Original Article

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Comparative analysis of the access to healthcare services and breast cancer therapy in 10 Eastern European countries

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Maria Dimitrova¹, Dragana Lakic², Guenka Petrova¹, Semir Bešlija³ and Josip Culig⁴

Abstract

Aim: The aim of this study is to compare the differences in breast cancer therapy, health-care service practices, and their availability in ten European countries—Albania, Bosnia and Herzegovina, Bulgaria, Kosovo, Montenegro, Republic of North Macedonia, Croatia, Romania, Slovenia, and Republic of Serbia.

Methods: An inquire survey was conducted among oncologists in the participating countries. The questionnaire was of qualitative character and focused on several key areas as screening practices, diagnosing, treatment, and health-care procedures utilization. The results were processed through comparative and percentage analysis.

Results: All of the observed countries have national registries for breast cancer, but only in five, a mechanism of controlled action of early detection is implemented. Ninety percent of the countries have implemented in the national guidelines the European Society of Medical Oncology recommendations, while National Comprehensive Cancer Network is considered in only 50%. In all countries, digital mammography is a universal diagnostic method. Pathohistological analysis, including HER2 receptor expression and determination of the level of progesterone and estrogen receptors, is routinely performed in all countries prior to therapy. Some differences are observed in terms of FISH/CISH methods, determination of Ki-67 volume, and prognostic molecular assays. Trastuzumab is used as neo-adjuvant therapy in HER2-positive disease in all countries, while in Bosnia and Herzegovina and Croatia, only pertuzumab is used. Psychological support is integrated into the professional guidelines for treatment and monitoring in Bosnia and Herzegovina, Bulgaria, and Serbia.

Conclusions: The international guidelines should be followed strictly, and some improvements in the health policies should be made in order to decrease the differences and inequalities in the availability of the breast cancer (BC) health services in the Central and Eastern European countries.

Keywords

Breast cancer, Eastern Europe, health-care resources, utilization, mapping

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Introduction

Breast cancer is the most common cancer disease in women—the fifth reason for mortality worldwide and the first in Europe.¹ One in every eight women in the European Union will be diagnosed with BC before the age of 85.² Studies have shown that the increased incidence of BC may be related to changes in the lifestyle, increase in sedentary lifestyle, weight gain, obesity, and the tendency of increased age at first birth.³

BC places substantial economic burden as almost 6 billion euros are the estimated health-care costs across the European Union every year.^{1,4} Studies have shown that the health-care resource utilization is dependent on the stage of

the disease and the choice of treatment.⁵ Early screening in high-risk individuals may be feasible and effective in countries with resource constraints.⁶ Although breast screening programs are already present at almost all European Union

¹Faculty of Pharmacy, Medical University of Sofia, Sofia, Bulgaria

²Faculty of Pharmacy, University of Belgrade, Belgrade, Serbia

³Oncology Clinic, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina

⁴University of Applied Health Sciences, Zagreb, Croatia

Corresponding author:

Maria Dimitrova, Faculty of pharmacy, Medical University of Sofia, Sofia 1000, Bulgaria.

Email: mia_dimitrova@yahoo.com

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countries, still there are considerable differences in the age, amount of covered population, and the applied techniques.⁷

In spite of updated international treatment guidelines, however, there is still a risk of inequalities in some countries. Treatment guidance could be influenced by country's specific cancer outcome indicators such as incidence; mortality and survival; access to health-care services including screening, treatment and care, and benefit/cost or cost/ effectiveness ratios; restricted health-care resource utilization; and budget constraints.8-10 A report of the European Commission concerning the challenges of cancer shows that some of the main reasons for these inequalities, especially in the Eastern European countries, could be attributed to differences in the lifestyles, socioeconomic status, different level of implemented preventive actions, the organization of screening programs, and the infrastructure and distribution of health-care facilities. 11 Important limitations and differences among Central and Eastern European (CEE) patients are also observed in terms of availability and costs of new medicines and drug shortages for medicines with well-established use, included in the list of "essential" medicines. 12

The objective of the present study is to evaluate and compare the differences in BC therapy and health-care service practices as well as their availability in ten European countries—Albania, Bosnia and Herzegovina, Bulgaria, Kosovo, Republic of North Macedonia, Croatia, Romania, Slovenia, and Republic of Serbia.

We wanted to evaluate whether there are health-care services and practices which are not available in all countries under consideration.

