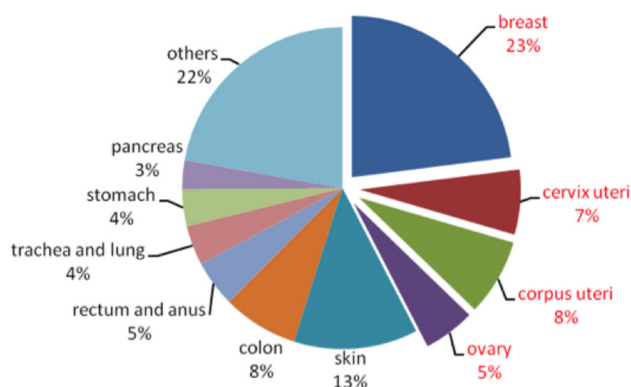
Introduction

In 2008 there were 12.7 million cancer cases diagnosed worldwide and 7.6 million deaths. Of these, almost half were women - 6.1 million new cases and 3.3 million deaths. Malignant diseases of the breast and genitals are the most common cancers in women worldwide - 2.4 million new cases per year. Breast cancer ranks first with 23.2% (1.4 million cases) of all incident cancers and the genitals (corpus uteri, cervix uteri and ovary) 17.3% (1.0 million cases) of them [1]. Incidence rates for breast cancer vary from 19.3 per 100,000 women in Eastern Africa to 89.7 per 100,000 women in Western Europe. The highest in-

cidence rates are observed in developed regions of the world. The incidence of breast cancer is increasing in most countries. Slower increase of incidence rates is observed for uterine and ovarian cancers. The incidence of cervical cancer is decreasing as a consequence of effective screening. In Europe in 2012 there were 1.6 million new cancer cases in females and 779,000 deaths. Breast cancer ranks first with 28.9% (464,000 cases) and gynecological cancers (corpus uteri, cervix uteri and ovary) 13.9% (223,000 cases) of all cancers in females. The incidence of breast cancer is highest in the countries of Northern and Western Europe (over 120/100,000 women) and lowest in Central and Eastern Europe – about 70/100,000 women.

Table 1. Number of cases, age-standardised rates (ASR) per 100 000 and average annual percent changes (AAPC) for the period 1993 – 2009, for breast and gynecological cancers among Bulgarian females

| | 1993 | | 2009 | | AAPC |
|------------------------|------------------|------------|--------------|------------|----------|
| <i>Site, ICD10</i> | <i>Cases</i> | <i>ASR</i> | <i>Cases</i> | <i>ASR</i> | <i>%</i> |
| | <i>Incidence</i> | | | | |
| Breast, C50 | 2720 | 42.1 | 3809 | 55.2 | 1.7* |
| Cervix uteri, C53 | 795 | 14.0 | 1072 | 18.7 | 2.4* |
| Corpus uteri, C54 | 943 | 13.8 | 1278 | 17.3 | 2.0* |
| Ovary, C56 | 657 | 10.6 | 862 | 13.0 | 2.6* |
| | <i>Mortality</i> | | | | |
| Breast, C50 | 1055 | 14.8 | 1234 | 14.9 | - 0.8* |
| Cervix uteri, C53 | 317 | 4.8 | 356 | 5.4 | - 1.0 |
| Corpus uteri, C54 | 186 | 2.4 | 242 | 2.9 | 4.9* |
| Ovary, C56 | 323 | 4.6 | 395 | 5.2 | 0.9 |

* significant values ($p < 0.05$)**Figure 1.** Percent distribution of all incident cancer cases in Bulgarian women, 2009.**Figure 2.** Percent distribution of all cancer deaths in Bulgarian women, 2009.

The incidence of gynecological cancers is relatively high in Central and Eastern Europe, and lower in Northern and Western Europe [2]. In Bulgaria, there are over 3,700 cases diagnosed with breast cancer annually and over 3,300 with gynecological cancers. Projections for 2013 are for 3,934 new cases with breast cancer and 3,568 with female genital cancers, which confirms the heavy burden of these malignant diseases for Bulgarian women [3].

The purpose of this study was to estimate the burden of breast and gynecological cancers in Bulgaria, analyzing trends of incidence, mortality and survival for the past two decades.

