

# Cancer prevention

## Breast cancer

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## Prevention and Screening of Cancer Diseases

Prevention is an integral part of complex oncology care and fundamentally influences the overall outcomes, as well as the cost-effectiveness of cancer treatment. It is important for every doctor to adopt **oncopreventive thinking**, in terms of primary, secondary, tertiary and even quaternary prevention.

**Primary prevention** aims to reduce the likelihood of an invasive tumour development. It involves continuous education against smoking and other toxic substance abuse and the promotion of healthy diets and healthy lifestyle. More specific primary prevention strategies include systematic detection and treatment of precanceroses such as mucosal dysplasia and polyps, urothelial papillomas, suspicious nevi, chronic lesions and inflammations. Another example of primary prevention is the recent introduction of vaccination against viruses associated with certain types of cancer, e.g., human papillomavirus vaccination to prevent cervical cancer or hepatitis B vaccination to reduce the risk of hepatocellular carcinoma by avoiding chronic viral hepatitis and cirrhosis. However, the capacities of general cancer prevention are rather limited.

**Secondary prevention** attempts to diagnose an invasive tumour at the earliest and localized stage, that is, at the point when it has not clinically metastasized yet. Early tumour detection provides patients with a chance for long-term cure, mainly by means of surgery and without any significant burden of anti-cancer treatment. Secondary oncological prevention primarily employs non-invasive techniques for the investigation of target tissues and organs. The risk of the most common malignancies increases with age, particularly after forty years and regular preventive testing is therefore necessary, especially in this age group. Active identification of hereditary risks of cancer among relatives or warning signs of cancer (such as the presence of blood in stool) is also an important part of secondary prevention strategies. Targeted screening further includes skin examination, lymph node palpation, standard blood and urine tests, faecal occult blood test or colonoscopy, mammographic and complete gynaecological examination in women, prostate-specific antigen (PSA) testing in men, etc. Ultrasound screening of the liver, pancreas and kidneys is commercially available in some institutions, as tumours of these organs are typical for late onset of symptoms usually thus often present at an advanced and incurable stage. The responsibility for secondary prevention lies mainly with general practitioners, gynaecologists, urologists and other ambulatory specialists, or specialized oncopreventive workplaces, such as screening mammography or preventive colonoscopy centres.

**Tertiary prevention** is aimed at early detection of tumour recurrence in cancer survivors. It also comprises screening of treatment-induced toxicities and comprehensive long-term follow-up of the oncology patient, provided mainly by the oncology centre where the patient was treated, or other specialized outpatient departments. A durable treatment response in cancer survivors also increases the chance of developing a second malignancy of another primary tumour that should be identified during the follow-up period. The frequency of second malignancies reaches as much as 15-20% and with the increasing prevalence of cancer diseases in the population, it is becoming a considerable challenge for the healthcare system and oncopreventive services.

**Quaternary prevention** may seem like a paradox, since it addresses cases of advanced and incurable tumours, usually in the fourth clinical stage with metastatic spread. Yet, even in these cases, it is necessary to anticipate the course of the disease and, in particular, potential complications of the

tumour that may invalidate the patient for the rest of his life, regardless of whether it counts in the order of weeks, months or sometimes even years. Quaternary prevention aims to avoid unnecessary suffering by preventing skeletal-related events in high-risk patients, ensuring the derivation of the bowel, gall bladder or urinary tract before malignant obstruction appears, or by providing timely analgesic treatment. An integral part of quaternary prevention is appropriate psychosocial support and other ancillary services to maintain a patient's active lifestyle or, on the contrary, provide palliative sedation at the point when the patient's discomfort turns into unbearable suffering.

While primary and secondary prevention are generally well-known and broadly applied concepts, tertiary prevention is considered only as a part of the oncology routine and quaternary prevention is sometimes confused with passive palliation. However, the ability to prevent problems and complications associated with advanced-stage deadly diseases is the most ethical counterpart to the introduction of euthanasia.

