

# Malignant Neoplasms of Breast and Female Genital Organs (C50, C51-C58) in the Osijek-Baranja County, Croatia

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## ABSTRACT

Breast cancer (C50) and neoplasms of female genital organs (C51-C58) represent one of the most frequent cancer groups among females in economically developed countries. The Institute of Public Health of the Osijek-Baranja County in collaboration with different county institutes provide updated information on the cancer occurrence and trends in the Osijek-Baranja County (OBC). The aim of this article is to provide information on the tendencies relating to these cancer groups in the OBC during the period from 2001 to 2009, which will be the first report on these cancer sites on a county level in Croatia. This article processes data on cancer incidence and mortality, appertaining age distribution, median age, cancer survival and length of stay in the county hospitals collected in period 1996–2010. In the OBC, the overall incidence rates of breast, cervix uteri, corpus uteri and ovary cancer were, using the EU standard population, 82.9, 13.0, 19.0 and 14.5/100,000, respectively, and are all characterized by a declining tendency in the second period except breast cancer. The overall breast incidence rate resembles the Croatian average and way exceeds the corresponding Central and Eastern Europe incidence rates, but is still bellow the Northern Europe ones. Also, the overall mortality rates of breast, cervix uteri, corpus uteri and ovary cancer were 29.6, 5.0, 8.1 and 9.6/100,000, respectively, and are all featured by a increasing tendency. The cancer 5-year relative survival rate from breast, cervix uteri, corpus uteri and ovary cancer in period 2001–2005 amounted to 64.2%, 66.1%, 57.4% and 43.0%, respectively. The overall median ages at diagnosis of breast, cervix uteri, corpus uteri and ovary cancer totalled 61.9, 56.4, 66.4 and 60.8 years, respectively, while the median ages at death from these cancers were 68.7, 65.7, 70.3 and 67.6 years, respectively. During the entire 9-year period, the average length of stay in hospital due to breast, cervix uteri, corpus uteri and ovary cancer were 12.1, 14.8, 18.5 and 11.3 days, respectively. The length of stay in hospital decreased for all but for ovary cancer. Implementation and consolidation of women's awareness of these cancers and relating early diagnostic activities within the OBC population seem to be the most effective ways to reduce the appertaining risks and thus to encourage changes in the lifestyle.

**Key words:** cancer, age-standardized mortality rate, age-standardized incidence rate, 5-year relative survival rate, age distribution, breast cancer (C50), cervical cancer (C53), ovarian cancer (C56), endometrial cancer (C54), neoplasms of female genital organs, C51-C58, median age at diagnosis, median age at death, length of stay in hospital, Osijek-Baranja County, Croatia

## Introduction

### Breast cancer

In European females, breast cancer was the most common cancer in the year 1995. It accounted for 26% of all newly registered cancers and was the leading cause of death in females. It was associated with 17% of all deaths from cancer in females<sup>1</sup>. In 2012, the share of breast can-

cer in all female cancers amounted to 28.8% (94/100,000, using the EU standard population) while its share in all cancer deaths among females totalled 16.8% (23/100,000). There were significant differences between certain European regions in this view, though. In Croatia, the breast

cancer incidence and mortality rate were 83 and 25/100,000, respectively (2004)<sup>2,3</sup>. The established risk factors for breast cancer refer to low age at menarche, nulliparity, high age at first childbirth, short time from last full-term pregnancy, oral contraceptive use, low physical activity, alcohol intake and obesity<sup>4</sup>. The 5-year relative survival rate from breast cancer among European females diagnosed in period 1995–1999 amounted to 79%<sup>5</sup>. The basic factors affecting survival rate from breast cancer include stage at diagnosis, availability and quality of treatment, screening programmes and low socioeconomic status<sup>6–8</sup>. Comparing period 1990–1994 with period 2000–2004, the breast cancer mortality in the EU declined from 20.8 to 18.1/100,000 (–13%) at all age. The biggest decline, from 16.7 to 12.6/100,000 (–25%), was registered among females of the 35–44 age group<sup>9</sup> mainly due to improved treatment with anti-estrogens and chemotherapy as well as due to the impact of screening mammography<sup>10,11</sup>. According to the 2012 data, the mortality rate in the EU increased to 21.1/100,000<sup>12</sup>. In the USA, the age distribution of breast cancer incidence is disclosed by the fact that more than 2/3 of all breast cancer cases were aged from 45 to 74 and they were almost equally distributed between age groups 45–54, 55–64 and 65–74 (peak incidence appeared in the 55–64 age group). In the same country, the age distribution of death from breast cancer was characterized by a shift of 10 years into an older age. More than 2/3 of death cases occurred within the 55–84 age group, with most deaths in the 75–84 age group<sup>13</sup>. In the USA, the median ages at diagnosis and at death amounted to 61 and 68 years, respectively<sup>13</sup>. The median age at breast cancer diagnosis in Croatia was around 62 years in 2005<sup>14</sup>.

#### *Ovarian and endometrial cancer*

The epidemiology of both ovarian and endometrial cancer is closely intertwined. The same personal risk factors (late menarche, early age at first birth, breastfeeding, oral contraceptives) can be attributed to the occurrence of either of these cancers. The incidence rates of endometrial and ovarian cancer in Europe totals 10.4 and 8.4/100,000 in Southern Europe and 14.6 and 11.8/100,000 in Central and Eastern Europe and Northern Europe, respectively.

The mortality rate from endometrial cancer ranges from 1.8 to 3.4/100,000, and from ovarian cancer from 4.2 to 5.5/100,000<sup>15,16</sup>. The endometrial and ovarian cancer incidence rates increased sharply during the perimenopausal years and reach peak well after the menopause. The endometrial cancer incidence rates drop after age 70, but the ovarian cancer incidence rates continue to rise with aging<sup>13</sup>. In Denmark and the USA, the median age of patients at diagnosis of these two cancers is between 61 and 64 years<sup>17,18</sup>.

In the USA, the survival rates from ovarian cancer mostly vary according to age, disease stage and kind of treatment. The early disease stage is featured by a 5-year survival rate above 70%, but only 15% for those diagnosed in the advanced disease stage. Younger women di-

agnosed with this cancer combat the disease more easily than older women and hence the former manage to stay alive longer on average. The 5-year relative survival rate at diagnosis in females aged 15–39 is nearly 70%. On the other hand, this rate is only 12% for females over 80<sup>19</sup>. The mean age-adjusted 5-year relative survival rate from ovarian cancer is highest in Nordic countries (36.3%, except Denmark) and Central Europe, intermediate in Southern Europe and lowest in Eastern Europe<sup>19</sup>.

In Europe, the 5-year relative survival rate at diagnosis from endometrial cancer was lower among patients aged 65 to 74 (78%) compared with approximately 90% among patients under 65<sup>20</sup>.

#### *Cervical cancer*

The overall incidence rate of cervical cancer in Europe is 10.6/100,000. A significantly lower rate has been found in Western Europe. It is accompanied with a downward trend (more advanced prevention programmes). On the other hand, Central and Eastern European countries are marked with a significantly higher incidence rate (in correlation to the intensity of organized screening)<sup>21–23</sup>. In Europe in general, the incidence rate of cervical cancer varies between 6.9/100,000 in Western Europe to 14.7/100,000 in Central and Eastern Europe and Northern Europe. The mortality rate from cervical cancer in Europe ranges from 2/100,000 in Western Europe to 6.2/100,000 in Central and Eastern Europe<sup>15</sup>. In Croatia, the incidence rates of cervical cancer in 2006 were 13.4/100,000 (using the EU standard population) and 10.6/100,000 (using the world standard population)<sup>24</sup>. The mortality rates from cervical cancer declined in most European countries between 2000 and 2010 (4.8 and 4/100,000, respectively). This does not apply to Bulgaria, the Former Yugoslav Republic of Macedonia, Croatia, Greece and Ireland. The mortality rate in Croatia went up in the same period<sup>25</sup>. In 2004, the mortality rate in Croatia totalled 12.7/100,000<sup>26</sup>. The 5-year relative survival rate from cervical cancer diagnosed between 1995 and 1999 in European countries was 62.6 years<sup>5</sup>. The European Union achieved, in periods 1997–2002 and 2004–2009, minor progress with respect to the 5-year survival rates from cervical cancer, but this progress was not uniform across countries<sup>25</sup>. In the USA, the median age at diagnosis of cervical cancer in all females was 48 years and the median age at death was 57 years, based on the 2004 to 2008 SEER data<sup>13</sup>.

In the USA, the mean length of stay in hospital concerning females with gynaecologic cancer with comorbid medical conditions or with postoperative complication (8.6 days and 11.9 days) in surgery departments was significantly longer than the length of stay in females with neither comorbid medical condition nor postoperative complication<sup>27</sup>.

The aim of this study is to describe and compare data for malignant neoplasm of breast (C50) and the data on malignant neoplasms of female genital organs (C51–C58) with the demographic (gender, age, median age) and statistical features of the referring cancer patients (inci-

dence and mortality rate, survival rate, length of stay in hospital) and is focused on obtaining information on the status of this group of cancer in the OBC in relation to the corresponding status of this disease in Croatia and Europe in period 2001–2009.