Materials and methods

This is a four-step inquiry research. We use the inquiry approach as a qualitative, investigational, and focus group questioning via a structured self-prepared questionnaire, followed by answers analysis and their external validation.¹³ The first step was the creation of the questionnaire from an international team of clinical experts and representatives from the patients' organization in each country. The second step was the answers' systematization and discussion, and the fourth step was the validation of the results. The questionnaire was prepared following the recommendations for BC therapy. 14,15 The questionnaire consists of 5 opened questions and 81 closed (74 yes or no and 7 multiple choice). The questionnaire was created and distributed in English language and focused on the screening practices, diagnosing, treatment, and health-care procedures utilization (supplementary material). The questions were separated in several groups of indicators:

Availability of patients' registries and centers for excellence care of BC;

Requirements for early screening and compliance with international guidelines for screening, diagnosis, and treatment of BC and the availability of national recommendations:

Applied methods for diagnosis of BC;

Therapeutic schemes for treatment of BC;

Possibilities for rehabilitation and psychological help for patients diagnosed with BC.

The questionnaire was disseminated to ten European countries—Albania, Bosnia and Herzegovina, Bulgaria, Kosovo, Republic of North Macedonia, Monte Negro, Croatia, Romania, Slovenia, and Republic of Serbia was conducted. The selected countries are neighboring from the Balkan area with similar historical and economic development. The questioning was organized through the e-mail contact. A pilot testing was performed after creation of the questionnaire with 2 of the countries (Bulgaria and Croatia).

One leading oncologist and one representative of patients' organization per country participated in the survey, thus reaching 100% response rate. Interviewed participants were asked to fulfill the available health-care services and procedures in the country, either provided on the basis of the regulatory decisions or as established practice in the hospitals or society. The oncologists were selected from the national specialized centers for oncology therapy out of the cohort of the national oncology consultants. The attempt was to gather the high-level oncologists in the country, working in a tertiary health care, specialized in BC therapy. All of the oncologists were consulting a variety of national institutions such as ministries of health and health insurance institutions. Of all nationally representative patients' organizations, those of patients with BC were selected. Several e-mail and electronic meetings were held to discuss the questionnaire. Only oncologists and chairs of patients' organization who agree to participate were included.

Systematization of the answers focused on availability and differences in the medical practice and health-care services, including medicines, rehabilitation, and BC registries. After collecting the answers and systematizing them, the research team discusses any available discrepancies with the representatives of all organizations.

The whole process took approximately one and a half year. The final step was the results validation by the local experts in 2019. Validation was performed from the experts working in the academia and where possible governmental institutions responsible for health-care policy and funding (Bulgaria, Serbia, and Croatia).

The ethical committee at the Medical University of Sofia waived the requirement for ethical approval for this study because of its inquiry design, in accordance with the national legislation and the institutional requirements.

Table 1. Data on health-care human resource and health facilities distribution.

Country	Population (No, 2019)	Total number of cancer cases (2018)	Breast cancer incidence (%, 2018)	5-year prevalence (all ages, breast cancer, No, 2018)	Approximate number of medical oncology centers (including independent medical oncology units and facilities) 2019	National Cancer Comprehensive Center (No, 2019)	Approximate number of oncologists in the country (per 10,000 all cancer patients, 2019)
Albania	28,80,913	8294	11.7%	2992	7	I	8
Bosnia & Herzegovina	33,00,998	14,385	9.6%	4310	4	1	15
Bulgaria	70,00,117	35,378	11.4%	13,179	>20	1	13
Croatia	41,30,299	25,221	11.3%	10,793	16	1	10
Kosovo ^{16,17}	19,32,744	2514	4.35%	No information available	I	I	4
Montenegro	6,27,988	2366	17.8%	1505	1	1	25
Republic of North Macedonia	20,85,056	7807	12.8%	3085	>20	I	17
Romania	1,93,64,558	83,461	11.5%	35,298	>60	2	36
Serbia	87,72,228	47,960	12.1%	18,621	30	5	28
Slovenia	20,78,654	13,503	10.2%	5582	3	I	23

Data available from: International Agency for Research on Cancer. The Global Cancer Observatory 2019; Medical Oncology Status in Europe Survey (MOSES). Phase II. ESMO MOSES Task Force 2006; WHO Cancer country profiles 2020. Available at: https://www.who.int/cancer/country-profiles/en/. Accessed on: March 2020.

Statistical analysis

Owing to the qualitative character of the study, comparative and percentage analysis was applied to evaluate the results. The results were processed with Excel.

Results

Health-care human resource and health facilities distribution in oncology

The BC incidence varies among the survey countries from 4.35% in Kosovo to 17.8% in Montenegro. All countries have at least one national cancer comprehensive center, but the number of medical oncology centers varies from 1 in Kosovo and Montenegro to more than 60 in Romania. The number of medical oncology specialists per 10,000 patients with cancer also varies—from 4 in Kosovo to 36 in Romania—Table 1.