Methods

Data from the Bulgarian National Cancer Registry for women diagnosed with cancer of breast (C50, ICD10), cervix uteri (C53), corpus uteri (C54) and ovary (C56) during 1993 – 2009 were analyzed. Mortality data for the same period and sites was provided by the National Statistical Institute [4]. Age-standardized incidence and mortality rates (ASR) per 100,000 persons were calculated using the world standard population [5]. Average annual percent changes (AAPC) for 1993-2009 were estimated by Joinpoint regression [6]. Significant trends were set at $p < 0.05$. The observed survival was analyzed with the Life Table method for two periods: 1993-1997 and 2005-2009. All patients were followed-up until 31.12.2011. Wilcoxon test was used to estimate significant differences between the two periods. Data were processed with SPSS13 and Excel2007. Maps for breast and cervical cancer incidence in 2008 [7] were made with Instant Atlas, demo version [8].

Results

Breast and gynecological cancers (cervical, uterine and ovarian) comprised almost half of all incident cancer cases in Bulgarian women and about one third of all cancer deaths in females (Figures 1 and 2). Breast cancer was the most common site (23% of the new cases), followed by cancer of the uterine body (8%), cervix (7%) and ovary (5%). While breast cancer was the most common cause of death (18% of all cancer deaths in females), gynecological cancers occupied a different place in the structure of mortality compared to incidence: ovary (6%), cervix (5%) and uterine body (4%).

Incidence and mortality rates of the most frequent cancers among Bulgarian women were found to be increasing. ASRs for 1993 and 2009, along with the average annual percent changes are presented in Table 1. Incidence was increasing more

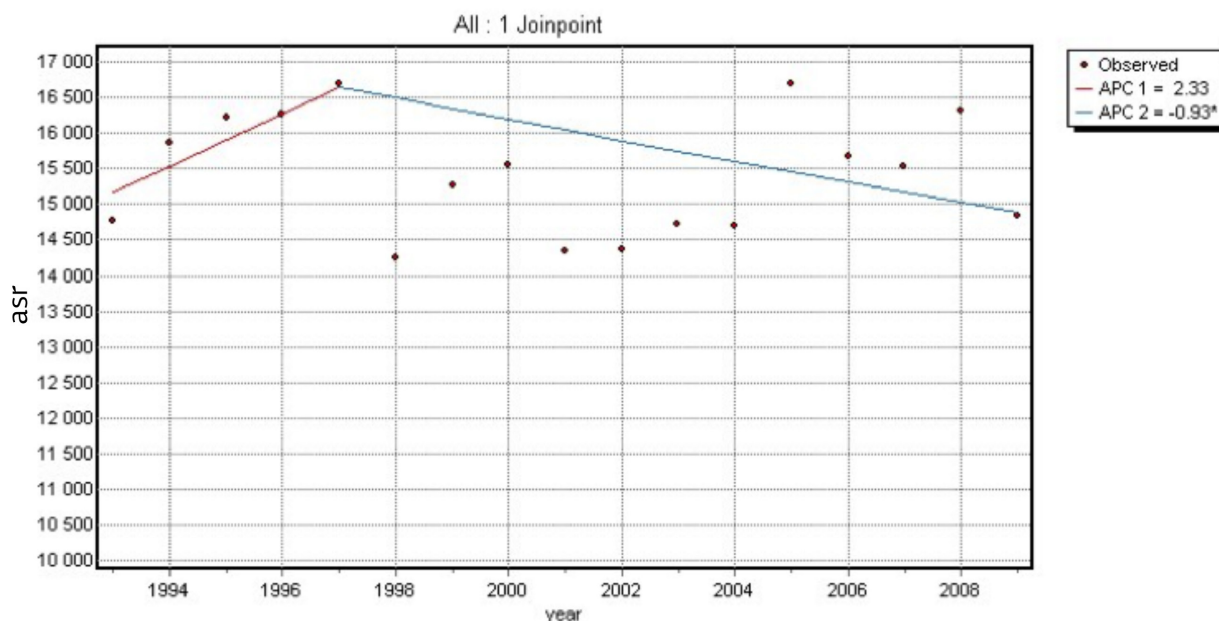


Figure 3. Trends of breast cancer (C50, ICD10) mortality for the period 1993 – 2009.

