

## ORIGINAL ARTICLE

# Trend analyses of breast cancer incidence and mortality in Vojvodina

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## Summary

**Purpose:** Breast cancer is the most common type of malignant tumor in women and one of the most significant public health problems in the world. The purpose of this work was to determine breast cancer epidemiology in the Autonomous Province of Vojvodina in a 20-year period (1993 to 2012) by determining breast cancer incidence and mortality in female population and analyzing the trend in the specified period.

**Methods:** The research involved the population of women in Vojvodina in the period from 1993 to 2012. Data were obtained from the Register for malignant neoplasms of Vojvodina. Incidence and mortality trends were analyzed by a joinpoint regression analysis.

**Results:** A total of 20,242 cases of breast cancer were registered in the observed period. Standardized incidence ratio

in 2012 was 71.2/100,000. The trend of incidence increased with an average annual percentage of growth of 2.10. A total 10,062 deaths due to breast cancer were documented. Standardized incidence ratio in 2012 was 28.6/100,000. An increase of mortality rate by 1.70% per year was recorded in the period from 1992 to 2006 and a decline in the mortality rate by 1.56% was noticed afterwards. The highest percentage of deaths due to breast cancer was recorded in a group aged 60-69 years (26.7%).

**Conclusions:** Our results indicated an unfavorable increasing trend in breast cancer incidence, while favorable trend in mortality was noticed after 2006.

**Key words:** breast cancer, incidence, mortality, epidemiology

## Introduction

Breast cancer is one of the most significant public health problems in the world. GLOBOCAN reported 2,089,000 new cancer cases for 2018, while the number of deaths due to breast cancer worldwide is estimated to 626,000 for the same year [1].

Estimated standardized incidence rate for the Republic of Serbia is 75.2/100,000, which is quite similar to the average incidence rate in Europe (74.4/100,000). On the contrary, estimated standardized mortality rate in the Republic of Serbia

(21.9/100,000) is noticeably higher than the European average (14.9/100,000). Serbia has higher mortality rates in comparison to all other European countries, except Montenegro [1]. It is important to emphasize that breast cancer is the third leading cause of death in Serbia in women older than 45 years [2].

In Vojvodina, standardized breast cancer incidence rate in 2012 was 71.2/100,000 (the total number of newly diagnosed cases was 1334), and

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standardized mortality rate was 28.6/100,000 (the total of 549 deaths) [3].

In addition to high cancer incidence rates, even more alarming is the constant increase of new cancer cases, especially in the countries where the rates used to be low. Breast cancer is the most common cancer in women in developed as well as in developing countries according to the 2012 and 2018 data. Every fourth woman is diagnosed with breast cancer, which speaks in favor of the significance of this issue [1]. Furthermore, breast cancer is among the most frequent causes of death from malignant diseases and is ranked fifth in Europe with the standardized mortality rate of 14.9/100,000 [4,5].

According to European Cancer Information System (ECIS) data, breast cancer in Europe ranked first in the structure of the patients diagnosed with this disease and patients who died from all the localizations of the malignant tumors with rates 29.5% and 17.5%, respectively [6].

Therefore, the purpose of this study was to explore the epidemiological situation of breast cancer in the area of Autonomous Province of Vojvodina in 20-year period (1993 to 2012), by determining breast cancer incidence and mortality in female

population, as well as to analyze trends in the specified time period.

## Methods

Descriptive epidemiological methods were used to process the data. Data were obtained from Vojvodina Cancer Registry, Oncology Institute of Vojvodina.

We determined the percentage ratio of breast cancer in the total number of cancer cases in Vojvodina in the observed period from 1993 to 2012. Three types of cancer incidence and mortality rates were calculated: crude, specific (age-specific) and standardized incidence and mortality rates. Rates were expressed per 100,000 persons. Calculations were based on the 10-year age group. The age-standardized rates (ASR) were calculated by direct standardization, using the world standard population. The data were analyzed chronologically.