## Materials and Methods

### Data source

Although the representativeness of their data might be challenged, mandatory county hospitals data reports, county bureaus of statistics and the County Register of Deaths still represent the only available source of information on the profile of cancer in the OBC. All data from the 2001–2009 period originate from these institutions. The cohort studied in this article included all people with cancer who were registered as the patients in one of two hospitals in the OBC in the time period from 1996 to 2010. Based on these sources, a database of people who were hospitalized in the area of the OBC for any reason whatsoever (including cancer) has been generated<sup>28,29</sup>. The data on each of the hospitalized patients have been supplemented with data obtained from the Register of Deaths.

Data on every person with cancer are accompanied with their chronological order of illness and hospitalization. The database involved all hospitalizations and all data on ONKO or BSL forms (mandatory statistical patterns for all hospitalized patients in Croatia). The ONKO form is a mandatory statistical report on every hospitalized cancer patients in Croatia. The BSL form is a mandatory statistical report on every hospitalized person, regardless of the causes of hospitalization. All cancer patients coming from this area are hospitalized in state-owned (public) hospitals since there are still the only hospitals here.

### Statistical analysis

The cancers were classified according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10), codes C50 and C51-C58. The cancer incidence and mortality estimates in the period from 2001 to 2009 were prepared for all cancers based on gender and for age groups 0–19, 20–44, 45–64, 65+ by the year at cancer diagnosis. Based on the 2001 census, the analysis covered a total population of 330.506 people in the OBC. The Croatian National Health Insurance is a universal health insurance that covers all or almost all costs (depending on a personal choice of the type of insurance) of treatment of Croatia citizens and provides them with the same chances of recovery. Therefore, this article can be said to comprise the entire population of cancer patients treated in the OBC.

Age-standardized rates were calculated as the number of new cases (incidence) or deaths (mortality) in specific age groups per 100,000 persons each year, and were age-adjusted to the EU standard population.

Descriptive statistics were used for both age and gender. The survival rates denote the outcome up to 5 years after diagnosis. This applies to cancer patients who were diagnosed with cancer during the 2001–2005 period. All survival estimates were age-adjusted on the basis of four age groups. The analyses were conducted using age-specific rates, the age-standardization-direct method and 95% confidence intervals (95% CI). The standardized incidence and mortality ratios as well as the 95% confidence intervals were computed for C50 and C51-C58 pursuant to the year at cancer diagnosis. Also, both ratios were stratified according to the year at cancer diagnosis, age and gender. The median age is the observation ranked in the middle; that is 50% of patients are diagnosed at an older age and 50% are diagnosed at a younger age compared to the median. The EU standard population was used in the analysis<sup>30</sup>. The length of stay was determined according to the date of admission and to the date of discharge with regard to the index admission. The SAS statistical package (version 9.1, SAS Institute INC, Cary, NC, USA) was used for the statistical analysis<sup>31</sup> and Microsoft® Office Excel® 2007.

## Results

### Median age

The overall median ages at diagnosis (OMADg) and at death (OMAD) from breast cancer (C50) were 61.8 and 69.4 years, respectively (Tables 1 and 2). The difference between the overall OMADg and OMAD was 7.6 years. The both indicators showing not significant upward moderate trendlines,  $R^2=0.308$  and  $R^2=0.143$ , respectively. Concerning female patient of 65+ years (Table 1), there was significant strong OMADg upward trendline for the whole group of malignant neoplasms, C00-C96 as well as for malignant neoplasm of cervix uteri, C53 ( $R^2=0.688$ ,  $t(7)=3.928$ ,  $p<0.01$  and  $R^2=0.834$ ,  $t(7)=5.930$ ,  $p<0.01$ , respectively). Among all cancer sites C50-C58 for all age groups, only C53 (OMADg=55.6 years) showed significant strong upward trendline ( $R^2=0.759$ ,  $t(7)=4.695$ ,  $p<0.01$ ). With regard to cancer sites cervix uteri (C53), corpus uteri (C54) and ovary cancer (C56) OMADg were 55.6, 65.2 and 61.0 years, respectively. The difference between the OMADg and OMAD from these cancer sites were 9.8, 6.4 and 6.4 years, respectively.

Concerning female patient of 65+ years (Table 2), there were significant strong OMAD upward trendlines for malignant neoplasm of breast (C50,  $R^2=0.565$ ,  $t(7)=3.015$ ,  $p<0.02$ ) and for malignant neoplasm of corpus uteri (C54,  $R^2=0.529$ ,  $t(7)=2.803$ ,  $p<0.05$ ). Cancer sites C53, C54 and C56 were marked with the OMAD of 65.4, 71.6 and 67.4 years, respectively (Table 2).

### Incidence and mortality rate

Tables 3 and 4 show the overall age-standardized incidence (OIR) and mortality rates (OMR) from breast cancer (C50) and cancers of female genital organs (C51-C58). In the entire 9-year period, 12 males were diagnosed with

**TABLE 1**  
THE MEDIAN AGE AT DIAGNOSIS FOR MALIGNANT NEOPLASMS OF BREAST AND FEMALE GENITAL ORGANS (C50, C51-C58)  
IN THE OBC, PERIOD 2001–2009

ICD <sup>10</sup>	Age group	OMADg	COD(S)	Trendline	Strength	Significant trend t-Test (df)
C50		61.9	y=61.09x0.008, R <sup>2</sup> =0.168	UW	moderate	–
C51		66.6	y=64.24x0.029, R <sup>2</sup> =0.044	UW	weak	–
C52		63.7	y=70.67x–0.06, R <sup>2</sup> =0.055	DW	weak	–
C53		55.6	y=47.63x0.103, R <sup>2</sup> =0.759	UW	strong	t(7)=4.695, p<0.01
C54	All age groups	65.2	y=62.29x0.034, R <sup>2</sup> =0.272	UW	moderate	–
C55		71.0	y=76.36x–0.11, R <sup>2</sup> =0.097	DW	weak	–
C56		61.0	y=62.09x–0.01, R <sup>2</sup> =0.065	DW	weak	–
C57		67.2	y=34.44x0.428, R <sup>2</sup> =0.701	UW	strong	–
C58		51.3	N/A	–	–	–
C51-C58		61.7	y=59.63x0.024, R <sup>2</sup> =0.28	UW	moderate	–
C50-C58		61.8	y=60.49x0.014, R <sup>2</sup> =0.308	UW	moderate	–
C50	20–44	39.4	y=40.12x–0.01, R <sup>2</sup> =0.092	DW	weak	–
	45–64	55.7	y=55.34x0.003, R <sup>2</sup> =0.030	UW	barely	–
	65+	73.3	y=73.26x0.000, R <sup>2</sup> =0.005	UW	barely	–
C51	20–44	38.6	y=43.00x–0.09, R <sup>2</sup> =0.176	DW	moderate	–
	45–64	54.9	y=53.85x0.018, R <sup>2</sup> =0.066	UW	weak	–
	65+	76.8	y=76.18x–1E–0, R <sup>2</sup> =0.000	DW	barely	–
C52	20–44	36.8	N/A	–	–	–
	45–64	57.0	y=69.27x–0.11, R <sup>2</sup> =0.105	DW	weak	–
	65+	77.1	y=72.73x0.042, R <sup>2</sup> =0.228	UW	moderate	–
C53	0–19	19.6	N/A	–	–	–
	20–44	36.0	y=35.83x0.002, R <sup>2</sup> =0.000	UW	barely	–
	45–64	54.1	y=55.84x–0.02, R <sup>2</sup> =0.310	DW	moderate	–
	65+	73.9	y=67.91x0.051, R <sup>2</sup> =0.834	UW	very strong	t(7)=5.930, p<0.01
C54	20–44	36.7	y=37.58x–0.01, R <sup>2</sup> =0.018	DW	barely	–
	45–64	56.9	y=56.81x0.001, R <sup>2</sup> =0.001	UW	barely	–
	65+	73.7	y=72.09x0.016, R <sup>2</sup> =0.279	UW	moderate	–
C55	20–44	38.5	N/A	–	–	–
	65+	74.6	y=73.28x0.018, R <sup>2</sup> =0.158	UW	weak	–
C56	0–19	6.5	y=0.161x2.372, R <sup>2</sup> =0.254	UW	moderate	–
	20–44	36.4	y=34.13x0.046, R <sup>2</sup> =0.052	UW	weak	–
	45–64	55.5	y=54.02x0.018, R <sup>2</sup> =0.389	UW	moderate	–
	65+	73.5	y=73.42x0.000, R <sup>2</sup> =8E–05	DW	barely	–
C57	45–64	55.6	N/A	–	–	–
	65+	78.8	y=187.6x–0.48, R <sup>2</sup> =0.702	DW	strong	–
C58	45–64	51.3	N/A	–	–	–
C51-C58	0–19	9.8	y=5.756x0.033, R <sup>2</sup> =4E–05	DW	barely	–
	20–44	36.4	y=36.09x0.008, R <sup>2</sup> =0.012	UW	barely	–
	45–64	55.7	y=55.77x–1E–0, R <sup>2</sup> =0.019	DW	barely	–
	65+	73.9	y=72.35x0.015, R <sup>2</sup> =0.688	UW	strong	t(7)=3.928, p<0.01
C50-C58	0–19	9.8	y=5.756x0.033, R <sup>2</sup> =4E–05	DW	barely	–
	20–44	38.0	y=36.09x0.008, R <sup>2</sup> =0.012	UW	barely	–
	45–64	55.7	y=55.77x–1E–0, R <sup>2</sup> =0.019	DW	barely	–
	65+	73.6	y=72.35x0.015, R <sup>2</sup> =0.688	UW	strong	t(7)=3.928, p<0.01