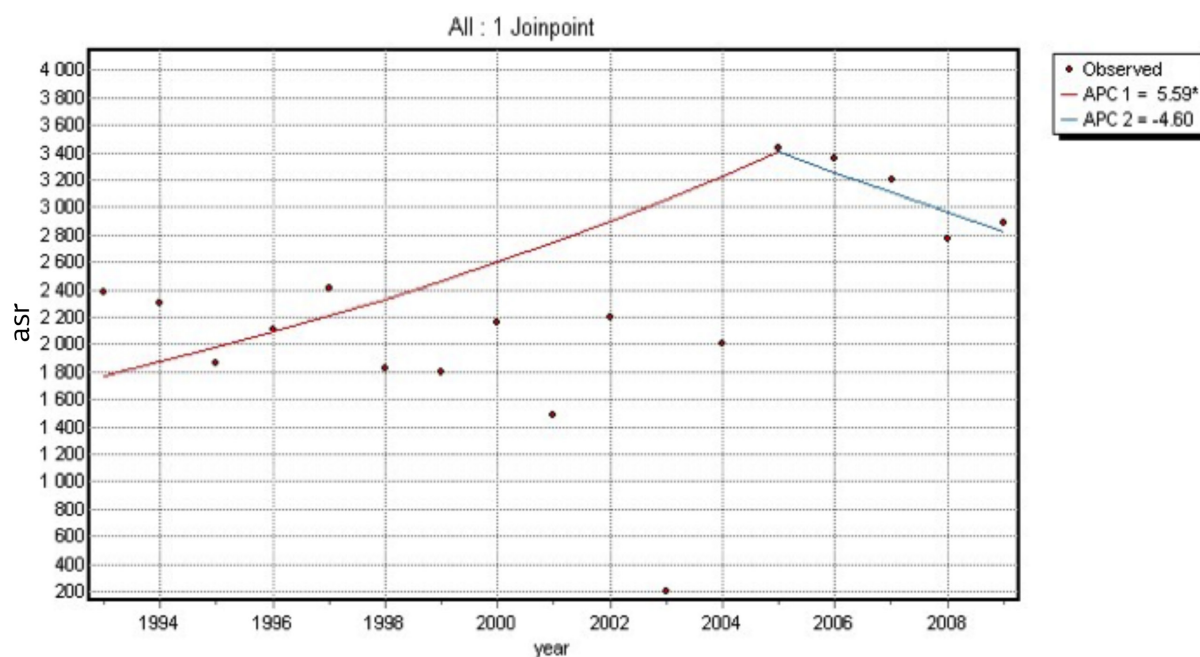


Figure 4. Trends of uterine cancer (C54, ICD10) mortality for the period 1993 – 2009.

rapidly in ovarian cancers (2.6% annually). Increase in mortality was most pronounced in corpus uteri (4.9% annually), followed by the ovary (0.9%). Mortality rates for breast cancer were significantly decreasing by - 0.8% per year for the study period. Trends of mortality rates in breast and corpus uteri cancers are shown in Figures 3 and 4. A significant decrease in breast cancer mortality after 1997 and a non-significant decrease in corpus uteri after 2005 were noticed.

Age-specific incidence was highest in women aged about 60 years for breast cancer, uterine body

and ovary, while for cervical cancer it was highest for the 40-45 years age group (Figure 5).

The proportion of women diagnosed over the age of 60 was highest in the uterine body, followed by breast and ovarian cancers. In 2009 there was an increase for all sites of 5-10% of the cases diagnosed in this age group, compared to 1993 (Figure 6).

Stage distribution for 1993 and 2009 is shown on Figure 7. A greater proportion of cases diagnosed in stage I in 2009 than in 1993 for all the 4 sites was registered. A decrease of stage II cases