Patients' registries

All of the observed countries have cancer patients' registries, but only in 5 of them, they are publicly available—Table 2.

Early screening and applied methods for diagnosis of BC

Only in five of the countries—Bosnia and Herzegovina, Croatia, Kosovo, Romania, and Serbia—there is a mechanism of controlled action of early BC detection.

In 90% of the countries the diagnosis and treatment of BC is implemented through the activity of multidisciplinary teams and according to national guidelines. Ninety percent of the countries follow the European Society of Medical Oncology (ESMO) recommendations, and only 50% (Bulgaria, Kosovo, Republic of North Macedonia, Serbia, and Slovenia) conform to both ESMO and NCCN (National Comprehensive Cancer Network)—Table 3.

We can assume the most of the critical prerequisites for BC information and standards of therapy are available, excluding the mechanisms for early detection (Figure 1).

Applied methods for diagnosis of BC

In all countries, participating in the survey, digital mammography is used for the diagnosis of BC. Magnetic resonance imaging (MRI) is not routinely used only in Albania and Romania, and positron emission tomography—computed tomography (PET/CT) is not applied in Albania, Kosovo, Macedonia, and Romania. Core needle biopsy is applied in 90% of the countries as the only exception is Albania. Fine-needle aspiration biopsy (FNAB) is not applied only in Romania and Serbia. Repeated biopsy regularly performed for confirmation of metastatic breast cancer (MBC)/site in 80% of the countries—Table 4.

Pathohistological analysis is performed in all countries prior to therapy initiation. Level of HER2 receptor expression and determination of the level of estrogenic and progesterone receptors is routinely determined in each of the participating countries. Some differences, however, are observed in terms

Table 2. National cancer registries.

Country	Registry	Institution	Publically available	Source
Albania	Albania National Cancer Registry	University Hospital Center, Oncological Institute	X	
Bosnia and Herzegovina	Population-based Cancer Registry of the Federation of Bosnia and Herzegovina	Institute of Public Health, Epidemiology Department	X	
Bulgaria	Bulgarian National Cancer Registry	National Oncological Hospital	\checkmark	https://www.sbaloncology.bg/index.php/bg
Croatia	Croatian National Cancer Registry	Croatian Institute of Public Health	\checkmark	https://www.hzjz.hr/wp-content/ uploads/2013/11/Bilten-2014_final.pdf
Kosovo	Kosova Cancer Registry	National Institute of Public Health	X	n.a.
Montenegro	Registry of Malignant Neoplasms of Montenegro	Institute of Public Health	X	
Republic of North Macedonia	Cancer Registry in the Republic of North Macedonia	Center for statistical processing of health data	X	
Romania	Bihor County Cancer Registry	Spitual Clinic Judetean	Χ	
	Cluj Regional Cancer Registry	Oradea, Clinica de Oncologie	$\sqrt{}$	www.iocn.ro
	Timisoara Regional cancer Registry	Oncology Institute Public Health Institue	$\sqrt{}$	www.ispt.ro
Serbia	Central Serbia Cancer Registry Vojvodina Cancer Registry	Institute of Public Health Institute of Oncology	$\sqrt{}$	www.batut.org.rs www.onk.ns.ac.rs
Slovenia	Cancer Registry of Republic of Slovenia	Institute of Oncology Ljublijana	\checkmark	www.onko-i.si/eng/crs/

 Table 3. Indicators for early detection and diagnosis of breast cancer and guidelines.

Countries	Controlled action for early detection	Multidisciplinary team engagement for diagnosis	National guidelines for diagnosis and treatment	ESMO handbook compliance for diagnosis and treatment of BC	NCCN guidelines for diagnosis and treatment of BC
Albania	х		\checkmark		x
Bosnia and Herzegovina	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	x
Bulgaria	x	$\sqrt{}$	$\sqrt{}$	\checkmark	$\sqrt{}$
Croatia	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	x
Kosovo	$\sqrt{}$	X	x	$\sqrt{}$	$\sqrt{}$
Montenegro	x	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	x
Republic of North	x	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$
Macedonia					
Romania	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	×	х
Serbia	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$
Slovenia	x	\checkmark	$\sqrt{}$	$\sqrt{}$	\checkmark

ESMO: European Society of Medical Oncology; BC: breast cancer; NCCN: National Comprehensive Cancer Network.

of fluorescence in situ hybridization/chromogenic in situ hybridization (FISH/CISH) methods, determination of Ki-67 volume (90% of the countries) and the application of prognostic molecular assays (only in 30% of the countries)—Table 5.