COD(S) – Coefficient of determination (strength), OMADg – overall median age at diagnosis, period 2001–2009, ICD<sup>10</sup> – International Statistical Classification of Diseases and Related Health Problems, 10th Revision, N/A – not available, DW – downward trendline, UW – upward trendline, R – Relationship, df – degrees of freedom, «–» – to small data number or no significant (p>0.05)

**TABLE 2**  
THE MEDIAN AGE AND AT DEATH FOR MALIGNANT NEOPLASMS OF BREAST AND FEMALE GENITAL ORGANS (C50, C51-C58)  
IN THE OBC, PERIOD 2001–2009

ICD <sup>10</sup>	Age group	OMAD	COD(S)	Trendline	Strength	Significant trend t-Test (df)
C50		69.6	$y=67.65x+0.022, R^2=0.434$	UW	moderate	–
C51		77.5	$y=70.08x+0.055, R^2=0.17$	UW	moderate	–
36 C52		59.9	N/A	–	–	–
C53		65.4	$y=62.59x+0.025, R^2=0.172$	UW	moderate	–
C54	All age groups	71.6	$y=67.21x+0.043, R^2=0.384$	UW	moderate	–
C55		71.0	$y=79.21x-0.13, R^2=0.142$	DW	weak	–
C56		67.4	$y=70.03x-0.02, R^2=0.440$	DW	moderate	–
C57		69.3	$y=54.82x+0.139, R^2=0.241$	UW	moderate	–
C51-C58		69.1	$y=67.89x+0.010, R^2=0.088$	UW	weak	–
C50-C58		69.4	$y=67.47x+0.018, R^2=0.275$	UW	moderate	–
C50	20–44	41.3	$y=42.34x-0.02, R^2=0.074$	DW	weak	$t(7)=3.015, p<0.02$
	45–64	56.3	$y=56.72x-0.00, R^2=0.011$	DW	barely	
	65+	76.5	$y=74.80x+0.014, R^2=0.565$	UW	strong	
C51	45–64	57.2	N/A	–	–	–
	65+	79.0	$y=79.60x-0.00, R^2=0.000$	DW	barely	–
C52	45–64	59.9	N/A	–	–	–
C53	20–44	39.2	$y=39.78x-0.00, R^2=0.019$	DW	barely	–
	45–64	55.1	$y=55.60x-0.00, R^2=0.001$	DW	barely	–
	65+	75.3	$y=71.58x+0.027, R^2=0.243$	UW	moderate	–
C54	20–44	36.5	$y=21.27x+0.342, R^2=0.997$	UW	very strong	$t(1)=18.23, p<0.01$
	45–64	57.9	$y=58.80x-0.01, R^2=0.143$	DW	weak	–
	65+	76.0	$y=72.96x+0.026, R^2=0.529$	UW	strong	$t(7)=2.803, p<0.05$
C55	20–44	38.5	N/A	–	–	–
	65+	74.7	$y=74.52x+0.006, R^2=0.014$	UW	barely	–
C56	20–44	35.4	$y=36.79x-0.01, R^2=0.015$	DW	barely	–
	45–64	56.2	$y=54.16x+0.016, R^2=0.034$	UW	weak	–
	65+	74.5	$y=74.44x+0.000, R^2=0.000$	UW	barely	–
C57	45–64	51.1	N/A	–	–	–
	65+	73.0	$y=67.05x+0.047, R^2=0.083$	UW	weak	–
C51-C58	20–44	37.2	$y=36.54x+0.001, R^2=0.000$	UW	barely	–
	45–64	56.4	$y=57.25x-0.01, R^2=0.268$	DW	moderate	–
	65+	75.5	$y=73.51x+0.017, R^2=0.438$	UW	moderate	–
C50-C58	20–44	39.3	$y=39.93x-0.01, R^2=0.121$	DW	weak	–
	45–64	56.3	$y=56.93x-0.00, R^2=0.064$	DW	weak	–
	65+	76.1	$y=74.11x+0.016, R^2=0.693$	UW	strong	$t(7)=3.975, p<0.01$

COD(S) – Coefficient of determination (strength), OMAD – overall median age at death, period 2001–2009, ICD<sup>10</sup> – International Statistical Classification of Diseases and Related Health Problems, 10th Revision, N/A – not available, DW – downward trendline, UW – upward trendline, R – Relationship, df – degrees of freedom, »« – to small data number or no significant ( $p>0.05$ )

C50 cancer (overall incidence rate was 0.8/100,000), and 8 males died from this cancer in the same period (overall mortality rate was 0.5/100,000). This data are not processed in this article though.

The OIR and OMR for breast cancer (C50) in the entire period were 82.9/100,000 (SD±6.48, CI 70.2–95.6) and 29.6/100,000 (SD±3.64, CI 22.46–36.73), respectively. The OIR is featured by non significant barely down-

ward trendline while OMR showed significant strong upward trendline ( $R^2=0.656, t(7)=3.653, p<0.01$ ). Concerning the OIR in females diagnosed with C50 (Table 3), there was insignificant upward trendlines in age groups 45–64 and 65+ years ( $R^2=0.012$  and  $R^2=0.015, p>0.05$ , respectively) and median downtrend trendlines in age group 20–44 years ( $R^2=0.280, p>0.05$ ). Concerning the OMR (Table 4), there was strong significant upward

**TABLE 3**  
 THE OVERALL AGE-STANDARDIZED INCIDENCE RATE (OIR) IN THE OBC FOR MALIGNANT NEOPLASMS OF BREAST AND FEMALE GENITAL ORGANS (C50, C51-C58) PER 100,000 USING EU STANDARD POPULATION, PERIOD 2001–2009

ICD <sup>10</sup>	Age group	OIR	COD(S)	Trendline	Strength	Significant trend t-Test (df)
C50		82.9	y=82.18x0.001, R <sup>2</sup> =7E-05	DW	barely	–
C51		1.9	y=1.450x0.025, R <sup>2</sup> =0.000	UW	barely	–
C52		0.5	y=0.341x0.319, R <sup>2</sup> =0.192	UW	moderate	–
C53		13.0	y=11.69x0.061, R <sup>2</sup> =0.050	UW	weak	–
C54		19.0	y=25.13x-0.21, R <sup>2</sup> =0.407	DW	moderate	–
C55	All ages	0.4	y=0.796x-0.05, R <sup>2</sup> =0.051	DW	weak	–
C56		14.5	y=17.97x-0.16, R <sup>2</sup> =0.230	DW	moderate	–
C57		0.3	y=7.106x-1.52, R <sup>2</sup> =0.773	DW	strong	t(2)=2.609, p<0.05
C58		0.1	N/A	–	–	–
C51-C58		49.6	y=57.44x-0.10, R <sup>2</sup> =0.410	DW	moderate	–
C50-C58		132.5	y=139.6x-0.03, R <sup>2</sup> =0.109	–	N/A	–
C50	20–44	25.3	y=31.03x-0.15, R <sup>2</sup> =0.280	DW	moderate	–
	45–64	182.7	y=177.6x0.016, R <sup>2</sup> =0.012	UW	barely	–
	65+	257.5	y=245.3x0.026, R <sup>2</sup> =0.015	UW	barely	–
C51	20–44	0.6	N/A	–	–	–
	45–64	2.9	y=4.353x-0.17, R <sup>2</sup> =0.085	DW	weak	–
	65+	8.5	y=5.9x0.079, R <sup>2</sup> =0.005	UW	barely	–
C52	20–44	0.2	N/A	–	–	–
	45–64	1.0	y=2.346, R <sup>2</sup> =#N/A	UW	–	–
	65+	1.4	y=3.178, R <sup>2</sup> =#N/A	UW	–	–
C53	20–44	11.6	y=19.40x-0.42, R <sup>2</sup> =0.384	DW	moderate	–
	45–64	22.9	y=13.51x0.248, R <sup>2</sup> =0.048	UW	weak	–
	65+	29.0	y=12.36x0.525, R <sup>2</sup> =0.566	UW	strong	t(7)=3.021, p<0.02
C54	20–44	4.1	y=8.983x-0.33, R <sup>2</sup> =0.186	DW	moderate	–
	45–64	35.7	y=45.18x-0.20, R <sup>2</sup> =0.184	DW	moderate	–
	65+	78.8	y=88.00x-0.09, R <sup>2</sup> =0.089	DW	weak	–
C55	20–44	0.2	N/A	–	–	–
	65+	3.2	y=7.135x-0.01, R <sup>2</sup> =0.002	DW	barely	–
C56	0–19	0.8	y=2.519, R <sup>2</sup> =-3E-1	DW	barely	–
	20–44	5.2	y=9.258x-0.33, R <sup>2</sup> =0.170	DW	moderate	–
	45–64	29.5	y=35.65x-0.14, R <sup>2</sup> =0.307	DW	moderate	–
	65+	46.3	y=68.41x-0.33, R <sup>2</sup> =0.254	DW	moderate	–
C57	45–64	0.8	N/A	–	–	–
	65+	1.1	y=3.178, R <sup>2</sup> =1E-15	DW	barely	–
C58	45–64	0.3	N/A	–	–	–
C51-C58	0–19	0.8	y=2.519, R <sup>2</sup> =-3E-1	DW	barely	–
	20–44	21.8	y=35.65x-0.43, R <sup>2</sup> =0.312	DW	moderate	–
	45–64	93.1	y=101.7x-0.07, R <sup>2</sup> =0.093	DW	weak	–
C50-C58	65+	168.1	y=180.3x-0.05, R <sup>2</sup> =0.069	DW	weak	–
	0–19	0.8	y=2.519, R <sup>2</sup> =-3E-1	DW	barely	–
	20–44	47.1	y=65.94x-0.26, R <sup>2</sup> =0.430	DW	moderate	–
	45–64	275.8	y=281.5x-0.01, R <sup>2</sup> =0.023	DW	barely	–
	65+	425.6	y=425.1x-0.00, R <sup>2</sup> =0.000	DW	barely	–