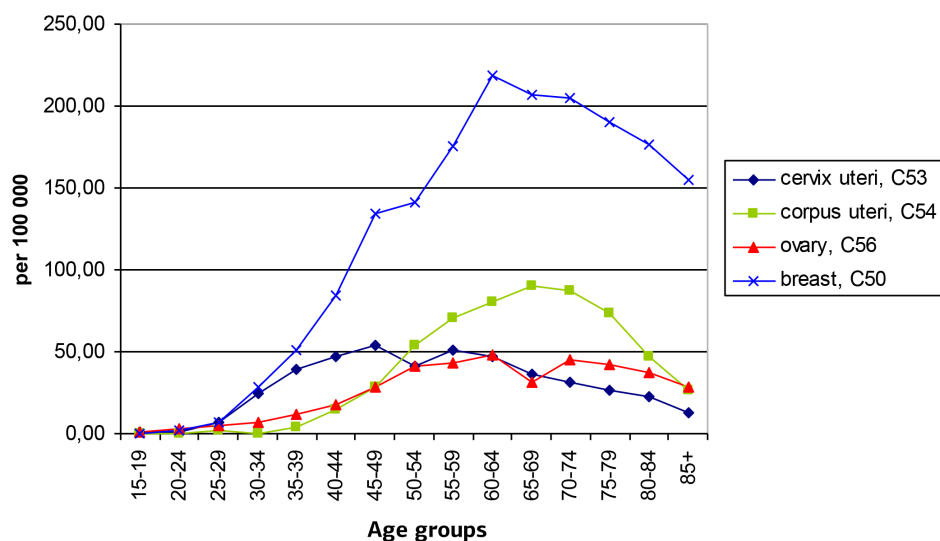


Figure 5. Age-specific incidence rates for cancers of the breast, corpus uteri, cervix uteri and ovary 2009.

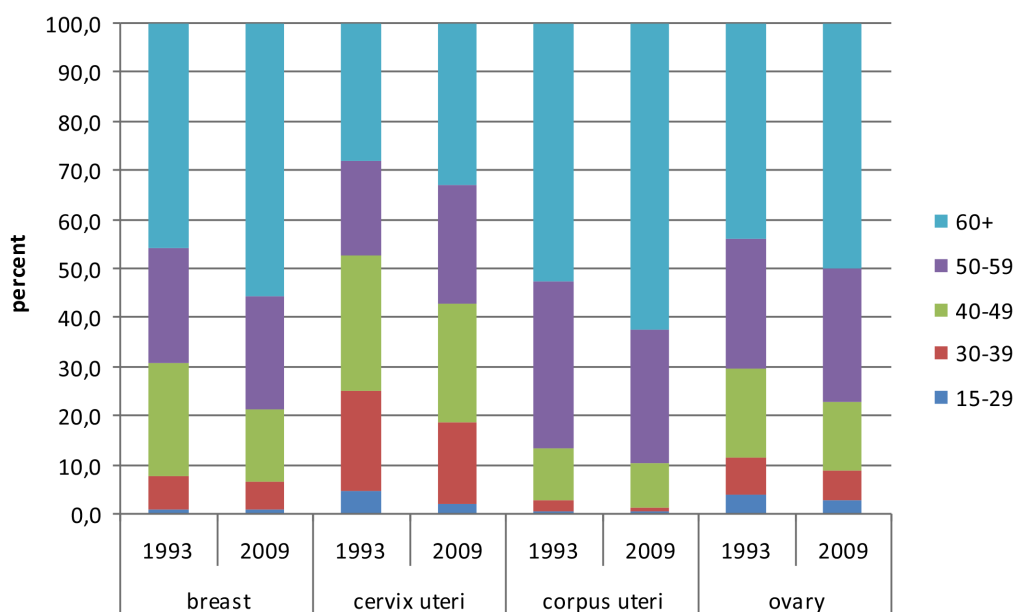


Figure 6. Age distribution of the newly diagnosed breast and gynecological cancers in 1993 and 2009.

Table 2. Observed 5-year survival rates for breast and gynecological cancer patients diagnosed during 1993-1997 and 2005-2009, followed-up till the end of 2011

| Site, ICD10 | Cervix uteri, C53 | | Corpus uteri, C54 | | Ovary, C56 | | Breast, C50 | |
|---------------------|-------------------|-----------|-------------------|-----------|------------|-----------|-------------|-----------|
| Period | 1993-1997 | 2005-2009 | 1993-1997 | 2005-2009 | 1993-1997 | 2005-2009 | 1993-1997 | 2005-2009 |
| 5-year survival (%) | 49.7 | 54.7 | 66.6 | 69.0 | 35.4 | 40.3 | 62.5 | 70.3 |
| p-value | < 0.0001 | | 0.024 | | < 0.0001 | | < 0.0001 | |

