

Pursuant to the Article 16, paragraph 2 of the Law on Health Care ("Official Gazette of RS", No. 107/05, 72/09 – Law, 88/10, 99.10, 57/11, 119/12 and 45/13 –Law) and Article 42, paragraph 1 of the Law on Government ("Official Gazette of RS", No. 55/05, 71/05 – correction, 101/07, 65/08, 16/11, 68/12 - US and 72/12),

The Government issues

**REGULATION
ON THE NATIONAL PROGRAM FOR EARLY DETECTION OF BREAST CANCER**

Article 1

This Regulation determines the National program for early detection of breast cancer and implementation of health care which includes activities to improve health, reduce mortality from breast cancer and improve the life quality of women.

Article 2

Activities to promote and preserve health are conducted by the National Program referred to in Article 1 of this Regulation which contains defined goals, activities and expected results.

The national program referred to in Article 1 of this Regulation is attached hereto as its integral part.

Article 3

On the date of entry into force of this Regulation, the Regulation on the national program for prevention of breast cancer ("Official Gazette of RS", No. 15/09) ceases to be valid.

Article 4

This Regulation shall enter into force on the eighth day of its publication in the "Official Gazette of the Republic of Serbia".

05 No.: 110-6916/2013
In Belgrade, 16 August 2013

THE GOVERNMENT

PRIME MINISTER

Ivica Dačić

NATIONAL PROGRAM FOR THE EARLY DETECTION OF BREAST CANCER

1. INTRODUCTION

Breast cancer is a global problem as the most common malignant tumor in women in the world, and in the Republic of Serbia it is one of the most common causes of premature death in women. The mortality rate from breast cancer is largely dependent on the success of the implementation of prevention programs.

Given the importance of the problem, the Ministry of Health, with the help of expert working groups, taking into account the recommendations of the WHO, analyzing screening programs in other countries and using the experience of various opportunistic screening programs, has developed a program for screening breast cancer in our country as well. The national program for early detection of breast cancer was adopted by the Government, and was published in the "Official Gazette of RS", No. 15/09.

Improvement of the National Program for early detection of breast cancer was done in 2012 and 2013, supported by the European Union and the project "Support to the implementation of the National Program to Fight Cancer in Serbia", the expert team of associates and working groups at the Ministry of Health.

The national program for prevention and early detection of breast cancer is in line with the recommendations of the World Health Organization, whose goal is "early detection of breast cancer, adequate diagnosis and therapy aimed to reduce mortality and improve quality of life of women."

2. SITUATION OVERVIEW

2.1. Epidemiology of breast cancer in the Republic of Serbia

Breast cancer is a global public – health problem, not only due to its epidemic proportions, but also because its consequences affect virtually all segments of society. During 2010, the world registered about 1.4 million new cases of the disease and over 450,000 deaths with this diagnosis. Epidemic wave of the disease affects both developed and developing countries. When it comes to the number of diseased women in 2010, the disease prevalence between countries was almost equal, while the developing countries had about 40% higher number of deaths. Study of the female population burdened with malignant diseases, which are used to plan health services and other resources related to health, as well as to assess the effectiveness and efficiency of preventive strategies, showed that breast cancer is the most significant cause of disease burden when it comes to malignant tumors in women, both globally and in our country. The risk to fall ill during life, or the cumulative probability of breast cancer is about 12.4%. This means that one in eight women can expect to have this illness during their lives. Breast cancer in many countries accounts for about 25% of all malignancies of the female population, in most developed countries even 28%, while in the structure of mortality it accounts for about 14-15%. In Serbia, 26% of all

patients and 17.5% of all deaths of women due to malignant tumors were diagnosed with breast cancer. The average standardized incidence rate of breast cancer in Central Serbia in the period 1999-2009 was 60.8/100,000, a mortality rate was 20.2/100,000. Similar values of incidence and mortality of breast cancer are registered in AP Vojvodina. In the countries of the European Union average annual incidence of breast cancer ranges from 57/100,000 (Greece) to 145/100,000 (Belgium), mortality rate from 18.4/100,000 (Spain) to 31.1/100,000 (The Republic of Ireland). The geographic distribution of breast cancer globally is not uniform. Areas which register the highest incidence of the disease are Western Europe, North America, Australia, New Zealand and some South American countries (Argentina), which is attributed to the higher prevalence of known risk factors for this disease in the mentioned regions. The European population is also polarized in terms of the frequency of breast cancer. The highest incidence rates are recorded in western and northern Europe, while the rates in southern and eastern Europe were significantly lower.