COD(S) – Coefficient of determination (strength), OIR – overall incidence rate, period 2001–2009, ICD<sup>10</sup> – International Statistical Classification of Diseases and Related Health Problems, 10th Revision, N/A – not available, DW – downward trendline, UW – upward trendline, R – Relationship, df – degrees of freedom, »« – to small data number or no significant (p>0.05)

**TABLE 4**  
 THE OVERALL AGE-STANDARDIZED MORTALITY RATE (OMR) IN THE OBC FOR MALIGNANT NEOPLASMS OF BREAST AND FEMALE GENITAL ORGANS (C50, C51-C58) PER 100,000 USING EU STANDARD POPULATION, PERIOD 2001–2009

ICD <sup>10</sup>	Age group	OMR	COD(S)	Trendline	Strength	Significant trend t-Test (df)
C50		29.6	y=21.22x0.222, R <sup>2</sup> =0.656	UW	strong	t(7)=3.653, p<0.01
C51		1.2	y=0.460x0.517, R <sup>2</sup> =0.302	UW	moderate	–
C52		0.1	N/A	–	–	–
C53		5.0	y=2.299x0.471, R <sup>2</sup> =0.412	UW	moderate	–
C54	All ages	8.1	y=5.704x0.214, R <sup>2</sup> =0.199	UW	moderate	–
C55		0.4	y=0.370x0.376, R <sup>2</sup> =0.422	UW	moderate	–
C56		9.6	y=9.299x0.014, R <sup>2</sup> =0.003	UW	barely	–
C57		0.3	y=0.482x–0.14, R <sup>2</sup> =0.172	DW	moderate	–
C51-C58		24.7	y=19.39x0.163, R <sup>2</sup> =0.707	UW	strong	t(7)=4.109, p<0.01
C50-C58		54.3	y=40.76x0.194, R <sup>2</sup> =0.871	UW	very strong	t(7)=6.874, p<0.01
C50	20–44	3.3	y=2.127x0.308, R <sup>2</sup> =0.165	UW	moderate	–
	45–64	44.3	y=39.90x0.052, R <sup>2</sup> =0.021	UW	barely	–
	65+	157.9	y=96.04x0.325, R <sup>2</sup> =0.676	UW	strong	t(7)=3.821, p<0.01
C51	45–64	0.3	N/A	–	–	–
	65+	9.9	y=4.254x0.429, R <sup>2</sup> =0.166	UW	moderate	–
C52	45–64	0.5	N/A	–	–	–
C53	20–44	1.5	y=3.280x–0.26, R <sup>2</sup> =0.356	DW	moderate	–
	45–64	8.3	y=3.234x0.590, R <sup>2</sup> =0.620	UW	strong	t(7)=3.379, p<0.02
	65+	21.2	y=9.803x0.459, R <sup>2</sup> =0.374	UW	moderate	–
C54	20–44	1.0	y=0.995x0.676, R <sup>2</sup> =0.394	UW	moderate	–
	45–64	7.6	y=5.918x0.126, R <sup>2</sup> =0.016	UW	barely	–
	65+	53.7	y=35.82x0.253, R <sup>2</sup> =0.332	UW	moderate	–
C55	20–44	0.2	N/A	–	–	–
	65+	3.2	y=3.291x0.432, R <sup>2</sup> =0.469	UW	moderate	–
C56	20–44	1.7	y=1.570x0.189, R <sup>2</sup> =0.118	UW	weak	–
	45–64	14.9	y=7.363x0.439, R <sup>2</sup> =0.517	UW	strong	t(7)=2.737, p<0.05
	65+	48.4	y=59.08x–0.18, R <sup>2</sup> =0.126	DW	weak	–
C57	45–64	0.3	N/A	–	–	–
	65+	1.8	y=3.178, R <sup>2</sup> =–3E–1	DW	barely	–
C51-C58	20–44	4.4	y=5.081x–0.10, R <sup>2</sup> =0.021	DW	barely	–
	45–64	31.8	y=18.23x0.349, R <sup>2</sup> =0.428	UW	moderate	–
	65+	138.1	y=119.5x0.093, R <sup>2</sup> =0.185	UW	moderate	–
C50-C58	20–44	7.7	y=5.763x0.088, R <sup>2</sup> =0.009	UW	barely	–
	45–64	76.1	y=59.10x0.165, R <sup>2</sup> =0.371	UW	moderate	–
	65+	296.0	y=214.8x0.213, R <sup>2</sup> =0.644	UW	strong	t(7)=3.558, p<0.01

COD(S) – Coefficient of determination (strength), OMR – overall mortality rate, period 2001–2009, ICD<sup>10</sup> – International Statistical Classification of Diseases and Related Health Problems, 10th Revision, N/A – not available, DW – downward trendline, UW – upward trendline, R – Relationship, df – degrees of freedom, »« – to small data number or no significant (p>0.05)

trendline in age group 65+ years (R<sup>2</sup>=0.676, t(7)=3.821, p<0.01).

The OIR and OMR from female genital organs (C51-C58) were 49.6 (SD±4.99, CI 39.86–59.42) and 24.7/100,000 (SD±3.3, CI 18.23–31.16), respectively (Tables 3 and 4). The changes in the OMR considering this group of cancer have the opposite trends to the C50. Non significant downward OIR trendline is a moderate (R<sup>2</sup>=0.410,

p>0.05) while a significant upward OMR trendline is a strong (R<sup>2</sup>=0.707, t(7)=4.109, p<0.01). Due to the both OIR and OMR, the most common cancer sites within the C51-C58 cancer group were malignant neoplasms of the cervix uteri (C53, 13.0 and 5.0/100,000, respectively), malignant neoplasms of the corpus uteri (C54, 19.0 and 8.1/100,000, respectively) and malignant neoplasms of the ovary (C56, 114.5 and 9.6/100,000, respectively).

**TABLE 5**  
THE 5-YEARS RELATIVE SURVIVAL RATES FOR MALIGNANT NEOPLASMS OF BREAST AND FEMALE GENITAL ORGANS (C50, C51-C58) IN THE OBC, PERIOD 2001–2005

TABLE 5A. The age group percentage of relative survival rates (number of survival cases)

ICD-10	0–19		20–44		45–64		65+		All ages	
C50	–	–	76.8	(66)	76.4	(304)	49.9	(171)	64.2	(541)
C51	–	–	100.1	(5)	75.8	(3)	35.5	(5)	54.9	(13)
C52	–	–	–	–	50.5	(1)	106.6	(2)	76.0	(3)
C53	100.1	(1)	79.6	(31)	66.6	(29)	50.2	(16)	66.1	(77)
C54	–	–	77.9	(14)	75.8	(63)	43.8	(51)	57.4	(128)
C55	–	–	–	–	–	–	0.0	–	0.0	–
C56	100.1	(3)	80.1	(12)	57.1	(39)	20.4	(14)	43.0	(68)
C57	–	–	–	–	67.4	(2)	106.6	(1)	76.0	(3)
C51-C58	100.1	(4)	80.6	(62)	67.2	(137)	37.1	(89)	54.5	(292)
C50-C59	100.1	(4)	78.6	(128)	73.3	(441)	44.6	(260)	60.4	(833)