Genetic counseling is performed in Bosnia and Herzegovina, Bulgaria, Serbia, and Slovenia. In none of the countries, the determination of BRCA1 and BRCA2 status is a routine practice, but only in Slovenia, the testing is covered by the health insurance.

Therapeutic schemes for treatment of BC

Neo-adjuvant therapy. Only in Bulgaria when planning neo-adjuvant therapy or when such is indicated, there is no rule to apply only chemotherapy or only hormone therapy. Trastuzumab is used as neo-adjuvant therapy in HER2-positive disease in all countries, while pertuzumab only in Bosnia and Herzegovina and Croatia. Lapatinib is prescribed as neo-adjuvant therapy only in Croatia—Table 6.

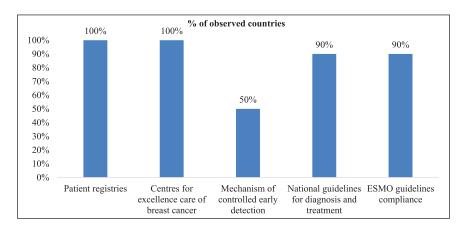


Figure 1. Availability of information and clinical standards.

Table 4. Indicators for applied methods for diagnosis of breast cancer.

Countries	FNAB (fine-needle aspiration biopsy) for BC diagnosis	Core needle biopsy for BC diagnosis	Sentinel test for BD diagnosis	Digital mammography for BC diagnosis	MRI for BC diagnosis	PET/CT for BC diagnosis	Re-biopsy for MBC/site
Albania		х	х	V	х	x	×
Bosnia and	$\sqrt{}$	\checkmark	\checkmark	$\sqrt{}$	\checkmark	\checkmark	\checkmark
Herzegovina							
Bulgaria	$\sqrt{}$	\checkmark	x	$\sqrt{}$	\checkmark	\checkmark	\checkmark
Croatia	$\sqrt{}$	\checkmark	\checkmark	$\sqrt{}$	$\sqrt{}$	\checkmark	\checkmark
Kosovo	$\sqrt{}$	\checkmark	×	$\sqrt{}$	$\sqrt{}$	x	x
Montenegro	$\sqrt{}$	\checkmark	\checkmark	$\sqrt{}$	$\sqrt{}$	\checkmark	$\sqrt{}$
Republic of North	$\sqrt{}$	\checkmark	×	$\sqrt{}$	$\sqrt{}$	x	\checkmark
Macedonia							
Romania	x	\checkmark	\checkmark	$\sqrt{}$	x	x	\checkmark
Serbia	$\sqrt{}$	\checkmark	\checkmark	$\sqrt{}$	$\sqrt{}$	\checkmark	$\sqrt{}$
Slovenia	\checkmark	\checkmark	\checkmark	$\sqrt{}$	\checkmark	\checkmark	\checkmark

BC: breast cancer; MBC: metastatic breast cancer; MRI: magnetic resonance imaging; PET/CT: positron emission tomography-computed tomography.

If neo-adjuvant therapy is unsatisfactory, capecitabine postoperatively is administered in 7 of 10 countries (except Bulgaria, Macedonia, and Serbia).

The volume of neo-adjuvant therapies per year in the compared countries varies from 5% to 100%. In more than 50% of the cases of breast malignancies, it is applied in Slovenia and Romania, and in Montenegro when indicated, it is prescribed in all patients—Figure 2.

Adjuvant therapy in ER-positive BC. In all countries, except Serbia, aromatase inhibitors are used as upfront therapy during 5 years when planning adjuvant therapy for estrogene receptor (ER)-positive disease in post-menopausal women. In Serbia, this therapy is applied only in HR + high-risk patients with contraindication to chemotherapy.

Tamoxifen, together with aromatase inhibitors, are applied for 5 years in all countries. Ten-year therapy of tamoxifen and aromatase inhibitors is prescribed in 9 of 10 countries (except Serbia), and in Bulgaria, the 10-year therapy is only for postmenopausal women with ER-positive BC.

Five-year LHRH agonist therapy together with aromatase inhibitors is used in eight of ten countries (except Romania and Serbia) and together with tamoxifen in nine of ten countries (except Serbia). Luteinising hormone releasing-hormone (LHRH) agonist therapy in Serbia is allowed for 3-year period.

Everolimus is used for treatment of ER-positive metastatic BC in 5 of the 10 countries (Albania, Bulgaria, Kosovo, Slovenia, and Montenegro). Palbocyclib is used only in Albania and Montenegro, and fulvestrant, in Bulgaria, Croatia, Kosovo, Romania, Slovenia, and Montenegro.