A recently published systematic analysis of incidence and mortality of breast cancer, including data from the Cancer register from 187 countries (including the Republic of Serbia), showed that the incidence of the disease globally has been growing continuously for 30 years and that this increase is 3.1% per year, while mortality varies. Analysis of the incidence of breast cancer in western European countries showed a trend of dramatic increase, especially in women older than 50 years, which is partly attributed to more frequent and earlier detection of disease or the effects of organized screening, but also to the effects of the demographic transition, leading to an increase in the number of women at risk of the disease.

When it comes to mortality from breast cancer, there is an evident trend of decline in the United States and other developed countries. In Europe, mortality from breast cancer in recent decades has different tendencies, i.e. ranging from a 30% decrease in the United Kingdom of Great Britain and Northern Ireland to a 25% increase in the Republic of Estonia. In addition to increasing incidence, especially in the older age groups, there is an evident effect of early detection on reducing mortality.

Breast cancer is the most common malignant tumor in women in the Republic of Serbia. Every year about 4,000 new cases of this disease are registered, which represents more than a quarter of all malignant disease in women.

Breast cancer takes 1,600 women each year, representing about 18% of deaths from cancer.

Both the incidence and mortality are constantly growing. Crude mortality rates of breast cancer increased four times since 1970, from ten per 100,000 women to 40 in 2004. The standardized mortality rate increased over the same period for two and a half times (from 8.3 to 20.7).

Breast cancer is one of the leading causes of premature death in women. Measured by age of lost life, breast cancer is the third cause of death in women aged 45-64 years, after cerebrovascular diseases and ischemic heart disease.

In women in the Republic of Serbia, breast cancer is usually discovered at an advanced stage. At the time of diagnosis, in more than half of the women the diseases spread from breast to regional lymph nodes, skin or are already distant metastases, which significantly reduces their chances for recovery. An important indicator is the size of the tumor at the time of detection: in only 30% of women breast cancer is detected while of smaller sizes, up to 2 cm; proportion of tumors that can not yet be felt, and are revealed by mammography screening is negligible. In women whose breast cancer is detected in operable stage, radical surgeries are usually done;

percentage of radical surgery ranges from 20 to 45%, depending on the institution where the interventions are performed.

2.2. Breast cancer prevention

The increase in breast cancer incidence is recorded in all developed and developing countries and is attributed to the increasing standards and changing lifestyles. Since present possibilities for primary prevention i.e. prevention of breast cancer is very limited, preventive activities are directed at early detection and reduction in mortality from breast cancer.

Thanks to organized programs of prevention and early detection of breast cancer and the timely implementation of appropriate treatment, most developed countries recorded a significant decrease in mortality from this disease in the last decade.

2.3. The implementation of the National program for early detection of breast cancer

National program of early detection of breast cancer (hereinafter referred to as screening) is implemented by organizing mammographic screenings in healthy women aged 50 to 69 years. Detection of breast cancer at an early stage, beside the high chance of cure, enables application of radical surgical interventions, faster recovery, reduced disability, better life quality as well as reducing the costs of treatment and indirect costs of illness.

Screening is a recognition of hitherto unrecognized disease, using a screening test in apparently healthy population that shows no signs of illness. The aim of screening is to reduce the incidence and mortality of the disease for which screening is organized. The screening can be organized or opportunistic.

Opportunistic screening represents the unsystematic application of screening tests as part of regular inspection. This includes women who themselves ask for examination or refer to a medical doctor for other reasons. This type of screening has been conducted in the Republic of Serbia for many years.

Organized screening is organized, mass calling the target population for screening mammograms and interpretation of images, accompanied by quality control and reporting. Organized screening is done in cycles over several years (one, two or three years).

Screening allows not only to detect breast cancer at an early stage, but also to detect precancerous changes whose removal prevents the development of malignant changes. Mostly in developed countries where the screening has been successfully applied for several decades, a dramatic decline in mortality from breast cancer has been recorded.

The screening test is a test applied for early detection of disease. The screening test should be highly sensitive, specific, easily applicable and relatively inexpensive. Screening test for organized breast cancer screening is mammography.

A successful screening should have:

- 1) a large population coverage (coverage should aim for at least 75% of the target population of women);

- 2) treatment of women with positive mammographic findings and their disposal;
- 3) the collection of data through an information system;
- 4) quality control.