Oncopreventive examination can be offered to a healthy individual irrespective of his genetic or occupational risks in the form of a **preventive oncological examination** or via a **national screening program**. The essentials of a preventive oncological examination are specified by the Decree of the Ministry of Health of the Czech Republic, namely by Decree No. 70 from the year 2012. The examination is provided by GPs and some outpatient specialists. It is also commercially available within some complex oncology centres.

In the Czech Republic, we have the following cancer screening programs (updated on 29<sup>th</sup> October 2024):

- Colorectal cancer screening program
- Breast cancer screening program
- Cervical cancer screening program
- Lung cancer screening program
- Prostate cancer screening program

## Colorectal cancer screening

All asymptomatic men and women aged over 50 years are eligible for colorectal cancer screening in the Czech Republic. Those individuals who meet the criteria of high-risk groups for colorectal cancer are not eligible for the screening program. Special surveillance regimes exist for patients with positive personal or family history of colorectal cancer, adenomatous polyps, familial adenomatous polyposis (FAP), hereditary nonpolyposis colorectal cancer (HNPCC), or inflammatory bowel disease (IBD).

Two screening options are available:

1. repeated **FOBT** (= faecal occult blood test)
2. **screening colonoscopy**

These examinations can be indicated by a GP or a gynaecologist.

### FOBT

In case of a **negative** test result (FOBT-):

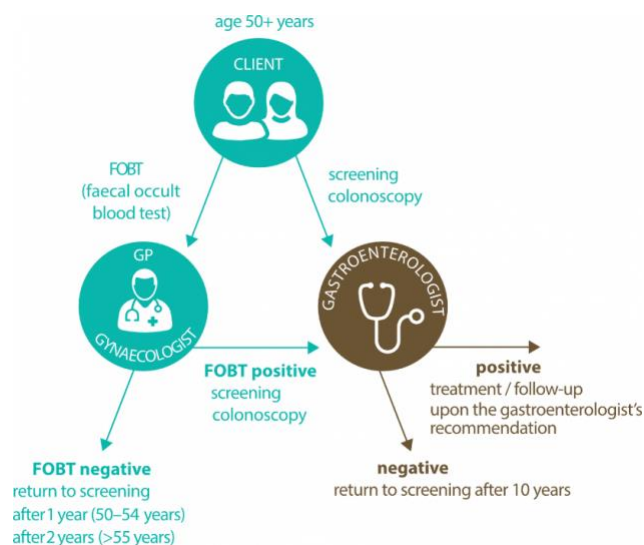
- FOBT is repeated each year in persons aged 50–54 years
- FOBT is repeated every two years in persons aged over 55 years

In case of a **positive** test result (FOBT+), screening colonoscopy is indicated.

### Screening colonoscopy

Screening colonoscopy is an alternative screening option for those individuals who decided not to undergo FOBT. This examination is reimbursed from the public health insurance for individuals aged over 50.

- In case of a **negative** result of screening colonoscopy, another colonoscopic examination is indicated after a 10-year-interval.
- In case of a **positive** result of screening colonoscopy, further diagnostic and therapeutic procedures follow the recommendations for patients at a high risk of colorectal cancer.



## Breast cancer screening

**Breast cancer screening** consists in regular mammography examinations of asymptomatic women aged over 45 in order to detect a possible malignant tumour of breast at a very early stage. A **mammogram** is an X-ray picture of the breast. In case of negative result the examination should be repeated in 2 years.

Thanks to the screening, approximately 3200 out of more than 7000 breast cancers per year are diagnosed in asymptomatic stages, such as Tis and T1 (representing 80 % of all cases). In a non-screened population, T1 and Tis stages constitute only one-third of newly diagnosed cases. This corresponds to worse prognosis and quality of life in non-screened patients, as well as higher health care costs.