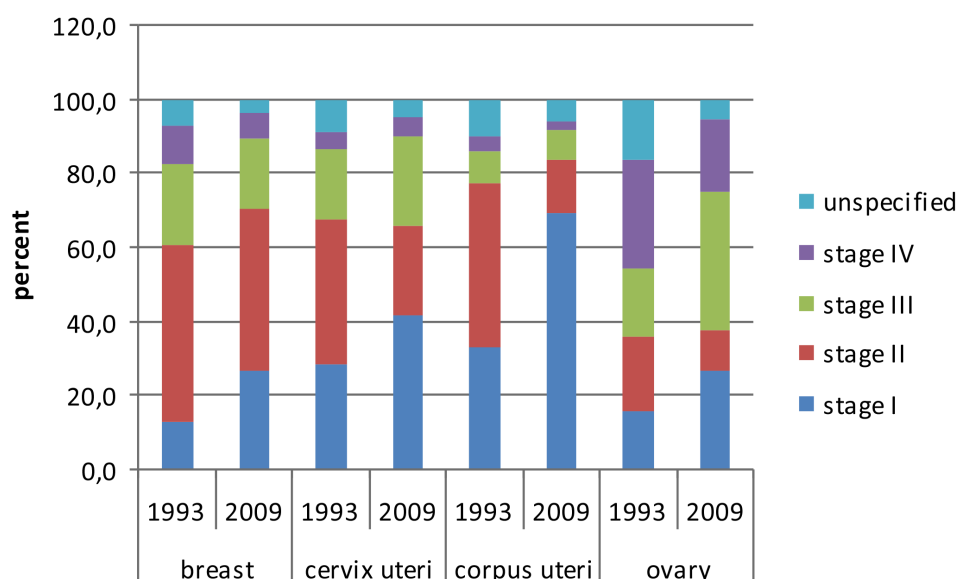


Figure 7. Stage distribution of the newly diagnosed breast and gynecological cancers in 1993 and 2009.

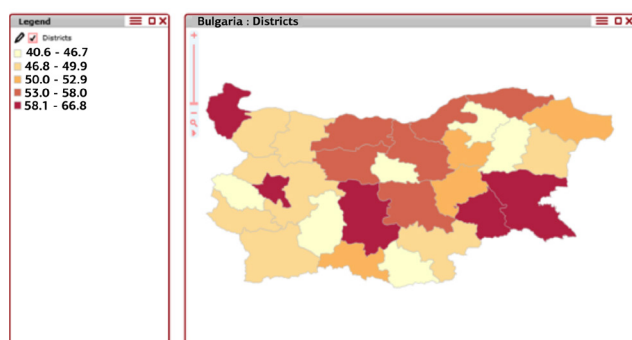


Figure 8. Age-standardized (world standard) incidence rates per 100,000 of breast cancer in females by district in Bulgaria, 2008.

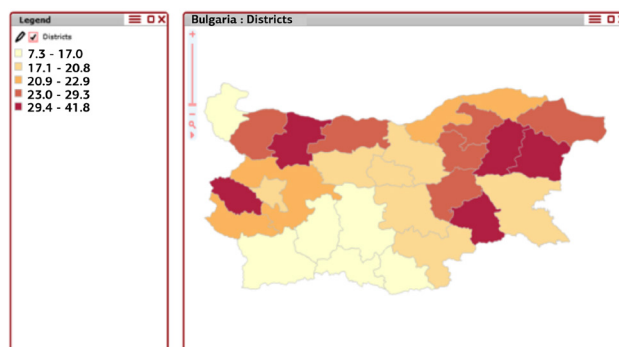


Figure 9. Age-standardized (world standard) incidence rates per 100,000 of cervical cancer by district in Bulgaria, 2008.

was observed, with the exception of breast cancer, which in 2009 increased slightly, while stage III cases decreased. A significant reduction in stage IV and unspecified stage was noted.

A difference in the incidence rates of breast cancer by regions was registered - ranging from 30 to 70 per 100,000 women. The highest ASRs were in the largest cities of the country. The difference between the most affected and least affected areas was 2.6 times (Figure 8).

The incidence of cervical cancer varied from 7 to 30 per 100,000 women. It was lowest in areas with a predominantly Muslim population. The difference between the most affected and least affected areas was 4.6 times (Figure 9).

Survival for all sites increased by 3 to 8% over the study period. The largest increase was seen in breast cancer, followed by ovarian and uterine cancers (Table 2).