Opportunistic screening has been performed in the Republic of Serbia, which showed the following shortcomings:

- 1) women's lack of information about the ways of early detection of breast cancer;
- 2) low coverage of the target population of women through regular clinical and mammographic examinations;
- 3) lack of quality control, training and work quality control – interpretation of mammographic findings;
- 4) inadequate data collection and reporting, thus no real results;
- 5) insufficient involvement of local governments in the activities to improve the health of women.

3. OBJECTIVES OF THE NATIONAL PROGRAM

3.1. General objective

Reduction of women's mortality from breast cancer in the Republic of Serbia.

3.2. Specific objectives

- 1) Raising awareness of women about the importance of regular examinations and early detection of breast cancer, and informing about the importance of screening;
- 2) strengthening the capacity of health institutions for the implementation of screening in terms of ensuring a sufficient number of trained personnel and equipment;
- 3) establishing a system of data collection and management during implementation
 - 1) screening;
 - 4) establishment of quality control services in the implementation of screening;
 - 5) involving local authorities and civil society in the implementation of screening.

4. LEGISLATURE AND SCREENING PARTICIPANTS

4.1. The legal framework

The basis for the implementation of organized screening are the following regulations:

- Health Protection Act ("Official Gazette of RS", No. 107/05, 72/09 - dr. Law, 88/10, 57/11, 119/12 and 45/13 - dr. Law);

- Health Insurance Act ("Official Gazette of RS", No. 107/05, 109/05, 57/11, 110/12 and 119/12);
- Regulation on the national program of health care for women, children and youth ("Official Gazette of RS", No. 28/09);
- Regulations on the nomenclature of health services at primary health care level ("Official Gazette of RS", No. 24/09 and 59/12);
- Public Health Strategy of the Republic of Serbia ("Official Gazette of RS", No. 22/09)
- Decision on the plan of development of health care in the Republic of Serbia ("Official Gazette of RS", No. 88/10);
- Decision on establishing standards for accreditation of health facilities ("Official Gazette of RS", No. 28/11).

4.1.1. Social care for the health of the population in the Republic of Serbia

Within the early detection of the disease, according to the Health Protection Act (hereinafter the Act), shall be targeted at preventative care or screening, according to the respective republic programs. Implementation of screening, according to Article 11, paragraph 15 of the Act, falls within the social care for the health of the population in the Republic of Serbia, and in accordance with Article 45, paragraph 1 of the Law on Health Insurance health care is insured in full force at the expense of the budget of the Republic of Serbia as well as for persons covered by screening according to the respective republic programs.

4.1.2. Activities of the selected physician in the screening implementation

The health care system and the organization of health services are regulated by the Act, according to which the medical activity is performed at the primary, secondary and tertiary levels (Art. 79, 88, 89, 90 and 91). In the process of health care implementation at the health center physician the elected physician conducts all activities defined by the Act (Art. 95, 98 and 99), including work on the identification and elimination of risk factors for the disease and implementing screening programs in accordance with special programs issued pursuant to the Act.

Screening as an activity is mentioned in the Strategy of Public Health of the Republic of Serbia ("Official Gazette of RS", No. 22/09), while the screening provisions are discussed in the Regulation on the national program of health care in women, children and youth ("Official Gazette of RS" No. 28/09), as a way of achieving the objective – preserving and improving the health of women in reproductive age.

4.1.3. Protection at work

Protection at work in the field of screening is regulated with various regulations. The ISO 15189:2008 quality standard of Medical laboratories is applied for the protection at work – special requirements for quality and competence.

Protection of carcinogenic substances and biological materials is achieved pursuant the Law on Safety and Health at Work ("Official Gazette of RS", No. 101/05), Regulations on preventive measures for safe and healthy work when exposed to biological hazards ("Official Gazette of RS "No. 96/10), Regulations on preventive measures for safe and healthy work at the workplace (" Official Gazette of RS ", No. 21/09) and Regulations on preventive measures for safe and healthy work when exposed to carcinogens or mutagens (" Official Gazette of RS ", No. 96/11).

4.2. Participants in the screening implementation

Breast cancer screening is carried out on the territory of the Republic of Serbia in the form of organized decentralized program.