## Cervical cancer screening

**Cervical cancer screening** is performed during regular gynaecological examinations. The aim is to reveal any precancerous changes in the cervix or early stages of cervical cancer.

Regular gynaecological examinations are widely accessible to all women from the age of 15, protecting them from specific types of cancer. Gynaecological examinations as part of prevention are covered by public health insurance once a year. The check-up includes an examination of the external genitalia and an examination in gynaecological mirrors, where a colposcopic exam of the cervix is first carried out, followed by a cervical smear. For women aged 35, 45 and 55, the presence of HPV is also tested in the cervical smear. Palpation of the uterus and ovaries is performed in all women. If necessary, a rectal examination is also performed. A vaginal ultrasound examination is also an option.

Cervical cancer screening is done using the **cervical smear test** which is taken by your gynaecologist during the preventive examination. This is a simple procedure that only takes about ten minutes and involves little more than a vaginal examination. During the examination, a sample of cells will be taken from your cervix using a small spatula or brush. These cells will be sent to an accredited cytology laboratory, where they will be examined under a microscope to search for any abnormal cervical cells. The results are then sent back to your gynaecologist.

In case of a normal result, the risk for cervical cancer is low and the woman should continue regular screening (once a year).

In case of a pathological result, depending on the result, it is advised to have one of the following: (a) another cervical smear in three to six months, (b) a colposcopy, which is a procedure that allows the doctor to examine your cervix more closely.

## Lung cancer screening

All current smokers or ex-smokers at the age from 55 to 74 who have smoked 20 and more pack-years are eligible for lung cancer screening programme. How are the pack-years counted? One pack-year means that a person smoked one pack of cigarettes a day for one year (or 2 packs for half a year, or half a pack for 2 years, etc.). To participate in this programme, 1 pack of cigarettes a day for 20 years.

The client has to speak first to his/her GP who indicates the examination by a pulmonary specialist. He or she will ask questions, take a medical history and carry out a standard lung examination. If the client smokes, he or she will offer help to stop smoking.

The pulmonary specialist indicates a **low dose CT scan, called LDCT (low dose computed tomography)**, which uses low doses of radiation. The radiologist will evaluate and describe the result and pass it on to your outpatient lung doctor or GP.

In case the result is:

- negative: they will discuss the result with the client and schedule the next CT scan on the recommended screening schedule, i.e. in 1 or 2 years
- indeterminate: they will most likely recommend a repeat LDCT, i.e. a scan usually between 6-8 weeks and 1 year
- positive: they will arrange further investigations and arrange a consultation at a cancer centre or pneumo-oncology centre
- other finding (other lung disease): they will arrange further investigations and take care of the patient

## Prostate cancer screening

The GP or an outpatient urologist who is already monitoring the patient for another medical condition may be able to refer him to the programme.

Men aged 50-69 years are eligible for the screening that consist of **the PSA test**.

Depending on the results, your doctor will plan your next follow-up procedure:

- If the PSA value is within 1.0 µg/l, the next test will be in 4 years
- If the PSA value is between 1.0–2.99 µg/l, a follow-up test will be performed in 2 years
- If your PSA is 3.0 µg/L or higher, the patient will be referred to the care of a certified urologist who will perform additional examinations and tests and who will decide on further follow-up