Breast cancer incidence and mortality trends were estimated by joinpoint regression analysis. The Joinpoint Regression Program is a trend analysis software developed by the United States National Cancer Institute (US NCI) for the analysis of data from the Surveillance Epidemiology and End Results Program (SEER). Joinpoint analysis was used to identify the best-fitting point, where a statistically significant change (called the "joinpoint") had occurred, and to determine the trends between joinpoints.

**Table 1.** Breast cancer incidence and mortality (numbers, crude rates and age-standardized rates) in women in Vojvodina for the period 1993-2012

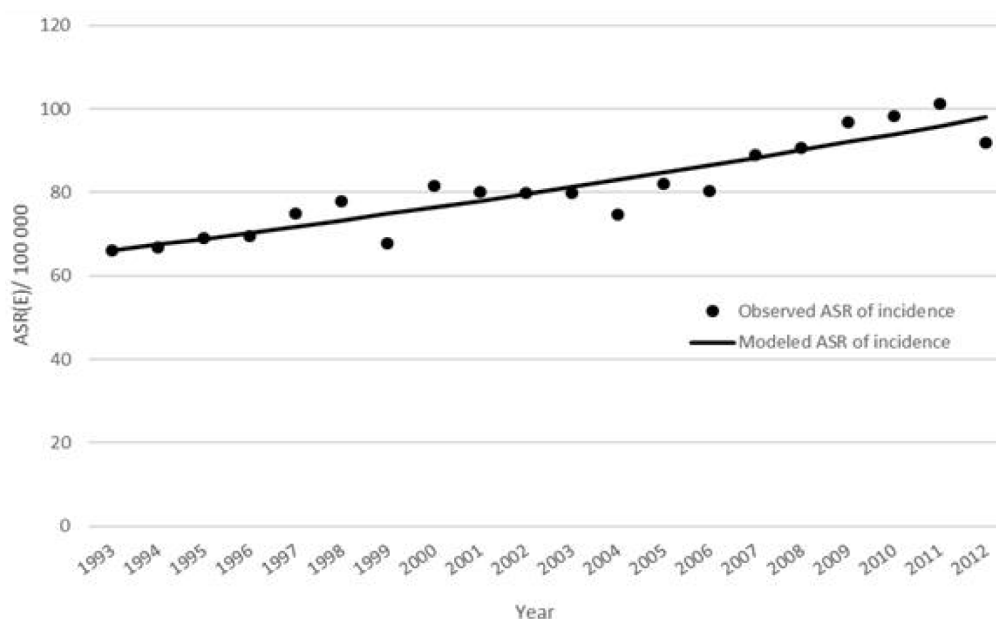
Year	Incidence			Mortality		
	N	Rate	ASR*	N	Rate	ASR*
1993	777	75.6	53.1	410	39.8	27.4
1994	795	77.5	52.9	409	40.1	26.9
1995	831	80.4	62.1	398	38.5	28.7
1996	836	81.7	54.4	416	40.5	27.4
1997	898	88.0	58.9	462	45.0	29.3
1998	931	91.4	61.6	476	46.3	30.1
1999	812	79.9	53.4	509	49.9	31.3
2000	981	96.8	63.6	510	50.5	32.9
2001	971	94.2	63.8	485	47.0	31.6
2002	1025	98.3	64.7	482	46.2	29.2
2003	1034	96.8	63.8	525	49.3	31.2
2004	960	90.8	58.8	555	52.5	32.9
2005	1054	99.9	64.8	577	54.4	32.9
2006	1046	99.2	63.1	572	54.9	33.8
2007	1160	110.5	69.1	560	54.1	33.2
2008	1198	114.8	70.7	549	52.6	31.9
2009	1261	122.0	75.9	550	52.8	31.3
2010	1291	121.6	78.1	531	49.6	31.1
2011	1340	131.5	78.0	578	57.3	33.3
2012	1241	122.2	71.2	508	50.2	28.6

\*ASR: age standardized rate (using world standard population)