4.2.1. Republic Expert Board for the implementation of programs for early detection of malignant diseases

Republic Expert Board for the implementation of programs for early detection of malignant disease (hereinafter referred to as the REB), formed by the Minister of Health for expert supervision over the implementation of organized screening, which through the defined annual plan, performs the following actions:

- 1) provides guidelines for screening programs and performs expert verification of screening programs, considers and adopts models and changes in screening programs;
- 2) provides guidelines for the organization, coordination, monitoring and evaluation of screening programs;
- 3) determines the list of indicators in the process of implementing screening;
- 4) determines and approves the plans in implementing screening and adopts the report on the plan execution and submits them for approval to the Ministry of Health, as well as the models in the implementation of screening programs and their changes;
- 5) conducts the activities in accordance with the plan of activities;
- 6) establishes the draft criteria, standards and norms pertaining to screening programs;
- 7) provides technical support to the Office for the Prevention of malignant diseases;
- 8) Evaluates the screening training program;
- 9) establishes programs of promotional activities related to screening programs, as well as plans for research in the field of screening programs;
- 10) makes proposals for the engagement of individuals or groups of experts to address certain issues in the field of screening and conducts other activities pursuant to the Act and the Minister of Health;
- 11) REB submits reports on its work to the Ministry of Health on a quarterly, semi-annual and annual basis.

4.2.2. The Institute of Public Health of Serbia "Dr Milan Jovanovic Batut"

The Institute of Public Health of Serbia "Dr Milan Jovanovic Batut" provides the necessary expert and logistical (technical) support to the Office for the Prevention of malignant diseases.

The information system of the Institute of Public Health of Serbia "Dr Milan Jovanovic Batut" represents the IT support in implementing screening programs, or collects data from the institutes of public health, forms continually updates appropriate electronic databases. Updated database is available to the Office for the Prevention of malignant diseases.

4.2.3. The Office for the Prevention of malignant diseases

The Office for the Prevention of malignant disease was established at the Institute of Public Health of Serbia "Dr Milan Jovanovic Batut".

The Office for the Prevention of malignant disease is responsible for the implementation of organized screening and performs the following actions:

- 1) coordinates, organizes, monitors and evaluates the implementation of organized screening and provides technical support to other participants in its implementation;
- 2) coordinates training in the areas of screening, in accordance with the plan for the implementation of screening;
- 3) prepares the draft plan for the implementation of screening;
- 4) performs activities of the five-year and annual plans in implementing screening of its competence (education coordination in the field of screening, organizing promotional activities);
- 5) submits the proposal of five-year and annual plans in implementing screening, including a financial plan, to the Ministry of Health and REB, and submits periodic and annual reports on the implementation plan to the Ministry of Health;
- 6) suggests REB changes, additions and new screening programs and models for their implementation to REB;
- 7) prepares and proposes REB draft of criteria, standards, norms and indicators related to the implementation of screening;
- 8) prepares and proposes REB suggestions of guidelines and regulations for screening;
- 9) prepares and proposes REB single form for collecting data on screening (population, test results, etc.);
- 10) issues instructions for preparing reports of the institutes of public health and health centers on the implementation of screening;
- 11) plans and conducts research in the field of screening;
- 12) prepares proposals for the program of promotional activities related to screening;
- 13) submits reports on the screening implementation to the Ministry of Health screening at least once a month;
- 14) performs other activities in the field of screening, with the consent of the REB.

4.2.4. The institutes of public health

The institutes of public health coordinate the implementation of screening in the territory they are established for and perform the following activities:

- 1) appoint screening coordinator and his deputy;
- 2) daily communication and cooperation with representatives of health centers are provided through a designated coordinator and his deputy;
- 3) coordinate and organize health centers and local self-government (representatives of population groups) in order to educate, motivate and increase the response of the local population to screening;
- 4) appoint their representatives in the team for the coordination of screening at the level of health center;
- 5) provide assistance to health centers in the preparation of action plans for the implementation of screening and approve the action plans;
- 6) collect and update data from health facilities which conduct screening (health centers, hospitals) according to a unique pattern, process this data and transmit them in the form reports to the Office for the prevention of malignant disease at least once a month;
- 7) prepare an annual report on the implementation of organized screening and submit it to the Office for the prevention of malignant diseases.

4.2.5. Health center

Health center is the carrier of screening in the territory it is established for.

Health center forms a team to coordinate the implementation of screening, whose member and representative of the institutes of public health it is. Among the team members for coordination of screening implementation persons responsible for screening are appointed.

Health center provides information to screening participants, motivates women invited for screening, receives participants' calls and records the time of arrival to screening.