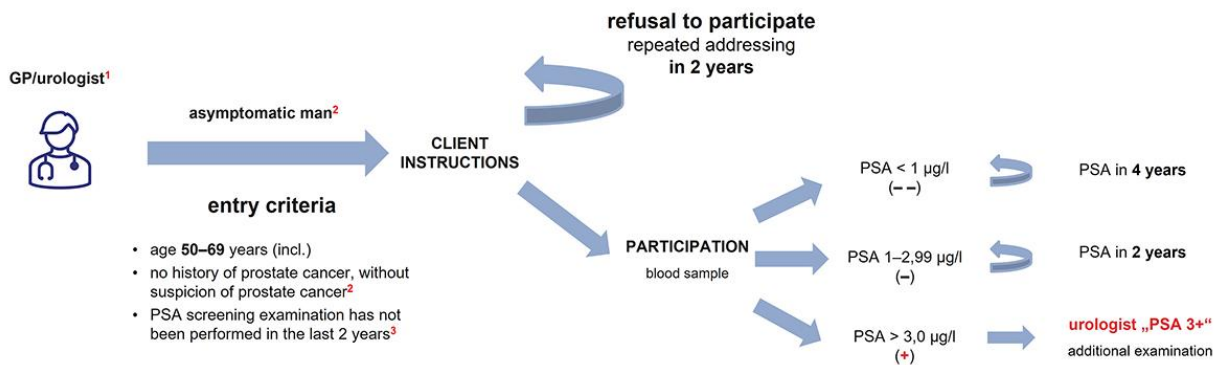
PSA (prostate-specific antigen), is a protein that enables sperm movement and is produced by the epithelial cells of the prostate gland. In the case of a violation of the internal structure of the prostate gland, part of the PSA gets into the blood and the increase in the level can then be detected by a test.

PSA levels in the blood may be increased in men with prostate cancer, benign prostate enlargement, but also after a prostate infection or after certain activities that may bias the results of the test (and should therefore be avoided before the PSA test).

Benefits of the PSA test:

- The test can detect prostate cancer before it manifests itself as health symptoms.
- Early treatment of prostate cancer can prevent further spread of the tumour and increase your chances of recovery and prolonged life.

An increase in PSA levels does not necessarily mean cancer. The suspicion must first be confirmed or disproved by subsequent examinations. MRI and prostate biopsy (taking a sample from the prostate with a biopsy needle) are the key to confirming the diagnosis. Only examination of these samples by a pathologist gives certainty that a cancerous tumour is present in the prostate.



<sup>1</sup> if under the dispensary care of a urologist, then the programme is offered only by the urologist

<sup>2</sup> in case of symptoms, man is referred to urologist for further diagnosis

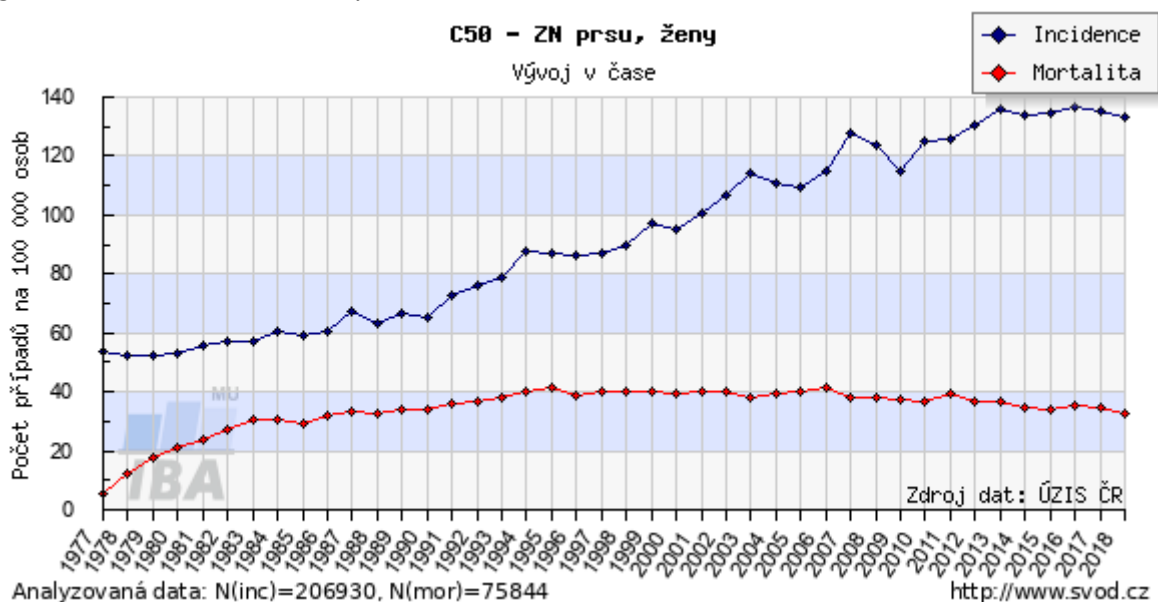
<sup>3</sup> proceed according to Methodological Recommendation 1B (Metodická doporučení – Upřesnění Metodiky realizace populačního pilotního programu časného záchytu karcinomu prostaty v ČR)