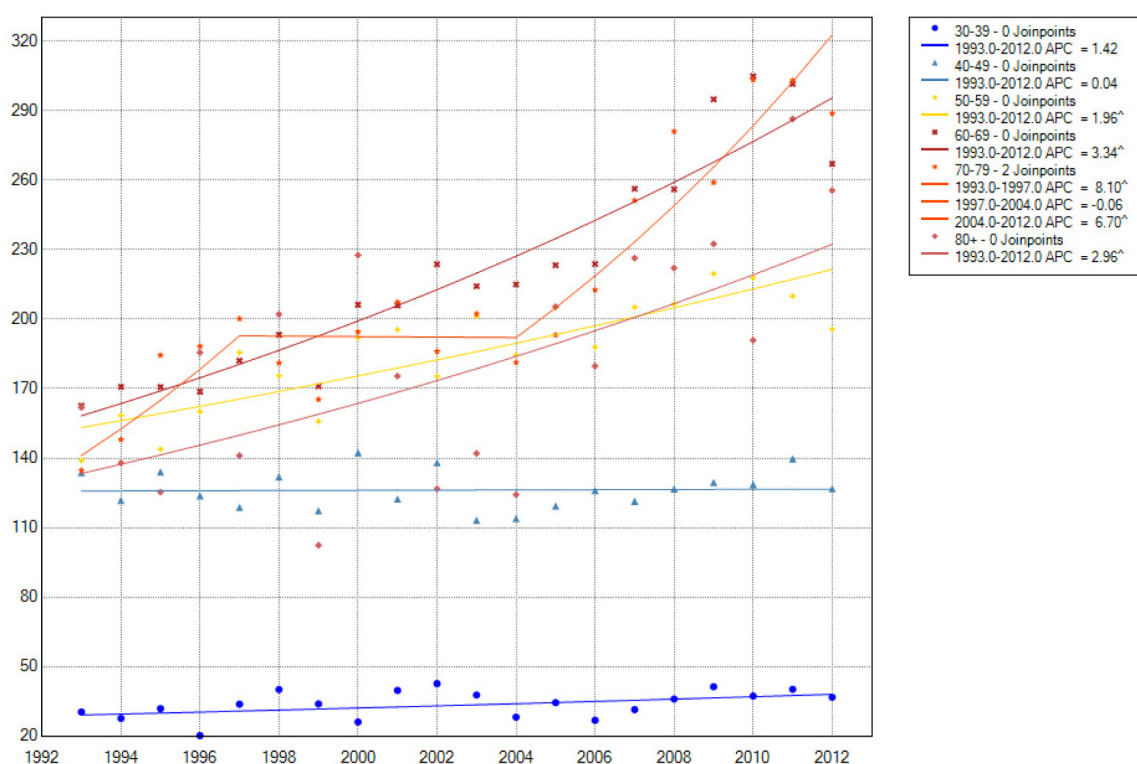
## Results

During 1993-2012, 20242 women with breast cancer were registered in the Autonomous Province of Vojvodina. In Vojvodina, breast cancer was the most common neoplasm in women in comparison with other cancer localizations, as it ranked first both in the structure of all patients diagnosed (25% in 2012), as well as in the total number of deaths

due cancer (19% in 2012). During the observed period, the number of cancer cases ranged from 777 (1993) to 1340 (2011). 10,062 women died as a consequence of the mentioned illness. During the observed period, the number of new breast cancer cases ranged from 398 (in 1995) to 578 (in 2011). The absolute number of new cases diagnosed with breast cancer and breast cancer-related deaths, the crude incidence and mortality rates and standard-