Health Center performs the following activities:

- 1) every year in collaboration with the institute or the National Institute of Public Health it issues an action plan for the implementation of screening;
- 2) organizes and conducts calling target population;
- 3) keeps call records which should contain (by date and shift) the number of: invited women, managed contacts, the women who refused to participate in screening, examined women, those who were not found at the given address and after repeated calls;
- 4) implements organized screening in separate time and/or place from providing health care to other patients;
- 5) the team for coordination and implementation of screening has a database and submits pattern reports to the competent institute or the public health department.

4.2.6. Mammography unit

Mammography unit is made by mammography apparatus and associated equipment for the analysis of mammography film (negatoscope or mammography workstation).

4.2.7. Medical institutions of secondary and tertiary health care

Medical institutions of secondary and tertiary health care appoint a coordinator and a nurse who are responsible for implementing screening. They keep records on the number of informed and examined women in the screening, the final outcome of the screening, they monitor the implementation of clinical way and report to the department/Institute of Public Health once a month.

Women with positive mammography findings within the screening program are directed to further diagnostic procedures in accordance with the Guide for good clinical practice. The time period from the referral issuance from the health center to the examination in the health institutions of the secondary and tertiary levels should be as short as possible (no longer than two weeks). These medical institutions provide services required to complete the diagnosis and perform necessary treatment (palpation, biopsy, surgical treatment, radiotherapy, chemotherapy, palliative care, etc.). These services are not part of screening, but the part of the routine services of these health institutions, but reporting on them is required for the analysis of the screening results.

4.2.8. Local government

In coordination with the institutes and departments of public health, health centers, representatives of religious and ethnic communities, associations of citizens, the media, representatives of local governments perform actions to educate and motivate women to respond to the call for an organized screening program.

4.2.9. The mass media

In agreement with the participants of organized screening, as well as with the Ministry of Health, the mass media play an important role in the process of education, motivation and increasing response of women, through activities: national and local media campaigns ("leaflets", brochures, posters, billboards, radio jingles TV spots, contributions to the website of the Ministry of Health and the Office for the prevention of malignant diseases, social networks, etc.); press conferences; press releases; interviews; and specially designed programs.

5. METHODOLOGICAL GUIDELINES FOR BREAST CANCER SCREENING

5.1. Screening model in the Republic of Serbia

Breast cancer screening is performed on the territory of the Republic of Serbia as organized decentralised program.

Target population: women 50-69 years of age.

Population coverage: tends to at least 75%.

Screening cycle: two years.

Screening implementation carrier: elected physician, medical doctor gynecology specialist.

Screening test: mammography.

Interpretation of mammography records: two-fold by two independent skilled medical doctors, radiology specialists.

The end of the screening process: the screening process ends after additional procedures (ultrasound breast examination and target mammography).

Further diagnostic procedures and follow-up: health centers, hospitals, clinical centers and institutes.

Quality control and final evaluation of screening process implementation is performed by the Ministry of Health.

Announcing results, determining the dynamic and content of the follow-up, including referrals to further diagnostics are performed by the elected medical doctor gynecology specialist according to radiologist's recommendations, and pursuant to the Guide for good clinical practice in diagnosing and treatment of breast cancer from 2012/2013.

5.2. Information, education, communication and social mobilisation

Prior to the beginning of screening implementation it is necessary to define the strategy of information, education, communication and social mobilisation, operation plan for its realization and its time frame, as well as to determine persons responsible for performing the mentioned activities at all levels.

The strategy for municipalities covered by health center represents a part of annual action plan of the health center activities prepared by the team for screening coordination that submits it for adoption to the institute or public health department.

5.3. Identification of target population

Screening helps identify the target group of women, from 50 to 69 years of age. Screening evidence is based on the list of the insured by The Republic Department for health insurance and other citizens and their right to health protection, regarding the regulations determining the area of personal data protection.

Coordination team for screening implementation in a health center, in cooperation with the institute or public health department, prepares the target population list.

5.4. Invitation plan

The invitation plan is made by the institutes or public health departments in cooperation with health centers.

Health centers, in accordance with their personnel and spatial capabilities and the calling plan, organize inviting and testing of women, providing them the possibility of testing off working hours.

The invitations should include at least half of the target population per year.

Mammography is scheduled during morning and afternoon hours for synchronising personal and working duties of women called for screening.

5.5. Invitation

The invitation letter is delivered by mail.

The invitation letter includes:

- 1) invitation with the phone number of health centers in order to make an appointment for testing;
- 2) information on the purpose and importance of screening (information leaflet).

Inviting can exceptionally be done by telephone. In this case, the woman is given an information leaflet during testing.