## Breast cancer

### Epidemiology

Breast cancer is the most common malignancy in women worldwide. The incidence rates have been increasing, especially in developed countries of Western Europe and the USA. The incidence increases with age, the highest rates are reported in the age group from 50 to 75 years. Despite increasing incidence, mortality rates in the Czech Republic remain stable or have even slightly decreased in the past few years – see *Fig. 1*. This resulted in higher breast cancer prevalence, i.e., the number of women living with the diagnosis of breast cancer, which is the highest of all solid tumours. This favourable trend is mainly a result of early diagnosis and the availability of wider and more effective treatment armamentariums.

Figure 1: Incidence and mortality rates in breast cancer



### Etiology

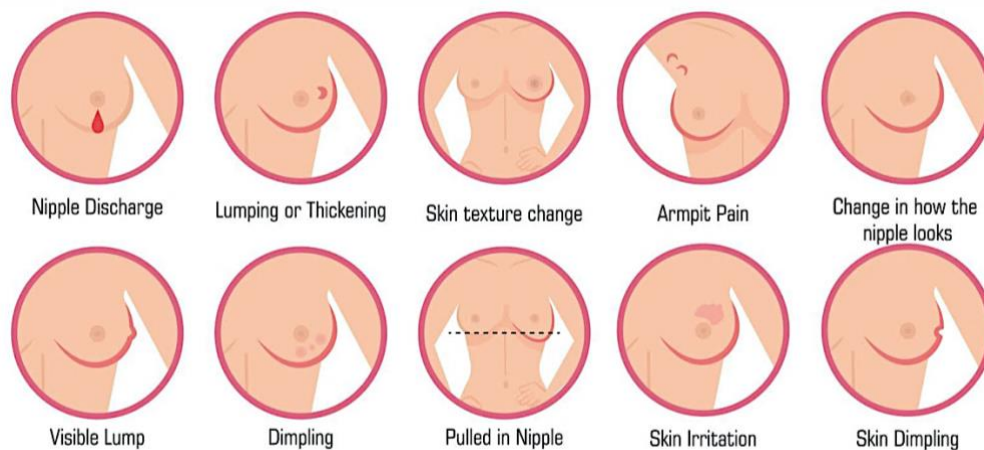
The etiopathogenesis of breast cancer (BC) is not entirely understood. Several risk factors for the development of breast cancer have been identified. Approximately **5-10 % of BCs** are associated with **genetic** predispositions, among which **BRCA1** and **BRCA2** mutations are the most frequent factors that confer a higher risk of BC. Women with these mutations have an 84% chance of developing a BC in their lifetime. The risk of breast cancer is also higher in patients with a positive family history, especially in women with first-degree relatives with breast cancer, irrespective of BRCAness. Other risk factors include history of irradiation (e.g., in patients who underwent treatment of Hodgkin's lymphoma), early menarche and late onset of menopause (after the age of 50), premalignant changes in the breast, hormone replacement therapy (mainly estrogen + gestagen combined preparations), higher alcohol intake, obesity and lack of physical activity.