TABLE 5B. Relative survival trend

ICD-10	Years					COD(S)	Trendline	Strength	Trend t-Test
	2001	2002	2003	2004	2005				
C50	62.2	61.0	67.5	67.3	61.9	$y=61.70x-0.034$ , $R^2=0.180$	UW	moderate	$t(3)=0.811$ , $p>0.05$
C51	100.1	0.0	33.8	40.5	76.0	–	–	–	N/A
C52	100.1	–	101.3	0.0	101.3	–	–	–	N/A
C53	80.1	50.6	70.9	76.0	52.4	$y=72.75x-0.12$ , $R^2=0.127$	DW	weak	$t(3)=0.660$ , $p>0.05$
C54	62.3	66.9	44.0	52.0	56.6	$y=63.10x-0.12$ , $R^2=0.251$	DW	moderate	$t(3)=1.002$ , $p>0.05$
C55	0.0	–	0.0	–	0.0	–	–	–	N/A
C56	38.9	41.0	54.5	42.2	41.1	$y=40.62x-0.065$ , $R^2=0.096$	UW	weak	$t(3)=0.564$ , $p>0.05$
C57	–	–	50.6	–	101.3	–	–	–	N/A
C51-C58	59.2	54.0	50.6	54.5	52.5	$y=57.79x-0.06$ , $R^2=0.569$	DW	strong	$t(3)=1.990$ , $p>0.05$
C50-C59	61.0	58.0	61.3	62.9	58.1	$y=60.39x-0.00$ , $R^2=0.002$	DW	barely	$t(3)=0.077$ , $p>0.05$

»« – no cases, 0 – no survival cases, COD(S) – Coefficient of determination (strength), N/A – not available

These three cancer sites comprise 86.1% of cancer in this group. Therefore, remaining cases of cancer within this group are not discussed in this article due to their small number. Concerning the OIR in females diagnosed with C51-C58, there were strong upward trendlines for C53 in age group 65+ years and moderate one for age group 45–64 years ( $R^2=0.566$  and  $R^2=0.384$ , respectively); for cancer sites C54 and C56 there were weak or moderate downward trendlines.

Concerning the OMR, there was strong upward trendline for malignant neoplasms of the cervix uteri (C53) in age group 45–64 years ( $R^2=0.620$ ,  $t(7)=3.379$ ,  $p<0.02$ , Table 4), moderate for C53 and C54 in age 65+ years ( $R^2=0.374$  and  $R^2=0.332$ , respectively); a strong downward trendline for C56 in the age of group 45–64 ( $R^2=$

$0.517$ ,  $t(7)=2.737$ ,  $p<0.05$ ) and weak one in the age of group 65+ ( $R^2=0.126$ ).

Among sites of the C51-C58 cancer group (and well below breast cancer incidence rate), malignant neoplasms of the corpus uteri (C54) were characterized by the highest overall incidence rate of 19.0/100,000 ( $SD\pm 3.02$ , CI 13.09–24.93, Table 3). This cancer site showed a moderate downward trendline ( $R^2=0.407$ ), more pronounced in the age 45–64 ( $R^2=0.184$ ) years then in the age 65+ ( $R^2=0.089$ ). Also, the incidence rate of malignant neoplasm of ovary (C56, overall incidence rate was 14.5/100,000,  $SD\pm 2.72$ , CI 9.19–19.85) had a moderate downward trendline ( $R^2=0.230$ ) as well as it were in all age groups. Unlike the incidence rates of malignant neoplasms of the ovary and the corpus uteri, the inci-



**TABLE 6**  
 THE AGE DISTRIBUTION AT DIAGNOSIS FOR MALIGNANT NEOPLASMS OF BREAST AND FEMALE GENITAL ORGANS  
 (C50, C51-C58) IN THE OBC, PERIOD 2001–2009

TABLE 6A. Age group distribution (%) at diagnosis for cancer sites C50-C58

ICD-10	Age group	OIR	COD(S)	Trendline	Strength	Trend t-Test
C50	20–44	9.2	$y=11.76x-0.19, R^2=0.355$	DW	moderate	–
	45–64	47.3	$y=46.46x+0.013, R^2=0.031$	UW	weak	–
	65+	43.6	$y=41.87x+0.024, R^2=0.076$	UW	weak	–
C51	20–44	13.2	$y=30.12x-0.26, R^2=0.402$	DW	moderate	–
	45–64	23.7	$y=26.89x+0.075, R^2=0.008$	UW	barely	–
	65+	63.2	$y=55.67x+0.043, R^2=0.004$	UW	barely	–
C52	20–44	11.1	N/A	–	–	–
	45–64	44.4	$y=1230x-1.65, R^2=0.527$	DW	strong	–
	65+	44.4	$y=103.5x-0.23, R^2=0.182$	DW	moderate	–
C53	0–19	0.4	N/A	–	–	–
	20–44	28.3	$y=53.39x-0.49, R^2=0.505$	DW	strong	$t(7)=2.672, p<0.05$
	45–64	37.0	$y=29.52x+0.083, R^2=0.014$	UW	barely	–
	65+	34.3	$y=14.98x+0.511, R^2=0.587$	UW	strong	$t(7)=3.154, p<0.02$
C54	20–44	5.5	$y=8.501x+0.015, R^2=0.000$	UW	barely	–
	45–64	38.6	$y=37.02x+0.013, R^2=0.003$	UW	barely	–
	65+	55.9	$y=49.70x+0.082, R^2=0.143$	UW	weak	–
C55	20–44	10.0	N/A	–	–	–
	65+	90.0	$y=100, R^2=\#N/A$	–	–	–
C56	0–19	1.1	$y=6.142x-0.37, R^2=0.416$	DW	moderate	–
	20–44	10.9	$y=12.41x-0.00, R^2=0.000$	DW	barely	–
	45–64	43.1	$y=41.83x+0.029, R^2=0.012$	UW	barely	–
	65+	44.9	$y=49.96x-0.12, R^2=0.11$	DW	weak	–
C57	45–64	50.0	N/A	–	–	–
	65+	50.0	$y=1.838x+2.112, R^2=0.790$	UW	strong	–
C58	45–64	100.0	N/A	–	–	–
C51-C58	0–19	0.2	$y=2.818x-1.32, R^2=0.833$	DW	very strong	–
	20–44	4.9	$y=7.358x-0.35, R^2=0.245$	DW	moderate	–
	45–64	14.6	$y=15.43x-0.04, R^2=0.037$	DW	weak	–
	65+	18.1	$y=18.50x-0.02, R^2=0.027$	DW	barely	–
C50-C58	0–19	0.2	$y=2.818x-1.32, R^2=0.833$	DW	very strong	–
	20–44	10.6	$y=14.38x-0.23, R^2=0.336$	DW	moderate	–
	45–64	44.0	$y=42.90x+0.018, R^2=0.070$	UW	weak	–
	65+	45.2	$y=43.09x+0.030, R^2=0.113$	UW	weak	–

TABLE 6B. The overall proportion (%) of each cancer sites in relation to the gender

C50		62.2	$y=58.69x+0.038, R^2=0.237$	UW	moderate	–
C51		1.5	$y=1.146x+0.068, R^2=0.005$	UW	barely	–
C52		0.4	$y=0.305x+0.227, R^2=0.226$	UW	moderate	–
C53	All ages	9.2	$y=7.341x+0.147, R^2=0.185$	UW	moderate	–
C54		15.2	$y=18.60x-0.15, R^2=0.410$	DW	moderate	–
C55		0.4	$y=0.790x-0.13, R^2=0.094$	DW	weak	–
C56		10.9	$y=13.48x-0.16, R^2=0.193$	DW	moderate	–
C57		0.2	$y=2.283x-0.93, R^2=0.636$	DW	strong	–

TABLE 6C. The age group proportion (%) of each cancer sites

ICD-10	Age groups			All ages		
	0–44	45–64	65+			
C50	9.2	47.3	43.6	100.0	62.2	–
C51	13.2	23.7	63.2	4.0		–
C52	11.1	44.4	44.4	0.9		–
C53	28.7	37.0	34.3	24.2		–
C54	5.5	38.6	55.9	40.1		–
C55	10.0	0.0	90.0	1.1		–
C56	12.0	43.1	44.9	28.9		–
C57	0.0	50.0	50.0	0.6		–
C58	0.0	100.0	0.0	0.1		–
C51-C58	13.4	38.7	47.9	100.0	37.8	–
C50-C58	10.8	44.0	45.2	100.0		–

R – Relationship, COD(S) – Coefficient of determination (strength), N/A – not available, DW – downward, UW – upward, »« – to small data number or no significant ( $p > 0.05$ ), OIR – overall incidence rate

dence rate of malignant neoplasms of the cervix uteri (C53, 13.0/100,000,  $SD \pm 2.63$ , CI 7.82–18.13, Table 3) showed a weak upward trendline ( $R^2 = 0.050$ ). However, when compare trendlines in different age groups, a significant strong upward trendline exist in the age group 65+ years ( $R^2 = 0.566$ ,  $t(7) = 3.021$ ,  $p < 0.02$ ) and a moderate downward trendline in the age group 20–44 years ( $R^2 = 0.384$ ). Malignant neoplasm of other and unspecified female genital organs (C57) showed a significant strong upward trendline ( $R^2 = 0.773$ ,  $t(2) = 2.609$ ,  $p < 0.05$ ) related with a small and intermittent, incidence rate (degrees of freedom=2).

The overall mortality rate from breast cancer was 29.6/100,000 with a significant strong upward trendline ( $R^2 = 0.656$ ,  $t(7) = 3.653$ ,  $p < 0.01$ , Table 4). This upward trendline is most influenced by the mortality rates of patients aged 65+ years ( $R^2 = 0.676$ ,  $t(7) = 3.558$ ,  $p < 0.01$ ).