Coordination team for the implementation of screening in a health center in agreement with the competent institute or the public health department, periodically (every one to two months) checks women's response to calls for screening, using screening records which is constantly updated.

Repeated invitation is forwarded in a period not exceeding six months from the date of the first invitation.

In case a contact is not established even after six months, health center is required to provide a direct call along with an invitation letter. If after attempting a direct call by the health center, contact is not established, the woman is excluded from screening and is invited in the next cycle.

5.6. Determining the exact testing time

Screening participants confirm participation and testing appointment by phone, SMS, email or in person.

5.7. Testing

On the given date women (hereinafter referred to as screening participant) with a letter of invitation reports to the service for health care of women in a health center. Responsible health worker accepts her, takes the invitation letter, performs recording and sends her to the appropriate clinic specific for screening (or the clinic of the selected physician, doctor of medicine specialist in gynecology, but separately from regular patients).

The selected physician, doctor of medicine specialist in gynecology performs the following actions:

- 1) receives screening participants who made an appointment;
- 2) provides necessary information about screening;
- 3) gives screening participants to sign a statement if she does not want to participate in screening;
- 4) take anamnesis;
- 5) fills out a standard protocol (clinical pathways) in paper or electronic form;
- 6) refers a screening participant to mammography in the mammography unit with instructions to take the record of previous mammogram if she has them;

- 7) informs screening participants about the examination results (if the result is negative, a screening participant takes over a written report at the health center, and the result can be given over the telephone; in the case of a positive finding, screening participant is called within the period of no longer than three weeks) ;
- 8) suggests further diagnostic procedures to screening participants with positive mammographic findings with the recommendations of a specialist radiologist, and in accordance with the Guide for good clinical practice for the diagnosis and treatment of breast cancer;
- 9) reports weekly to the responsible person from the team for coordination in screening implementation at the health center on meeting the dynamics of the action plan.

5.7.1. Mammograms

Implementation of mammograms performed within screening is done by a radiology technician in the mammography unit.

A radiology technician performs the following actions:

- 1) completes the first part of the Protocol for screening for radiologists of health centers;
- 2) takes over previous mammograms;
- 3) performs mammograms;
- 4) forwards the current and previous mammograms to the doctor of medicine, radiology specialist.

5.7.2. The first reading of mammography image

The analysis of mammography image is performed by an educated medical doctor specialized in radiology at the health center, or the nearest hospital.

In health care facilities that have workstations, reading is done from the CD on a workstation. Health facilities that do not have a workstation, develop films and read snapshots with a negatoscope.

Each image is read by two independent radiologists (hereinafter referred to as the first reader). The first reading is done in a health center or a hospital.

The first reader performs the following actions:

- 1) describes a screening mammogram as positive or negative;
- 2) notes Breast Imaging Reporting and Data System (hereinafter referred to as BI-RADS) classification and marks the position of changes, if any;
- 3) meets the standard protocol for mammography;
- 4) forwards the protocol with the images on a CD or films to another radiologist.

5.7.3. The second reading of mammography image

The second reading of mammograms submitted on CDs is done on workstations in a medical institution of secondary or tertiary levels of health care. Second, independent radiologist performs the following activities:

- 1) repeats the reading of the image as the first reader, but irrespective of his findings;
- 2) fulfills a part of the protocol designed for the second reading;
- 3) forwards the protocol with images on CD or films to the third radiologist, if the findings on the first and second reading are not the same. CDs are kept in a medical institution where the second reading is performed.

Consensus and forwarding the findings to the selected physician, medical doctor specialist in gynecology:

Consensus is achieved if the findings from the first and second reading match. If the score with one specialist in radiology is BI-RADS 1, and with another radiologist BI-RADS 2, it is considered matching. Higher BI-RADS is entered in the definitive finding.

In all other differences in assessments by BI-RADS classification of the first and second radiology specialist, the third reading is necessary by a third independent radiology specialist – supervisor in the presence of (preferably) two radiologists who performed the first independent readings. After the consensus of opinion of all three radiologists, a final decision on mammographic findings is made and entered into the assessment protocol of BI-RADS classification from the consensus.

If after the third reading BI-RADS classification is 4a, 4b and 5, in addition to the findings it is necessary to write whether it is necessary to supplement the diagnostic with an ultrasound breast examination as well as targeted mammograms (with magnification, compression, etc.).

A medical doctor specialized in radiology at the health institution of secondary or tertiary health care, who in the course of one year reads at least 2,000 mammograms or is accredited to supervise, may be a supervisor.