Discussion

Trends of breast and gynecological cancers incidence rates are similar globally. In our study the highest increase in incidence was observed in ovarian cancer, followed by uterine body and breast cancer. Increasing incidence of ovarian cancer is related to increased infertility, stimulation of ovulation and in vitro fertilization [9], which are on the increase during the last decade in Bulgaria. Improved survival for ovarian cancer without significant change in stage distribution is explained by the larger number of patients re-operated for tumor reduction and new chemotherapy regimens that have proven efficacy. Patients with ovarian cancer are diagnosed in stage III-IV in 60% of the cases, when the treatment option for patients with suboptimal cytoreduction is chemotherapy. With the introduction of taxanes (espe-

cially paclitaxel), the superiority of cisplatin combined with paclitaxel compared with the previous standard of cisplatin plus cyclophosphamide was confirmed [10].

Results for Bulgaria correlate with these trends (increasing incidence and survival) and logically the most common cancer in women is the most common cause of cancer death. As a result of improved diagnosis, raised awareness and opportunistic screening programs in Bulgaria, an increase of 13 to 33% of cases diagnosed in stage I and a decrease in the proportion of stage II and III was observed for most of the sites. This, in turn, together with compliance with standards of cancer treatment, reduced the mortality in breast and cervical cancer and increased survival by 3 to 8% for all sites. Improved survival of patients with cervical cancer may be explained with the relative increase of diagnosis at an earlier stage and the use of more effective treatment methods - over the last decade the indications for performing surgery have expanded and the proportion of patients treated with radiotherapy has decreased. Considering that the incidence of breast cancer is highest in large cities, it would be logical to be associated with major risk factors (reduced fertility, later age at first birth and decreased lactation, excessive hormonal intake). The lowest incidence of cervical cancer in Southwestern Bulgaria can be related to customs and traditions of the people living there, (mostly Muslim population with less promiscuity, lower infection rate with HPV/ a proven etiologic factor for cervical cancer, and male circumcision contribute to this). HPV infection was found in 99% of the cases of cervical cancer and 4% in women of reproductive age with infection combined with different degrees of precancerous cervical lesions [11,12]. In Bulgaria, the lowest incidence of cervical cancer occurs in regions inhabited mostly by Turkish-speaking population and with Muslim religion. In Turkey cervical cancer is relatively rare (age-standardized incidence is 5.4 per 100,000) [13]. Despite the fact that over the last 20 years there is a tendency of increasing engagement of the younger age groups with cervical cancer, the highest risk is still for post-menopausal women and especially after the age of 60. The trend of increasing incidence of corpus uteri cancer in adults can be explained with the fact that the risk of developing the disease is increasing with age and, on the other hand, there is an increase of the years of menstruation [14,15]. In general, the average life expectancy of women has increased, as well as the proportion of those with obesity and diabetes, which are also risk factors

for endometrial cancer. Increasing proportion of elderly breast and gynecological cancer patients is also seen in other countries [16,17]. Among European countries, Greece has the lowest incidence and mortality from endometrial cancer. The low average height of Greek women, high frequency of induced abortions and low frequency of oestrogen replacement may contribute to the lower incidence of endometrial cancer in Greece [18]. Similar trends are found in other countries in Southeastern Europe and a significant reduction in mortality of breast and gynecological cancers has been recently reported in those countries that apply screening programs [19].

On the other hand, according to our results, the survival of patients with endometrial cancer is increasing at a slower rate. This is most likely due to the fact that over the last decade the proportion of non-cancer hospitals which treat patients with endometrial cancer has increased and this resulted in insufficient preoperative and surgical staging.

Conclusions

Breast cancer is the most common malignancy in Bulgarian women, followed by cancer of the uterine body, cervix and ovary. While breast cancer is the most common cause of cancer deaths, female genital cancers occupy a different place in the structure of mortality compared to their incidence - ovary, cervix and uterine body.

The fastest rate of increasing incidence is observed in ovarian cancer, followed by cervical cancer, uterine body and breast. Increase in the proportion of cases diagnosed in stage I from 13 to 33% for all sites was noticed. The country's districts are affected in a different degree, according to the distribution of major risk factors. The incidence of breast cancer is highest in large cities. The lowest incidence of cervical cancer is observed in regions in Southwest Bulgaria.

In all the sites except cervix, the most affected age group is over 60 years. The proportion of these patients increased in recent years.

There is a significant reduction in mortality of breast and cervical cancers.

There was an increase in survival in all sites by 3 to 8%.

The results indicate some differences in trends in incidence and mortality of the reviewed sites, compared with other European countries, highlighting the need for more strict adherence to integrated treatment standards and the necessity of introduction of population screening programs.

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