**Figure 1.** Joinpoint analysis of breast cancer incidence trends in women, Vojvodina, 1993-2012.



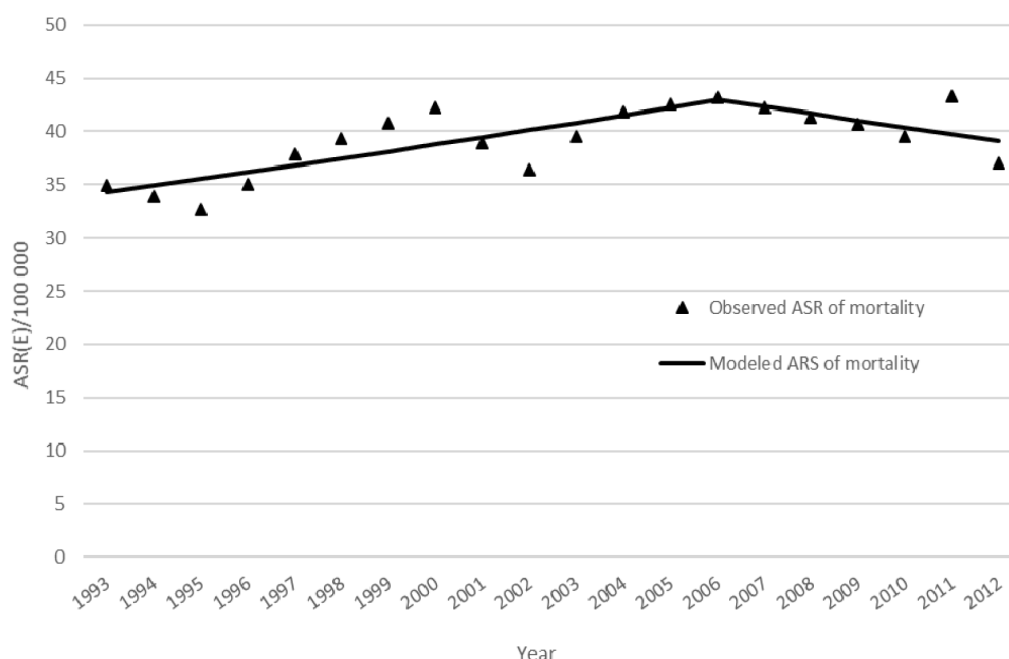
**Figure 2.** Joinpoint analysis of breast cancer incidence trends in women according to age groups, Vojvodina, 1993-2012.

ized incidence and mortality rates are presented in Table 1.

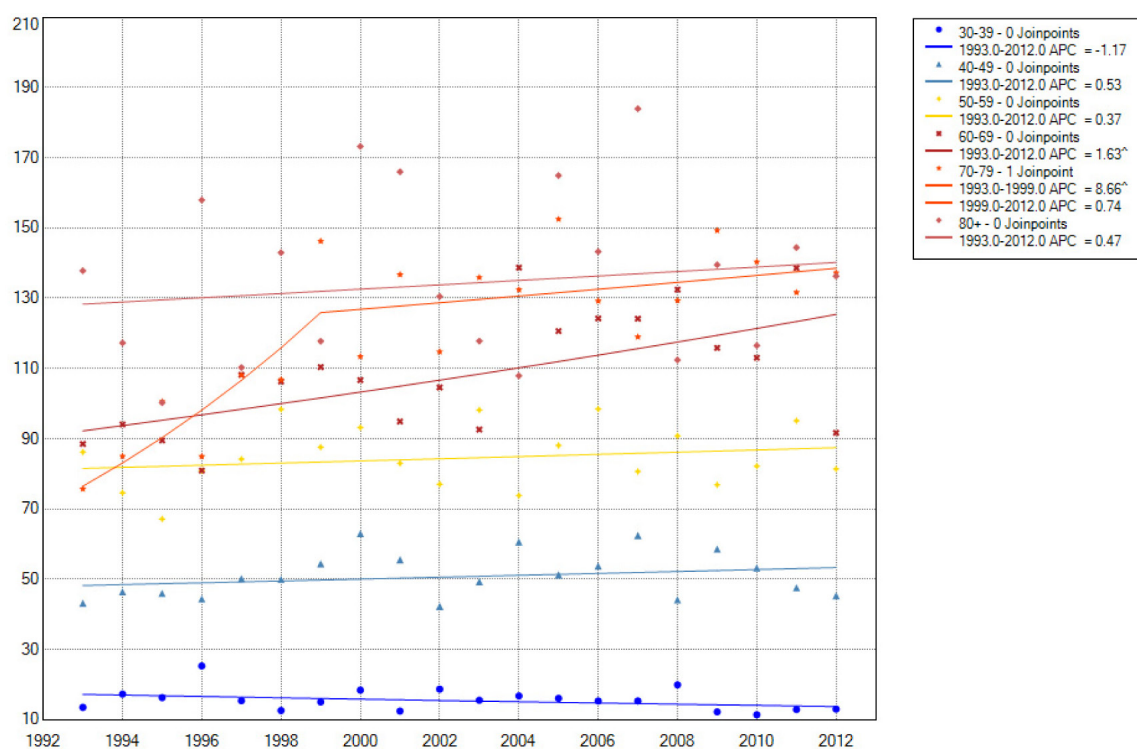
The standardized incidence rate ranged from 53.1/100,000 (in 1993) to 78.1/100,000 (in 2010). The age structure for all the breast cancer patients indicated that the highest percentage of patients belonged to those aged 55-64 (27.1%). The percentage of the patients younger than 40 was 5%. In the