Adjuvant therapy in HER2-positive BC. Trastuzumab therapy is prescribed for 12-month period in HER2-positive BC in all countries, but only in 2 (Romania and Albania), there is a practice for 3-month treatment period.

Trastuzumab could be combined with antracycline, taxane, and platinum-based therapy, but there are variations between the observed countries—Table 7.

In all countries, trastuzumab is prescribed for the treatment of metastatic BC, while ado-trastuzumab emtasine is

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Countries	WHO NHS scale classification for for tumor histological grade	NHS scale for tumor grade	NHS scale Determination of for tumor hormone receptors grade (ER, PgR)	Determination of the level of HER2 receptor expression	FISH (F)/CISH (C) method for determination of HER2 amplification	Determination Application of Ki67 volume of prognostic molecular assays	Application of prognostic molecular assays	Menopausal status determination based on sex hormones
Albania	>	>	>	>	U	×	×	×
Bosnia and Herzegovina	>	>	>	>	O	>	>	>
Bulgaria	>	>	>	>	ш	>	>	>
Croatia	>	>	>	>	U	>	×	>
Kosovo	>	>	>	>	U	>	×	>
Montenegro	>	>	>	>	U	>	×	>
Republic of North Macedonia	>	>	>	>	U	>	×	>
Romania	>	>	>	>	ш	>	×	>
Serbia	>	>	>	>	ш	>	×	>
Slovenia	>	>	>	>	ш	>	>	>

prescribed only in Bulgaria, Kosovo, Montenegro, and Slovenia. Pertuzumab is used in 5 of 10 countries—Albania, Kosovo, Macedonia, Romania, and Serbia. Lapatinib is used in 7 of 10 countries (except Albania, Bosnia and Herzegovina, and Macedonia).

Treatment of metastatic BC. Everolimus is used for treatment of ER-positive metastatic BC in 5 of the 10 countries (Albania, Bulgaria, Kosovo, Slovenia, and Montenegro). Palbociclib is used in Albania, Bulgaria, and Montenegro, and fulvestrant, in Bulgaria, Croatia, Kosovo, Romania, Slovenia, and Montenegro.

In all countries, trastuzumab is prescribed for the treatment of metastatic HER2-positive BC, while ado-trastuzumab emtasine is prescribed only in Bulgaria, Kosovo, Montenegro, and Slovenia. Pertuzumab is used in 6 of 10 countries—Albania, Bulgaria, Kosovo, Macedonia, Romania, and Serbia. Lapatinib is used in 7 of 10 countries (except Albania, Bosnia, and Herzegovina and Macedonia).

We should consider that fact that at the time of the survey, some of the medicines may not have been available in the countries, but owing to the constant update of the national reimbursement list, now they might be already included.

Bone metastases are treated with bisphosphonates in 9 of 10 countries with the exception of Serbia. Denosumab is prescribed only in Bulgaria, Croatia, Montenegro, and Slovenia.

Radiation therapy. Intensity-modulated radiation therapy (IMRT) when planning adjuvant therapy is applied in only 3 of the countries—Bulgaria, Romania, and Slovenia, while hypofractionation is not applied only in Bosnia and Herzegovina and Macedonia. Partial breast irradiation after breast conserving surgery is used only in Bulgaria and Kosovo. Integrated boost radiation is applied only in Bosnia and Herzegovina, Kosovo, and Romania.

Conformal radiation technique is used in 90% of the countries, except Kosovo, while conventional (2D) radiation technique is applied in Bosnia and Herzegovina, Bulgaria, and Romania. Integrated boost radiation is applied only in Bosnia and Herzegovina, Kosovo, and Romania.

Radiation of the thoracic wall after mastectomy with an electronic beam is applied in Albania, Bosnia and Herzegovina, Bulgaria, Kosovo, and Montenegro, while radiation with two or more tangential photon beams in not applied only in Albania and Kosovo. Boost radiation of the primary process sit with a direct electronic beam or with photon beams is applied in Bulgaria, Kosovo, Serbia, and Slovenia.

All countries compare the tolerance doses for organs at risk with the QUANTEC recommendations. In 6 of the countries-Albania, Bulgaria, Croatia, Slovenia, Romania, and Montenegro—specialists contour the left anterior descending coronary artery as an organ at risk, especially in left-sided BC.

During the course of radiotherapy in all countries, there is a check of the fields (EPID (electronic portal imaging device) and CBCT (Cone-Beam CT)) but there is a variation in the frequency—Table 8.

Table 6. Neo-adjuvant treatment practices among the compared countries.