There was a strong increase in the mortality rate considering all cancer sites of the C51-C58 cancer group ( $R^2 = 0.871$ ,  $t(7) = 6.874$ ,  $p < 0.01$ , Table 4) directly influenced by mortality rates of patients 45–64 years with malignant neoplasms of the cervix uteri and (C53) and malignant neoplasm of ovary (C56).

#### Five year relative survival rate

The 5-year relative survival rate from breast cancer was 64.2%. This cancer site implied a small difference in survival in age groups 20–44 and 45–64 (76.8% and 76.4%, respectively). In age group 65+ the survival rate was much lower, 49.9% (Table 5A). Within C51-C58 cancer group, malignant neoplasm of ovary (C56) was denoted by the lowest survival rate, only 43.0%. The difference between age groups in the survival rate from the C56 cancer site was great and rate varied a lot: age groups 20–44, 45–64 and 65+ revealed 5-year relative survival rates of 80.1%, 57.1% and 20.4%, respectively.

Neither cancer sites showed no significant upward or downward trendline (Table 5B). C50 and C56 featured moderate and weak upward trendline ( $R^2 = 0.180$  and  $R^2 = 0.096$ , respectively), while C53 and C54 showed weak and moderate downward trendline ( $R^2 = 0.127$  and  $R^2 = 0.251$ , respectively). Power mortality rates of C53 and C54 compared to C56 creates a non significant strong upward trendline for the entire group of cancer C51-C58 ( $R^2 = 0.569$ ,  $t(7) = 1.999$ ,  $p > 0.05$ )

#### Age distribution

The age distribution at diagnosis of breast cancer (C50), cervix uteri (C53), corpus uteri (C54) and ovary (C56) cancer sites differ from the respective age distribution at death. Although the age distribution at diagnosis of the C50 cancer site was rather similar in age groups 45–64 and 65+ (47.3% and 43.6%, respectively), there were much more patients who died from this cancer aged 65+ than aged between 45 and 64 (68.8% and 27.4%, respectively) showing a moderate upward trendlines (Tables 6A and 7A). The proportion of patients with C53 cancer site aged 65+ at diagnosis was 34.3% while the proportion of female patients of the same age at deaths was much higher, 58.0%. It was similar to the cancer sites C54 and C56.

Considering age distribution, there was a big difference between the 65+ age group and other age groups. Patients with breast cancer (C50), malignant neoplasm of the corpus uteri (C54) and malignant neoplasm of the ovary (C56) mostly died at the age of 65+ (68.8%, 79.0% and 66.0%, respectively, Figure 1). One needs to single out malignant neoplasms of the cervix uteri (C53) which entailed the fact that the 9.0% of patients died at the age from 20 to 44 (the highest percentage in this age group among C51-C58 cancer sites, (too small number of cases for C55)).

**TABLE 7**  
THE AGE DISTRIBUTION AT DEATH FOR MALIGNANT NEOPLASMS OF BREAST AND FEMALE GENITAL ORGANS  
(C50, C51-C58) IN THE OBC, PERIOD 2001–2009

TABLE 7A. Age group distribution (%) at death for cancer sites C50-C58

ICD-10	Age group	OMR	COD(S)	Trendline	Strength	Trend t-Test
C50	20–44	3.8	$y=4.983x-0.26, R^2=0.125$	DW	weak	–
	45–64	27.4	$y=35.01x-0.18, R^2=0.189$	DW	moderate	–
	65+	68.8	$y=60.76x+0.076, R^2=0.266$	UW	moderate	–
C51	45–64	6.9	N/A	–	–	–
	65+	93.1	$y=100, R^2=-6E-1$	DW	barely	–
C52	45–64	100.0	N/A	–	–	–
C53	20–44	9.0	$y=23.85x-0.46, R^2=0.529$	DW	strong	–
	45–64	33.0	$y=27.76x+0.110, R^2=0.065$	UW	weak	–
	65+	58.0	$y=57.45x-0.00, R^2=0.001$	DW	barely	–
C54	20–44	2.7	$y=2.338x+0.794, R^2=0.906$	UW	very strong	$t(1)=3.104, p<0.02$
	45–64	18.3	$y=39.00x-0.57, R^2=0.361$	DW	moderate	–
	65+	79.0	$y=65.99x+0.118, R^2=0.256$	UW	moderate	–
C55	20–44	10.0	N/A	–	–	–
	65+	100.0	N/A	–	–	–
C56	20–44	4.4	$y=3.789x+0.226, R^2=0.215$	UW	moderate	–
	45–64	29.6	$y=13.22x+0.523, R^2=0.420$	UW	moderate	–
	65+	66.0	$y=79.38x-0.16, R^2=0.354$	DW	moderate	–
C57	45–64	16.7	N/A	–	–	–
	65+	83.3	$y=100, R^2=-1E-1$	DW	barely	–
C51-C58	20–44	4.5	$y=6.292x-0.24, R^2=0.096$	DW	weak	–
	45–64	24.6	$y=21.81x+0.066, R^2=0.033$	UW	weak	–
	65+	70.9	$y=73.05x-0.02, R^2=0.036$	DW	weak	–
C50-C58	20–44	4.1	$y=4.317x-0.14, R^2=0.024$	DW	barely	–
	45–64	26.2	$y=28.56x-0.06, R^2=0.060$	DW	weak	–
	65+	69.7	$y=66.68x+0.027, R^2=0.080$	UW	weak	–

TABLE 7B. The overall proportion (%) of each cancer sites in relation to the gender

C50		54.2	$y=49.93x+0.051, R^2=0.189$	UW	moderate	–
C51		2.5	$y=1.369x+0.290, R^2=0.095$	UW	weak	–
C52		0.2	N/A	–	N/A	–
C53	All	8.5	$y=5.319x+0.272, R^2=0.190$	UW	moderate	–
C54	ages	15.9	$y=14.78x+0.028, R^2=0.005$	UW	barely	–
C55		0.9	$y=1.125x+0.075, R^2=0.012$	UW	barely	–
C56		17.4	$y=24.30x-0.24, R^2=0.466$	DW	moderate	$t(7)=2.471, p<0.05$
C57		0.5	$y=1.096x-0.23, R^2=0.825$	DW	very strong	$t(4)=4.342, p<0.01$

TABLE 7C. The age group proportion (%) of each cancer sites

ICD-10	Age groups			All ages		
	0–44	45–64	65+			
C50	3.8	27.4	68.8	100.0	54.2	–
C51	0.0	6.9	93.1	5.4		–
C52	0.0	100.0	0.0	0.4		–
C53	9.0	33.0	58.0	18.7		–
C54	2.7	18.3	79.0	34.7		–
C55	10.0	0.0	90.0	1.9		–
C56	4.4	29.6	66.0	37.9		–
C57	0.0	16.7	83.3	1.1		–
C51-C58	4.5	24.6	70.9	100.0	45.8	–
C50-C58	4.1	26.2	69.7	100.0		–

R – Relationship, COD(S) – Coefficient of determination (strength), N/A – not available, DW – downward, UW – upward, »« – to small data number or no significant ( $p>0.05$ ), OMR – overall mortality rate

**TABLE 8**  
THE TREND AND THE AVERAGE NUMBER OF HOSPITAL ADMISSION *PER* PATIENT FOR MALIGNANT NEOPLASMS OF BREAST AND FEMALE GENITAL ORGANS (C50, C51-C58) IN THE OBC, PERIOD 2001–2009

ICD <sup>10</sup>	ONOHA	COD(S)	Trendline	Strength	Significant trendline t-Test
C50	1.8	y=2.045x-0.09, R <sup>2</sup> =0.377	DW	moderate	–
C51	2.1	y=1.572x0.043, R <sup>2</sup> =0.009	UW	barely	–
C52	2.8	y=1.346x0.137, R <sup>2</sup> =0.010	UW	barely	–
C53	2.8	y=2.597x0.000, R <sup>2</sup> =3E-07	DW	barely	–
C54	1.9	y=1.865x-0.04, R <sup>2</sup> =0.031	DW	weak	–
C55	1.3	y=1.224x-0.26, R <sup>2</sup> =0.160	DW	weak	–
C56	3.1	y=3.541x-0.15, R <sup>2</sup> =0.187	DW	moderate	–
C57	2.0	y=19.60x-1.79, R <sup>2</sup> =0.983	DW	very strong	t(2)=10.75, p<0.01
C58	1.3	N/A	N/A	N/A	N/A
C51-C58	2.5	y=2.494x-0.02, R <sup>2</sup> =0.027	DW	barely	–
C50-C58	2.1	y=2.24x-0.06, R <sup>2</sup> =0.249	DW	weak	–

ONOHA – overall number of hospital admission per patient, DW – downward trendline, UW – upward trendline, N/A – not available, R – Relationship, COD(S) – Coefficient of determination (strength), ICD<sup>10</sup> – International Statistical Classification of Diseases and Related Health Problems, 10th Revision, »-« – to small data number or no significant (p>0.05)

### Cancer patient hospitalization

In the 2001–2009 period, a total of 1,561 females were diagnosed with the breast cancer C50 and they were admitted to the OBC hospitals 2,850 times where they spent a total of 34,607 days (Tables 10). An average patient was admitted to hospital 1.8 times during the course of their illness (Table 8) with a significant strong downward overall length of stay in hospital (OLOSH) trendline (R<sup>2</sup>=0.716, t(7)=2.717, p<0.05) of 12.1 days (Table 10). Comparing the number of hospital admissions (NOAH) and the LOSH, females aged 65+ spent on average 14.5 days in hospital, which is 4.7 days more than females aged 20–44 and 3.8 days more than females aged 45–64. The LOSH went down in all age groups, and very strong in age groups 65+ (R<sup>2</sup>=0.809, t(7)=3.641, p<0.01). In the same period, the LOSH of females diagnosed with C50 cancer declined significant sharply (R<sup>2</sup>=0.716, t(7)=2.713, p<0.05), but without change in the NOAH (R<sup>2</sup>=0.025, barely upward trendline). The greatest share in all hospitalizations (49.1%) referred to females aged 45–64.