Filled protocol for radiologists after the second and possibly third reading shall be submitted to the selected physician doctor of medicine gynecology specialist who referred a screening participant to mammography.

In case the first reading is performed in the general hospital, the form for a clinical path is filled out. In this case, a screening participant, submits a part of clinical path form with a final assessment by BI-RADS classification to the selected physician doctor of medicine specialist in gynecology.

5.7.4. Keeping mammograms

CDs submitted to a medical doctor specialized in radiology at the second reading, remain archived in the institutions where the second reading was performed.

5.7.5. Double reading of mammograms

Filled Protocol (clinical path) for a medical doctor specialized in radiology at health center is sent back to the health center, after a second, possibly third reading, also through the responsible person from the health center and delivered to the selected physician, doctor of medicine specialist in gynecology. Selected physician,

doctor of medicine specialist in gynecology at the health center shall include in his Protocol the results of the first, second and possibly third reading and notify the radiologist at the health center on the final assessment by BI-RADS classification.

A medical doctor specialized in radiology at the health center enters the results into the patient protocol of radiology service, that participate in screening, and the Protocol form for the radiologists at the health center remains in gynecological history of the screening participant. If both medical doctors, specialists in radiology declare that the result is positive (BI-RADS 4a, 4b, 5) it is necessary to read the same mammography the third time at the secondary and tertiary level, by a third medical doctor specialized in radiology and then enter final assessment by BI-RADS classification and possibly propose a additional procedure. In screening, additional procedures involve palpation breast examination, breast ultrasound examination and targeted mammography with compression, magnification or at a different angle.

5.7.6. Additional diagnostic procedures as a part of the screening program

Additional diagnostics is performed at the secondary and tertiary levels of health care. Selected physician medical doctor specialist in gynecology and issue a referral and with the Protocol for radiologists of the health center refers a screening participants to the additional procedure.

Screening coordinator in secondary and tertiary institutions organize additional procedures on the specific day of the week. After the completion of additional procedures, the patient returns to the selected physician specialist in gynecology with a medical report from a doctor specialized in radiology who conducted additional procedures at the secondary and tertiary levels of health care.

Selected physician specialist in gynecology then enters into his protocol the final assessment by BI-RADS classification, recording the screening mammography findings. Screening participants are not issued the mammograms, but are only given the film if they are developed in a health center. Data on the screening mammograms results remain in the gynecological records.

Necessary diagnostic procedures must be taken within six weeks of the health center referral.

Communicating the results to the screening participants, from mammography to the end of the diagnostics, must be carried out within six weeks.

5.7.7. Care of screening participants with positive mammographic findings

A medical doctor specialized in radiology at the health institutions of secondary or tertiary levels of care, fill out a part a form Clinical path for radiologists, where he enters which additional procedure was performed, the date and by which medical doctor specialized in radiology, the final assessment by BI-RADS classification, as well as a proposal for the type of necessary biopsy (stereotaxic vacuum-assisted biopsy, hereinafter SVAB or CORE biopsy) on the specialist's report.

A screening participant is, with final report by a medical doctor specialized in radiology at the health centers of secondary or tertiary level of health care, referred to her selected physician medical doctor specialized in gynecology who is responsible to

inform the medical doctor specialized in radiology at the health center on the final assessment by BI-RADS classification.

If the finding of additional procedures is positive, the selected physician medical doctor specialised in gynecology refers the patient to a surgeon at competent institution (clinically palpable changes with the BI-RADS grade 4a, 4b, 5).

If the breast changes are not palpable, such as microcalcification or the zones of disturbed architectonics, that cannot be visualised with ultrasound, the patients are referred with the suggestion for SVAB to the Institute for oncology of Vojvodina in Sremski Karlovci, Clinical center of Kragujevac and Clinical center of Nis, according to territorial affiliation.

All patients with clinically impalpable breast changes that can be visualized with ultrasound examinations and require CORE biopsy controlled by ultrasound are referred to the health institutions with technical conditions for performing this kind of biopsy and educated personnel.

5.8. Referring patients to further treatment or additional diagnostics not included in the screening program

If a patient underwent biopsy, she with a histopathological finding reports to the selected physician medical doctor specialised in gynecology who, depending on the type of diagnosed change, acts according to the recommendations of the Guide of good clinical practice for diagnostics and treatment of breast cancer.