observed period, breast cancer was registered in all age groups starting from those aged 10-14 (1 case).

The standardized mortality rate in the observed period ranged from 26.9/100,000 (in 1994) to 33.8/100,000 (in 2006). The highest number of women was registered in the age group 65-69 years (14%). The highest percentage of patients' deaths was detected in the age group of 60-69 years



**Figure 3.** Joinpoint analysis of breast cancer mortality trends in women, Vojvodina, 1993-2012.



**Figure 4.** Joinpoint analysis of breast cancer mortality trends in women according to age groups, Vojvodina, 1993-2012.



(26.7%), while women under 40 years constituted about 4.5 % of deaths due to breast cancer.

The cumulative risk of being affected by breast cancer up to the age of 74 ranged from 5.19 to 7.96 during the observed period, meaning 1 out of 20 to 1 out of 12 women will be affected during their lifetime in the absence of other fatal diseases. Additionally, the cumulative risk that resulted in death ranged from 2.61 to 3.50, meaning that 1 out of 40 women to 1 out of 30 women will develop breast malignancy up to the age of 74 in the absence of other fatal diseases.

Joinpoint analysis of the standardized incidence ratio showed an average increasing trend of 2.10% (95%CI=2.0-2.2;  $p<0.0$ ) (Figure 1).

The standardized incidence ratio trends demonstrated an increasing trend in all age groups (Figure 2). The highest increase was recorded in those aged 70-79 years (in the period from 1933 to 1997 and 2001 to 2012), and the lowest in those aged 40-49 (1993-2012).

The mortality trend was divided in two parts. An increase of mortality rate of 1.7% (95%CI=1.5-2.1;  $p<0.001$ ) per year was recorded in the period from 1992 to 2006. After that, a decrease in the number of deaths of 1.56% was observed (95%CI=-2.4. to -0.7;  $p<0.1$ ) (Figure 3).

The standardized incidence ratio trends of the 10-year age groups showed increasing trend in all the age groups (Figure 4). The greatest increase was recorded in those aged 70-79 years (in the period from 1993 to 1999). Decreasing trend in mortality was observed in the age group 30-39 throughout the whole observed period (1993-2012).

## Discussion

Descriptive breast cancer epidemiology provides the data reflecting the significance of this most common malignancy in women, since it is the most frequent neoplasm in female population (25% in 2012), as well as the most frequent cause of death (19% in 2012) in Vojvodina [4]. Vojvodina belongs to the area with high incidence rate and especially high breast cancer mortality rate in women in comparison to European Union (EU) and the surrounding countries [1].

Our results are in agreement with the data of the majority of European countries, where breast cancer is one of the leading health problems in women [7,8]. The real reason that lies behind the increase of breast cancer patients can only be assumed. Some of the reasons include: women with fewer children on average, the age of women giving their first birth is increasing and the number of obese women is also increasing.