A total of 949 females were diagnosed with the C51-C58 cancer group and they were admitted to the OBC hospitals 2,402 times where they spent a total of 35,882 days. An average patient was admitted to hospital 2.5 times (Table 8) during the course of their illness with a non significant moderate downward LOSH trendline (R<sup>2</sup>=0.327) of 14.9 days (Table 10). Among the most common cancer site in this group, the total number of patient with C53, C54 and C56 were 230, 381 and 274, respectively; they were admitted to the OBC hospitals 584, 784 and 883 times, respectively; they spent a total of 8655, 14,519 and 9968 days, respectively; an average hospital admission per patient were 2.8, 1.9 and 3.1 times, respectively (Table 8); the LOSH were 14.8, 18.5 and 11.3 days, respectively. Females diagnosed with malignant neoplasms of the corpus uteri (C54) stayed in hospital longer than

females diagnosed with other cancer sites of this cancer group (18.5 days, Tables 10). The LOSH trendlines for C53 and C54 moderately decreased (R<sup>2</sup>=0.224 and R<sup>2</sup>=0.451, respectively), while it moderately increased for C56 (R<sup>2</sup>=0.46). Contrary, the NOAH for C53 moderately increased (R<sup>2</sup>=374) while it moderately and strongly decreased for C54 and C56 (R<sup>2</sup>=465 and R<sup>2</sup>=609, respectively).

### Discussion

Malignant neoplasms of breast (C50) and female genital organs (C51-C58) within the OBC female population accounted for 34.8% (C50 – 21.6%, C51-C58 – 13.2%) of all newly registered cancer cases in the period from 2001 to 2009. In the same population and period of time, the proportion of C50-C58 cancer group in all cancer cases at death amounted to 35.5% (C50 – 17.6%, C51-C58 – 14.9%)<sup>32</sup>.

#### Breast cancer

According to the data stated in this article, incidence rate of breast cancer in the OBC decreased in the period 2001–2009. The overall incidence rate resembles the Croatian average and way exceeds the corresponding Central and Eastern Europe incidence rates, but is still below the Northern Europe ones<sup>33,34</sup>. A study on the breast cancer incidence in 35 countries (mostly European ones) from 1990 to 2002 has revealed that the incidence rate had an upward trend within that period of time<sup>35</sup>. Pursuant to the respective 2012 EUCAN data, most of these countries are still experiencing a rise in the number of newly registered breast cancer cases<sup>12</sup>. Concerning the same time period, similar data can be found at the national level too<sup>33</sup>.

A decline in the breast cancer incidence is undoubtedly related to the raised women’s awareness of this ill-

**TABLE 9**  
THE TREND AND THE AVERAGE NUMBER OF ADMISSION IN HOSPITAL FOR MALIGNANT NEOPLASMS OF BREAST AND FEMALE GENITAL ORGANS (C50, C51-C58) IN THE OBC, PERIOD 2001–2009

ICD-10	Parameters	Age group				All ages
		0–19	20–44	45–64	65+	
C50	ONOA	–	32.7	155.4	128.6	316.7
	Trendline	–	DW	UW	UW	UW
	Strength	–	weak	barely	weak	barely
C51	ONOA	–	0.4	2.9	6.6	9.9
	Trendline	–	UW	UW	UW	UW
	Strength	–	strong	moderate	moderate	moderate
C52	ONOA	–	0.1	0.9	1.7	2.7
	Trendline	–	–	UW	UW	UW
	Strength	–	–	barely	weak	moderate
C53	ONOA	0.1	15.2	26.8	22.8	64.9
	Trendline	–	DW	UW	UW	UW
	Strength	–	barely	moderate	moderate	moderate
C54	ONOA	–	5.0	34.4	47.7	87.1
	Trendline	–	DW	DW	DW	DW
	Strength	–	strong	moderate	weak	moderate
C55	ONOA	–	0.2	0.3	1.4	2.0
	Trendline	–	–	UW	DW	DW
	Strength	–	–	–	moderate	moderate
C56	ONOA	0.8	12.6	50.2	34.6	98.1
	Trendline	–	DW	DW	DW	DW
	Strength	–	barely	moderate	barely	strong
C57	ONOA	0.1	–	1.1	0.8	2.0
	Trendline	–	–	UW	UW	DW
	Strength	–	–	weak	moderate	weak
C58	ONOA	–	–	0.1	0.1	0.2
C51-C58	ONOA	1.0	33.6	116.8	115.6	266.9
	Trendline	UW	DW	DW	UW	DW
	Strength	moderate	moderate	moderate	barely	strong
C50-C58	ONOA	1.0	66.2	272.2	244.1	583.6
	Trendline	UW	DW	DW	UW	DW
	Strength	moderate	moderate	weak	weak	weak

ONOA – overall number of admissions in hospital, UW – upward, DW – downward, ICD10 – International Statistical Classification of Diseases and Related Health Problems, 10th Revision, t – significance of the coefficient of determination

ness. For about 20 years, Croatian women have been exposed to necessary information on the need of formal and informal breast cancer education provided more or less frequently by various media<sup>36</sup>. The extent of the effect of educational programmes on the quality of healthcare and changes of statistical indicators is best indicated by the data on the incidence rate in the OBC since the initiation of the national breast cancer prevention programme in 2006. The incidence rate rose sharply in 2007, then fell to the 2006 level and has kept falling ever since. Comparing to the data at the national level<sup>37–39</sup>, the overall mortality

rate was below the Croatian average in the time<sup>24,26,40</sup>. The data of concern is the significant mortality rate upward trend for all age groups and separately for age group 65+ years (Table 4).

The 5-year relative survival rate from breast cancer diagnosed among European females from 1995 to 1999 years was (5 years earlier) higher by 3.6 of percent points then appertaining survival rate in the OBC in the period 2001–2005 (64.2%)<sup>5</sup>. The data of the median age at diagnosis were almost the same in the USA, Croatia and in the OBC (61, 61.5 and 61.5 years, respectively), while the

**TABLE 10**  
 THE AGE GROUP AND CORRESPONDING TREND OF THE OVERALL LENGTH OF STAY IN HOSPITAL FOR MALIGNANT NEOPLASMS OF BREAST AND FEMALE GENITAL ORGANS (C50, C51-C58) IN THE OBC, PERIOD 2001–2009

ICD <sup>10</sup>	Parameters	Age group				
		0–19	20–44	45–64	65+	All ages
C50	OLOSH	–	9.8	10.7	14.5	12.1
	Trendline	–	DW	DW	DW	DW
	Strength	–	strong	weak	very strong	strong
	Trendline (t)	–	t (7)=2.801, p<0.05	t (7)=0.084, p>0.05	t (7)=3.641, p<0.01	t (7)=2.713, p<0.05
C51	OLOSH	–	19.5	17.2	24.5	22.1
	Trendline	–	DW	UW	UW	DW
	Strength	–	moderate	barely	weak	weak
C52	OLOSH	–	7.0	17.4	8.5	11.4
	Trendline	–	–	DW	DW	UW
	Strength	–	–	strong	barely	barely
C53	OLOSH	3.0	12.0	14.0	17.7	14.8
	Trendline	–	UW	DW	DW	DW
	Strength	–	barely	weak	strong	moderate
C54	OLOSH	–	17.1	16.7	20.0	18.5
	Trendline	–	UW	DW	DW	DW
	Strength	–	moderate	strong	strong	moderate
C55	OLOSH	–	24.5	14.0	11.1	13.1
	Trendline	–	–	DW	DW	DW
	Strength	–	–	moderate	strong	moderate
C56	OLOSH	13.0	8.6	9.5	14.8	11.3
	Trendline	–	UW	UW	DW	UW
	Strength	–	moderate	strong	moderate	moderate
	Trendline (t)	–	–	t (7)=2.420, p<0.05	–	–
C57	OLOSH	8.0	–	8.7	23.0	14.2
	Trendline	–	–	DW	UW	UW
	Strength	–	–	barely	very strong	strong
C58	OLOSH	–	–	2.0	2.0	2.0
C51-C58	OLOSH	11.3	11.7	12.9	18.0	14.9
	Trendline	UW	UW	DW	DW	DW
	Strength	very strong	barely	barely	moderate	moderate
	Trendline (t)	t (1)=22.34, p<0.01	–	–	–	–
C50-C58	OLOSH	11.3	10.7	11.6	16.2	13.4
	Trendline	UW	DW	DW	DW	DW
	Strength	very strong	moderate	weak	strong	strong
	Trendline (t)	t (1)=22.34, p<0.01	–	–	–	–

OLOSH – overall length of stay in hospital, UW – upward, DW – downward, ICD<sup>10</sup> – International Statistical Classification of Diseases and Related Health Problems, 10th Revision, t – significance of the coefficient of determination, »-« – to small data number or no significant (p>0.05)

figures on the median age at death in the USA were different from those collected in the OBC (68 and 69.1 years, respectively)<sup>13,14</sup>.