Countries	Neo-adjuvant therapy (only chemotherapy)	Neo-adjuvant therapy (only hormonal therapy)	Neo-adjuvant therapy (trastuzumab)	Neo-adjuvant therapy (pertuzumab)	Neo-adjuvant therapy (lapatinib)
Albania			\checkmark	x	х
Bosnia and Herzegovina	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	\checkmark	x
Bulgaria	x	x	$\sqrt{}$	x	x
Croatia	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$
Kosovo	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	x	x
Montenegro	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	x	x
Republic of North Macedonia	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	x	x
Romania	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	x	x
Serbia	$\sqrt{}$	$\sqrt{}$	$\sqrt{}$	x	x
Slovenia	\checkmark	$\sqrt{}$	\checkmark	x	x

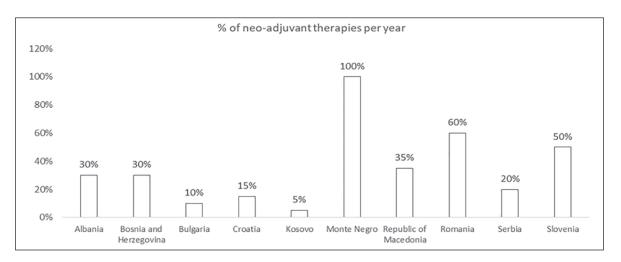


Figure 2. Percentage of neo-adjuvant therapies per year applied in the compared countries.

 Table 7. Trastuzumab-based adjuvant treatment practices among the compared countries.

Countries	$\label{eq:Trastuzumab} \ + \ \text{antracycline} \\ \text{therapy}$	Trastuzumab + platinum- based therapy	$\begin{array}{c} Trastuzumab + taxane \\ therapy \end{array}$
Albania	×	Х	V
Bosnia and Herzegovina	X	\checkmark	\checkmark
Bulgaria	X	\checkmark	$\sqrt{}$
Croatia	\checkmark	\checkmark	\checkmark
Kosovo	X	×	\checkmark
Montenegro	\checkmark	\checkmark	$\sqrt{}$
Republic of North Macedonia	\checkmark	\checkmark	$\sqrt{}$
Romania	X	\checkmark	$\sqrt{}$
Serbia	\checkmark	×	$\sqrt{}$
Slovenia	X	\checkmark	$\sqrt{}$

Rehabilitation and psychological help. Primary and secondary breast reconstruction at health insurance expense is provided in 7 of 10 countries (Bulgaria, Croatia, Macedonia, Montenegro, Romania, Serbia, and Slovenia).

Palliative care is provided in 90% of the countries, participating in the survey, except Bosnia and Herzegovina.

Psychological support is integrated into the professional guidelines for treatment and monitoring in Bosnia and

Table 8. Frequency of EPID and CBCT field check.

Countries	Check of the EPID and CBCT fields
Albania	Once a week
Bosnia and Herzegovina	Once a week
Bulgaria	Every day
Croatia	Once a week
Kosovo	Once a week
Montenegro	3 times per course
Republic of North Macedonia	No information
Romania	Once a week
Serbia	Once per course
Slovenia	During the first 3 days and then once a week, or depending on the radiation therapy technique

EPID: electronic portal imaging device; CBCT: Cone-Beam computed tomography.

Herzegovina, Bulgaria, and Serbia. Professional psychological help in the treatment centers is provided in 5 of the countries (50%)—Albania, Bulgaria, Croatia, Serbia, and Slovenia, however, out-of-hospital counseling centers for the maintenance and improvement of quality of life are present only in Albania and Bulgaria.

Medical students are provided with training in communication with patients in 6 of the countries—Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Macedonia, and Montenegro. Physicians also are trained in communication skills with patients in the aforementioned countries, except Croatia.

Only in 1 of the countries (Albania), there seems to be no cooperation between patients' associations and health-care institutions.

Discussion

The results from our study show that all of the observed countries have BC patients' registries, and only 50% (5 out of 10 observed countries) have a mechanism of controlled early BC detection via some type of screening.

BC registries are available in many countries and provide socio-demographic, epidemiologic, and clinical characteristics of patients, which might be used for comparative analysis and quality indicators comparison.¹⁸ The importance of registries is appreciated at the European level as data provider and for improving the quality of health care through the linkage of the available cancer registries.^{19,20}

In 90% (9 out of 10) of the observed countries, the diagnosis and treatment of BC is performed by multidisciplinary teams and is in compliance with national guidelines.²¹ In most of the countries, all health-care services concerning the treatment, diagnosis, and rehabilitation are according to international and mostly according to the European Society of Medical Oncology recommendations.^{22–24} Only one

exception is Romania according to experts' answers. However, some differences among the countries are in place concerning the type of health-care services and their financing. Some services, such as genetic testing, for example, in most of the countries are not covered with public expenditures. There are no significant variations in terms of diagnostic techniques and patho-histological analysis prior therapy initiation.