It is extremely important to realize appropriate communication with the screening participant at all levels. It includes explanations of all types of treatment and outcomes and acquiring an informed consent of the patient for further diagnostic procedure and treatment.

5.9 Collecting data and reporting

Data on the target population, sent invitations, response to screening, results of screening tests, all the necessary diagnostic and therapeutic procedures make a database at the health center. This database is necessary for the monitoring and estimation of screening implementation.

Records of sent invitations, given invitations and response to testing is conducted by the team for coordination of screening implementation at the health center. Mentioned activities are performed by a medical technician pursuant to the recommended standards.

5.9.1. Standard protocol (clinical path)

Reporting on the screening results is based on the minimal data set which must be collected to calculate the process and outcome indicators of the screening program.

The data necessary for the assessment of screening efficiency are created in every stage of screening implementation, thus a standardized and coordinated way of their collection is required. In order to avoid data loss, they should be collected at the time of their appearance. Thus the screening uses the standardized protocol (clinical path) that monitors the screening participant through every screening stage, from the beginning to the end, which refers to invitation, all visits to the physician and other

health workers, as well as to the performance and analysis of screening tests and other procedures included in the screening process at all levels of health care.

Data entry:

The protocol can be printed on paper, but the optimal data entry into the protocol is electronically which requires the following:

- 1) the existence of the protocol for the electronic data entry with accompanying software equipment;
- 2) the existence of computer equipment at every work place where a screening participant is;
- 3) network of all work positions, so that all screening performers have insight into the previous stage of the process;
- 4) connection with the institutes and departments for public health and the Office for the prevention of malignant diseases.

In case such system exists, all the data are entered only once at the work place where they occur, and the networking allows them to be available at all other work places, as well as to the centers for collecting data where through the databases they transform into the required indicators.

5.10. Data and indicators of program implementation

5.10.1. List of screening-collected data

All the collected data are given in the protocol (clinical path).

5.10.2. Indicators of program implementation

Screening indicators can be process and outcome indicators.

Process indicators are:

- 1) percent of women who responded to the invitation and reported to a health center after the first and following calls;
- 2) percent of women that underwent mammography;
- 3) percent of technically incorrect mammography;
- 4) percent of women called for additional diagnostic procedures (ultrasound, targeted mammography);
- 5) percent of women who underwent invasive diagnostic procedures (biopsy);
- 6) percent of malignant breast tumors which were diagnosed prior to surgical intervention;
- 7) percent of women with exempt and radical surgical interventions;
- 8) percent of returned invitations;
- 9) percent of women that did not respond to delivered invitations;
- 10) time interval between a screening test, final diagnosis and the beginning of therapy.

Outcome indicators are:

- 1) percent of positive mammograms BI-RADS 4a, 4b, 5;

- 2) changes in the mortality caused by breast cancer;
- 3) decrease in mortality which is possible to calculate from the ratio between the response and the number of detected invasive cancers, the response and the number of interval cancers by the tumor size, histological grade and the state of axillary glands.
- 4) Percent of patients with diagnosed cancer in situ;
- 5) Percent of patients with cancer and pathohistological type – disease stage at diagnosis.

Process and outcome indicators are the elements of periodical reports on performed activities at all levels, from health centers to the Ministry of Health.

Screening outcome indicators are the elements for planning further activities of the health system in order to decrease the incidence and mortality from breast cancer.

5.11. Quality assurance

Quality and success of the whole screening program in one country depends on the high quality of every step in the organized screening.

Each step of the screening must be explained in detail through instructions so the screening organization on the territory of one country could be as uniform as possible.

Social mobilisation requires adequate professional approach to greater population synced with demographic, social, educational and religious structure of the population. Special attention must be directed to marginalized groups and minorities. Inviting and informing during all screening stages must be conducted by ethnic, legal and moral principles, synced with educational and social status of women according to the instructions.

Uniform conditions of assuring the quality of mammography are necessary.

Uniform data collection through unique protocols and reports are necessary for monitoring and estimation of screening implementation.

Based on monitoring and estimation of screening implementation as collected data, quality control is performed on all screening stages: through response, mammography, reading of mammograms, supervisors and education.

5.12. Monitoring and evaluation of screening

Monitoring and evaluation of screening is planned and conducted by the Office for early detection of malignant diseases through a database of organized screening and periodical reports of the public health institutes and centers. Final evaluation of the screening is done by the Ministry of Health for each calendar year, based on the data and reports of the Office for early detection of malignant diseases.

6. FINANCING

The National program for early detection of breast cancer is financed pursuant to the law.