## Clinical presentation

Symptoms (*Fig. 2*) indicative of BC are changes in breast size and shape, nipple or skin retraction, cutaneous oedema (peau d'orange appearance – *Fig. 3*), erythema, nipple asymmetry, ulceration or eczema (*Paget's disease*), discharge from nipples (especially when haemorrhagic), breast pain, palpable lump in the breast, axillary or supraclavicular lymphadenopathy. Secondary upper extremity lymphedema may sometimes develop in an advanced BC with nodal involvement.

*Fig. 2: Symptoms indicative of BC.*



*Fig. 3: Locally advanced breast cancer with nipple retraction and incipient inflammatory skin reaction*

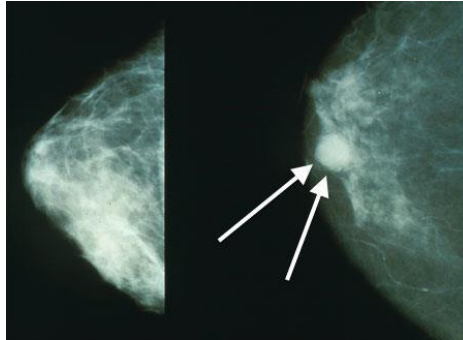


## Diagnostic evaluation and screening

**Imaging methods:** Mammography (MG) is an irreplaceable imaging method in breast cancer screening and diagnostics – see *Fig. 4*. Mammographic screening is indicated in women aged 45 years and older every 2 years. Dense breast tissue makes mammography less feasible and adjunctive ultrasound examination could be used in case of indeterminate findings. Breast ultrasound is also indicated in young, pregnant and *breastfeeding* women. MRI is part of a routine examination in high-risk women. Liver ultrasound and chest X-ray are used to evaluate distant metastases in patients at low risk of

metastases. Otherwise, a targeted CT scan or whole-body PET/CT scan is indicated, if clinical signs of metastatic disease are present.

*Fig. 4: Mammographic image of a breast tumour*



**Histopathology:** Any suspicious lesion should be confirmed by histology. Tissue sampling is usually provided by a core-cut needle biopsy. For further treatment decision-making, the histopathologic report should convey information about the type of breast cancer, grade, estrogen (ER) and progesterone receptor (PR) expression, proliferation and HER2 status.

**Tumour markers:** Markers, such as carcinoembryonic antigen (CEA) and CA 15-3 have no place in the primary diagnosis of breast carcinoma; however, they might be used to monitor the dynamics of metastatic disease.

### Prevention

The possibilities of primary prevention of breast cancer are rather limited. Preventable lifestyle factors include sufficient physical activity and healthy dietary habits. The use of long-term hormone replacement therapy (for more than 5 years) should be avoided, especially in high-risk patients. Women with genetic burden may be offered prophylactic bilateral mastectomy with subsequent reconstruction. Regular breast self-examination as well as annual breast palpation exam by a treating gynaecologist or GP plays a crucial role in the early diagnosis of BC.