Major differences are observed in the treatment schemes are observed between the observed countries—mainly in the application of pertuzumab, fulvestrant, and palbociclib as adjuvant therapy and the type of radiation therapy, but overall the majority of them comply with the international guidelines.

The results from this study comply with other published studies evaluating the affordability of BC care in the region. A study published in 2018 evaluates the access to screening programs, surgery, radiotherapy, pathology, palliative care, and antineoplastic medicines in the CEE countries. In a CEE country survey, some disparities are observed related to limitations in the access to screening programs and high-quality pathology. Surgical services are widely accessible among the observed countries, but sentinel node biopsy is not universally available throughout the region. The most substantial inequalities exist in the availability and costs of the medicines, especially with the newer and more expensive ones. 7,25 This potentially could pose a burden on patient self-financing or co-payment.

More variations are observed in terms of providing psychological help, especially in out-of-hospital counseling centers. According to our results such centers are present only in Albania and Bulgaria. In 80% of the countries, however, there are mechanisms for cooperation between healthcare institutions and patients' associations.

Psychological help is of a great importance to achieve emotional competence which is expected to have beneficial impact of the patient's satisfaction of the total process of care. ^{26,27} The patients association could play a significant role in supporting BC survivors. ²⁸

Studies suggest that these differences could be attributed to differences in the organization of health-care systems and socio-economic reasons. Differences also exist in the programs for cancer control activities among the Eastern European countries which leads to variations in the incidence and mortality trends. Philadelic This difference could also be attributed to differences in the lifestyle risk factors from one side and differences in the GDP per capita status for other. On the countries were suggested as the countries of the countries o

The study has several limitations. We selected the top ranked in the society BC oncologists, but some variations in practice patterns might exist between the oncologists in the same country. We consider that these variations might not influence the answers in the great extend because they focus more on the availability of the health-care resources that are evident for all professionals. Supplemented with the information from the patients' organizations, the comparison is as

closer as possible to the real-life practice. The second limitation is in the fact that the answers was provided by only one oncologist and patients' organizations' representative per country, but this was our primary idea to receive the best clinical practice point of view and to verify it through the patients. Additional validation was necessary after completing the manuscript because we wanted to be sure that there are no changes in the access to the health-care services.

Conclusion

BC continues to place substantial economic and social burden, especially in the CEE countries where the survival rates are still lower than in Western Europe. The reasons for this could be assigned to lack of screening practices and increased risk of late diagnosis, access to therapy, and specificities in the health system in the relation to the availability, access, and finance of the BC care services among the CEE countries. Strictly following the international guidelines and some improvements in the health policies should be placed in order to decrease the differences in the availability of the BC health services in the Central and Eastern European countries.

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Authors contribution

G.P. and M.D. contributed to the analysis and interpretation of data, drafting of the manuscript, and the critical revision and final approval. D.L. participated in the analysis and interpretation of the data, the critical revision, and final approval. S.M. contributed to the acquisition of the data, analysis and interpretation of the data, drafting the manuscript, and the final approval. J.C. participated in the drafting of the manuscript, the critical revision, and final approval.

Declaration of conflicting interests

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Ethical approval

The ethical committee at the Medical University of Sofia waived the requirement for ethical approval for this study because of its inquiry design, in accordance with the national legislation and the institutional requirements

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ORCID iDs

Maria Dimitrova https://orcid.org/0000-0002-4868-7775 Guenka Petrova https://orcid.org/0000-0001-8116-5138