Incidence trend showed a continuous increase in the territory of Vojvodina, throughout the whole observed period and in all age groups. Similarly, the annual incidence rate is increasing in the Eastern European countries and in the specific age groups 2-4% (15-39), 2-5% (40-49), 1-4% (50-69) and 1-6% (70+) [9,10].

Our results also indicated higher percentage of breast cancer mortality in comparison to European countries. Mortality rates decreased significantly in all age groups in the majority of the countries, especially in the countries of the Northern and Western Europe [11], however they were increased on the annual level in women aged over 55 in Ukraine, Moldavia and Cyprus [9].

The increase in cancer mortality trend in our country may be the consequence of absence of screening programs, as our country has been conducting national breast cancer screening program for women aged 50-69 since 2013 [12]. Randomized studies showed that the regular mammography in women aged 50-70 reduced cancer mortality by 25-30% [13-17]. In Vojvodina a decrease in the standardized mortality rate was recorded. Decrease in mortality can be explained by the improved novel therapies, such as the biological therapies, monoclonal antibodies and new hormonal therapies. SEER data (Surveillance, Epidemiology, and End Results Program) demonstrated reduction in breast cancer mortality of 1.9% per year in the period from 1998 to 2007 in USA [18].

In Europe, 20% of women get affected by breast cancer up to 50 years, 37% when aged 50-64, and 43% when older than 64 [5]. Our results showed that new cases and deaths due to breast cancer were less than 5% of women aged 40 years. According to the literature, the most important risk factor for the development of breast cancer is age [19]. Analysis of the structure of cancer patients showed that breast cancer is an illness of the middle-aged and older women. Around 78% of all cancers cases were diagnosed in those aged 55 and older. In the age groups 20-39 and 40-59 in the USA breast cancer is the leading cause of cancer-related death [20].

Even though a declining trend in breast cancer mortality has been recorded in Vojvodina, there is a worrying fact that a high percentage (around 40%) of the women deaths is recorded in women younger than 59. Also, every fifth death occurs in women under the age of 50 (20% approximately for the whole period). Compared with Croatia (a neighboring European country with high standardized mortality rates and similar age structure) it can be observed that the rate of younger women who died in Croatia was significantly lower (around 20% of deaths due to breast cancer in patients under 59

years of age and less than 10% of women under the age of 50). Some reasons for high mortality are diagnosing breast cancer in the later phase of disease or the different obstacles set by the patients and health system organization.

According to our results, non-significant decline in mortality was recorded in younger women in Vojvodina. In concordance with our results, similar situation was observed in EU countries where breast cancer mortality rate declined from 17.9/100,000 in 2002 to 15.2/100,000 in 2012. The predicted rate for 2020 is 13.4/100,000. Decrease in mortality (22% between 2002 and 2012) was highest in young women (20-49 years old). In EU, decrease was higher in the UK and other countries of the northern and western Europe than in the majority of the Central and Eastern Europe [11].

Even though there were more attempts to conduct breast cancer screenings, these programs were not conducted in Serbia until 2013. Target group were women aged 50-69. By the end of 2016, around one quarter of the municipalities in Serbia were included in the screening [22]. Preventive screening programs can result in early breast cancer detection and consequently in decrease of breast cancer mortality rate. We assume that decrease in mortality with national screening pro-

gram is expected in 10 to 15 years from the time of covering the target population with participation of 70 % or above.

Our conclusion is that in 1993-2012, the trends of breast cancer incidence in Vojvodina showed an unfavorable increase. The mortality trend was more favorable, as a decrease after 2006 was recorded. Variations in incidence and mortality rates reflect the influence of risk factors, availability of early breast cancer detection through screening programs, and efficient and available novel therapies. Health policy-makers and experts from this area should deal with the concerning increase in incidence and make the appropriate steps in decreasing breast cancer mortality in Vojvodina.

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## Conflict of interests

The authors declare no conflict of interests.

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