## The 6 steps to performing a breast self-examination



<p><b>1</b> Take a good look at your breasts in the mirror and start by looking for changes in the shape, size or position of your nipples.</p>		<p><b>Do you have any of these symptoms?</b></p> <ul style="list-style-type: none"> <li>☑ Breast or nipple pain</li> <li>☑ Nipple discharge</li> <li>☑ Nipple retraction or inversion</li> <li>☑ Change in size/shape of the breast or asymmetry of the position of the nipples</li> </ul>
<p><b>2</b> After you have checked your nipples, raise your arms in the air; you are going to look for any distortion of your breasts such as dimpling of the skin.</p>		<p><b>Do you have any of these symptoms?</b></p> <ul style="list-style-type: none"> <li>☑ Visible lumps</li> <li>☑ Skin dimpling</li> <li>☑ Redness</li> <li>☑ Swelling</li> </ul>
<p><b>3</b> It is best to lie flat when examining your breasts, either on your bed, or sofa or even in the bath. This allows your breast tissue to spread out and makes examination much easier.</p>		<p><b>Do you have any of these symptoms?</b></p> <ul style="list-style-type: none"> <li>☑ Palpable breast lump - if present is it hard or soft, smooth or irregular?</li> </ul>
<p><b>4</b> Then using firm pressure with flat fingers on your right hand press your breast tissue against the underlying chest wall and use your flat fingers press around each quarter of your left breast. Once you have done this then use your fingertips to press around your nipple. If you feel any lump or thickened area, then use both of your hands to try and identify if there is a lump present.</p>		<p><b>Do you have any of these symptoms?</b></p> <ul style="list-style-type: none"> <li>☑ Bleeding from the nipple</li> <li>☑ Breast asymmetry in terms of the feel of the breast and how lumpy it is</li> </ul>
<p><b>5</b> Repeat step 4 but on your right breast and using your left hand.</p>		<p><b>Do you have any of these symptoms?</b></p> <ul style="list-style-type: none"> <li>☑ Lumps</li> </ul>
<p><b>6</b> Finally, examine your left underarm area with your right hand, starting as high as possible in your armpit and running your fingers downwards looking for any lumps. Repeat this process on your right underarm using your left hand.</p>		<p><b>Do you have any of these symptoms?</b></p> <ul style="list-style-type: none"> <li>☑ Palpable lump in the armpit</li> <li>☑ Swelling of the arm</li> <li>☑ A tender swelling under the arm</li> <li>☑ Lymph node changes</li> </ul>

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### Therapy

Treatment of breast cancer is usually multimodal and includes locoregional methods, such as surgery and radiotherapy, as well as systemic treatment options like chemotherapy, hormone therapy and targeted agents. The treatment approach should be decided within a multidisciplinary tumour board, based on the tumour TNM stage, its phenotype, the patient's age, comorbidities and other predictive and prognostic factors.

### Hormonal treatment

The main predictive factor for hormone treatment is the level of ER and PR expression, which is positive in approximately 75 % of BC. Hormones binding to these receptors control the growth and activity of breast cancer cells, thus, by blocking the receptors or by decreasing hormone levels, we can influence tumour proliferation.

### Chemotherapy

Chemotherapy is indicated in hormone-negative, high-grade tumours with higher proliferation rates.

### Targeted treatment

Approximately **15 %** of breast cancers carry **HER2 gene amplification**. These tumours are more aggressive and have a worse prognosis. Currently, there are several drugs available in clinical practice that affect HER2 receptor signal transduction. A ground-breaking drug used in the treatment of BC was a monoclonal antibody against the HER2 receptor known as **trastuzumab**, which has dramatically improved the prognosis of HER2-positive BC. Other monoclonal antibodies include pertuzumab,

lapatinib, and lately also T-DM1 (a combination of trastuzumab and emtansine - a strong cytostatic drug bound to the monoclonal antibody).