Supplemental material

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References

- World Health Organization. Breast cancer: prevention and control, http://www.who.int/cancer/detection/breastcancer/en/ index1.html (accessed January 2019).
- Curado MP, Edwards B, Shin HR, et al. Cancer incidence in five continents (vol. IX, IARC Scientific Publications No. 160). Lyon: IARC Press, 2007.
- Stewart BW and Wild CP (eds). World cancer report 2014.
 Lyon: International Agency for Research on Cancer, 2014.
- Luengo-Fernandez R, Leal J and Sullivan R. Economic burden of malignant neoplasms in the European Union. In: *Presented* at ESMO 2012 congress, Vienna, 2012. 1415PD PR.
- Pallis A, Tsiantou V, Simou E, et al. Pharmacoeconomic considerations in the treatment of breast cancer. *Clinicoecon Outcomes Res* 2010; 22: 4747–6161.
- Teh YC, Tan GH, Taib NA, et al. Opportunistic mammography screening provides effective detection rates in a limited resource healthcare system. *BMC Cancer* 2015; 15: 405.
- Altobelli E and Lattanzi A. Breast cancer in European Union: an update of screening programmes as of March 2014 (Review). *Int J Oncol* 2014; 45(5): 1785–1792.
- 8. Bobridge A, Price K, Gill TK, et al. Influencing cancer screening participation rates—providing a combines cancer screening program (a "One stop" shop) could be a potential answer. *Front Oncol* 2017; 7: 308.
- Senore C, Giordano L, Bellisairio C, et al. Population based cancer screening programmes as a teachable moment for primary prevention interventions: a review of literature. Front Oncol 2012; 2: 45.
- Jerusalem G, Neven P, Marinsek N, et al. Patterns of resource utilization and cost for postmenopausal women with hormonereceptor-positive, human epidermal growth factor receptor-2-negative advanced breast cancer in Europe. *BMC Cancer* 2015; 15: 787.
- Coleman MP, Alexe DM, Alberht T, et al. Responding to the challenge of cancer in Europe. Ljubljana, Slovenia: Institute of Public Health of the Republic of Slovenia, 2008.
- Enniu A and Antone N. Access of affordable breast cancer care in Eastern Europe. Current Breast Cancer Reports 2018; 10: 170–178.

 Bowling A. Research methods in health: investigating health and health services. 2nd ed. Buckingham: Open University Press, 2002.

- Cardoso F, Kyriakides S, Ohno S, et al. Early breast cancer: ESMO clinical practice guidelines. *Annal Oncol* 2019; 30: 1194–1220.
- NCCN Clinical Practice Guidelines in Oncology. Breast Cancer Screening and Diagnosis V 1.2019, https://www.nccn. org/professionals/physician_gls/pdf/breast-screening.pdf (accessed February 2020).
- Turjaka AN, Berisha ML, Luci LG, et al. Breast cancer screening in Kosovo: Women's knowledge and behaviours. *Zdrav Var* 2010; 49: 153–159.
- Kosovo Agency of Statistics, 2016, https://ask.rks-gov.net/media/3709/health-statistics-2016.pdf (accessed March 2020).
- Hartmann-Johnsen OJ, Karesen R, Schlichting E, et al. Using clinical cancer registry data for estimation of quality indicators: results from the Norwegian breast cancer registry. *Int J Med Inform* 2019; 125: 102–109.
- Data linkage and cancer registries. ENCR Scientific Meeting General Assembly 26–28 September 2018, Copenhagen, Denmark.
- Abriata MG and Macías GR. Patients with breast cancer: report from a national hospital-based cancer registry in Argentina, 2012 to 2016. *J Glob Oncol* 2019; 5: JGO009050.
- National medical standards for systemic drug therapy evaluation of the therapeutic effect follow-up of malignant solid tumors in adults. *Bulgarian Oncology Society*, 2019, https://www.oncologos.eu/phocadownload/standarti-za-lechenie-2019.pdf (accessed September 2019).

- Cardoso F, Kyriakides S, Ohno S, et al. Early breast cancer: ESMO Clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2019; 30(10): 1674–1220.
- Cardoso F, Senkus E, Costa A, et al. 4th ESO-ESMO International consensus guidelines for advanced breast cancer (ABC 4). Ann Oncol 2018; 29(8): 1634–1657.
- 24. NCCN Clinical practice guidelines in oncology. Breast cancer. Version 3, 2019, https://www.nccn.org/professionals/physician gls/pdf/breast.pdf (accessed September 2019).
- Eniu A and Antone N. Access to affordable breast cancer care in Eastern Europe. Current Breast Cancer Reports 2018; 10(6): 170–178.
- Baudry AS, Lelorain S, Mahieuxe M, et al. Impact of emotional competence on supportive care needs, anxiety and depression symptoms of cancer patients: a multiple mediation model. Support Care Cancer 2018; 26(1): 223–230.
- Grassi L, Spiegel D and Riba M. Advancing psychosocial care in cancer patients [version 1; referees: 3 approved]. F1000 Res 2017; 6: 2083.
- 28. Wells K, Valverde P, Ustjanauskas AE, et al. What are patient navigators doing, for whom, and where? A national survey evaluating the types of services provided by patient navigators. *Patient Educ Couns* 2018; 101(2): 285–294.
- Dimitrova N, Znaor Z, Agius D, et al. Breast cancer in South-Eastern European countries since 2000: Rising incidence and decreasing mortality at young and middle ages. *Eur J Cancer* 2017; 83: 43–55.
- 30. Dafni U, Tsourti Z and Alatsathianos I. Breast cancer statistics in the European Union: incidence and survival across European countries. *Breast Care* 2019; 14(6): 344–353.