Between 1981 and 2000, the length of stay of patient with breast cancer in Canada hospitals declined from 26 days to 9.4 days (almost 64%, each year 3.2%) and the

number of hospital admissions during that period remain the same<sup>41</sup>. In the OBC, the length of stay over the 9-year period declined by 0.6% each year. Compare to the Canadian data referring to the year 2000, the average length of stay in OBC (14.7 days) was 5.3 days longer.

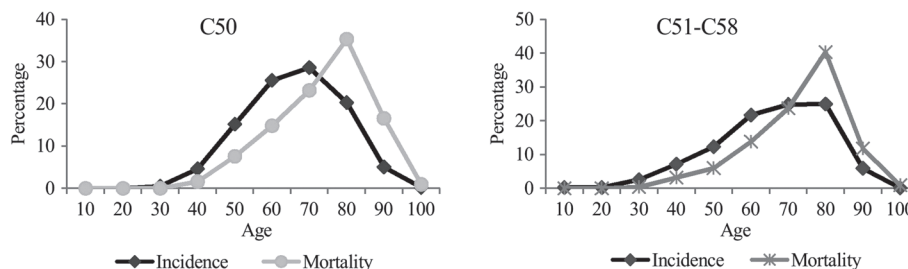


Fig. 1. The age distribution for malignant neoplasms of breast and female genital organs (C50, C51-C58) in the period 2001–2009.

In summary, female patients develop breast cancer and die both later and later, the incidence rate rises strongly until 2007, and then decline, five-year relative survival rate is extended and declined the number of hospitalizations per year, the number of hospitalizations per person/year and the length of hospitalization per year. Negative data is that the mortality rate increases significantly. The implementation and consolidation of female's awareness of these cancers and relating early diagnostic activities within the OBC population seem to be the most effective ways to reduce the appertaining risks and thus to encourage changes in the lifestyle.

#### Ovarian (C56) and endometrial cancer (C54)

In the OBC, the overall incidence and mortality rate from ovarian and endometrial cancer exceeded the relating EU rates. The incidence rate for endometrial cancer (C54) decreased in each age group as well as in all age's groups together. In the same period, the incidence rate of the C54 cancer site fell bellows the Croatian average<sup>40</sup>. The overall incidence rate of ovarian cancer (C56) was slightly below the Croatian average (Table 3). The incidence rate of the C56 cancer site moderate decreased in age groups 45–64 and 65+ years. Similarly to the situation with breast cancer, propaganda in public media and education of women exercises great influence on the decline of this incidence rate. Unfortunately, the mortality rates show a moderate increase for C54 cancer due to an increase in mortality rate in the age group 65+ years (Table 4). The mortality rate is nearly twice as high as in Europe. The 5-year relative survival rate from endometrial cancer (C54) in the OBC of 57.4% is well below the USA and EU rates (83% and 78%, respectively) whereas the survival rate from ovarian cancer of 43.0% is very close to the USA average (46%) and higher than the respective EU rate (36.3%)<sup>19,42,43</sup>. Comparing to the average length of stay in one hospital in the UK due to ovarian cancer (8.5 days)<sup>44</sup>, female patients with the same cancer spent 2.7 days more in the OBC hospitals (11.3 days) for the same reason. Compare to the Australian average, the length of stay in the OBC hospitals due to endometrial cancer was longer by 12.8 days<sup>45</sup>.

In summary, female patients develop endometrial cancer (C54) and die both later and later, the incidence rate decreased and declined the number of hospitalizations per year, the number of hospitalizations per person/year and the length of hospitalization per year. Negative data: the mortality rate and 5-year relative survival rates decreased. Female patients with ovarian cancer

(C56) showed negative trendline for median age at diagnosis and at death and upward mortality rate.

#### Cervical cancer (C53)

In the OBC, the overall incidence rate of cervical cancer (13.0/100,000) slightly increased in 2001–2009 period. It corresponded to Central, Eastern and Western European incidence rates and to the Croatian average. The overall mortality rate of 5.0/100,000 was lower then in Central and Eastern Europe (8.7 and 6.2/100,000, respectively), and lower than the Croatian average<sup>15,22,24</sup>. In the OBC, the incidence rate of the age group 45–64 experienced almost a threefold increase as well as a twofold increase in the age group 65+ years (Figure 7). Currently, there is no information which might, to some extent, explain the rise in the mortality rate. Compared to the 5-year relative survival rate in the EU<sup>5</sup>, the respective rate was higher in the OBC (62.6% and 66.1%, respectively). Compare to the length of stay in hospitals in Spain (15.2 days), females with cervical cancer in the OBC stayed shorter in hospital on average by 14.8 days<sup>47</sup>. A distinctive reduction in the incidence of cervical cancer over the past two decades in some European countries and North America suggests that in the OBC there is still no widespread screening and early treatment of pre-invasive lesions. Cervical cancer screening programs were first established in Croatia in the 2012.

In summary, in female patients with cervical cancer (C53) the median age at diagnosis was significantly shifts the older age, dies later, declined the number of hospitalizations per person/year and the length of hospitalization per year. Unfortunately, the 5-year relative survival rates decreased.

Implementation and consolidation of women's awareness of these cancers and relating early diagnostic activities within the OBC population seem to be the most effective ways to reduce the appertaining risks and thus to encourage changes in the lifestyle.

#### Limitations

Patients who were treated outside the hospitals in the OBC are not registered with the IPHO. Despite the efforts to obtain this information (it exist at the national level) in its original form, the authors were unable to obtain those data for unknown reasons. Therefore, these data on cancer in the OBC may differ from official state data on cancer in the OBC.

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## RAK DOJKE I ŽENSKIH SPOLNIH ORGANA U OSJEČKO-BARANJSKOJ ŽUPANIJI, HRVATSKA

### SAŽETAK

Rak dojke (C50) i rak ženskih spolnih organa (C51-C58) su među najučestalijim neoplazmama u žena u razvijenim zemljama. Zavod za javno zdravstvo Osječko-Baranjske županije u suradnji s različitim županijskim ustanovama vodi podatke oboljelih od raka s područja Osječko-Baranjske županije (OBC). Cilj je ovoga članka dati informaciju o raku dojke i raku ženskih spolnih organa u vremenu od 2001–2009 godine. Ovo je ujedno i prvi članak o ovim sijelima raka na razini jedne županije u Hrvatskoj. Članak obrađuje podatke o incidenciji i mortalitetu, dobnoj distribuciji, srednjoj dobi u trenutku dijagnoze i smrti, preživljavanje i dužinu hospitalizacije oboljelih od ove vrste raka za razdoblje od 1996 – 2010. U OBC prosječna stopa incidencije u šestogodišnjem razdoblju za rak dojke, ušća maternice, tijela maternice i jajnika (korištena je EU standardna populacija) je bila 82,9, 13,0, 19,0 i 14,5/100,000. Pojedinačno promatrane, stope za svaku vrstu raka padaju tijekom promatranog razdoblja, osim za rak dojke. Stopa incidencije za rak dojke u OBC slična je hrvatskom prosjeku, nadmašuje stopu incidencije u Srednjoj i Istočnoj Europi, ali je niža od one u Sjevernoj Europi. U OBC prosječna stopa smrtnosti u šestogodišnjem razdoblju za rak dojke, ušća maternice, tijela maternice i jajnika je bila 29,6, 5,0, 8,1 i 9,6/100,000 te sve stope raka pokazuju uzlazni trend. 5-godišnje relativno preživljavanje oboljelih od raka dojke, ušća maternice, tijela maternice i jajnika u vremenu od 2001–2005 godine je 64,2%, 66,1%, 57,4% i 43,0%. Prosječna srednja dob u trenutku postavljanja dijagnoze raka dojke, ušća maternice, tijela maternice i jajnika je bila 61,9, 56,4, 66,4 i 60,8 godina. Srednja dob u trenutku smrti oboljelih od raka dojke, ušća maternice, tijela maternice i jajnika je bila 68,7, 65,7, 70,3 i 67,6 godina. U devetogodišnjem razdoblju prosječna dužina boravka oboljelih od raka dojke, ušća maternice, tijela maternice i jajnika je bila 12,1, 14,8, 18,5 i 11,3 dana. Dužina hospitalizacije oboljelih od raka pada za sva sijela osim za rak jajnika. Podizanje svijesti žena OBC o raku dojke i raku ženskih spolnih organa, preventivnim pregledima, važnosti rane dijagnoze i promjene načina života su najučinkovitiji način smanje rizike od raka, odnosno njegovih posljedica na zdravlje.