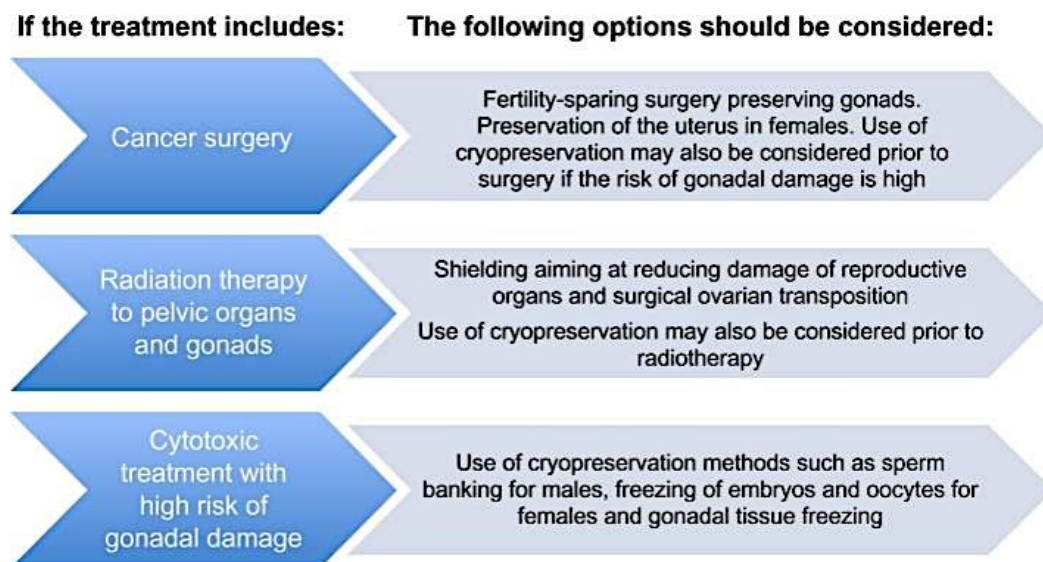
### **Surgery**

The aim of curative surgical treatment is a complete resection of the tumour and regional lymph nodes and it is therefore indicated in patients without any distant metastases. To date, breast-conserving procedures such as quadrantectomy (a partial or segmental mastectomy) or lumpectomy (removal of the tumour and normal tissue margin) are preferred. During the surgery, sentinel node biopsy (SNB) or lymph node sampling may be performed to rule out metastatic nodal spread. In case of positive results, surgery will proceed with axillary dissection. After radical mastectomy, reconstructive breast surgery may be indicated, either using the patient's own tissue (autologous) or by inserting an implant (alloplastic).

The principles of treatment by cancer stage are beyond the knowledge needed to take part in the TBL practice.

Triple-negative breast cancer (TNBC) accounts for about 10-15% of all breast cancers. The term triple-negative breast cancer refers to the fact that the cancer cells don't have estrogen or progesterone receptors (ER or PR) and also don't make any or too much of the protein called HER2. (The cells test "negative" on all 3 tests.) These cancers tend to be more common in women younger than age 40 or who have a BRCA1 mutation. Treatment options in triple-negative breast cancer are currently very limited and they are based mainly on chemotherapy (anthracycline, taxane, capecitabine, eribulin, vinorelbine or gemcitabine monotherapy or in combination).

Local and systemic treatment modalities for cancer may affect fertility. In the figure below you can see the fertility preservation approaches in oncologic surgery and in patients facing fertility threats due to radiation therapy and chemotherapy.



## Hereditary Cancer Diseases

### Epidemiology

Cancer is a multifactorial disease in the vast majority of cases. Both internal and external environmental factors, as well as genetic variability, play a part in tumorigenesis. Generally, age is considered the major risk factor. With ageing, the frequency of new somatic mutations increases, whereas the DNA repair capacity decreases. This leads to the accumulation of acquired DNA errors that may facilitate tumour growth. Life-long exposure to various mutational agents also contributes to a high cumulative risk of cancer.

Most cancers are caused by the accumulation of random somatic mutations in driver genes, such as tumour suppressor or DNA repair genes. The contribution of genetic factors might be variable. Familial cancer is often multifactorial and the role of genetic predisposition is inferior, whereas in hereditary forms, well-defined mutations have a significant impact. Familial occurrence of some cancers is attributable mainly to shared lifestyle risk factors and the inheritance of low-risk genetic mutations. In these cases, we speak of polygenic factors involved in cancer development.

About **5-10%** of all cancers are a part of a **hereditary cancer syndrome**. Most of these conditions are caused by a pathogenic mutation in a single gene (monogenic hereditary disease), particularly in a tumour suppressor gene, DNA repair gene, or less frequently, in an oncogene. Such mutations are present in all cells of the affected individual and in the case of autosomal-dominant inheritance pattern. They are transmitted with 50% probability, regardless of gender. On the other hand, penetrance, i.e., the clinical manifestation of a mutation, usually varies depending on gender and other genetic or non-genetic factors. Less often, syndromes can be inherited in an autosomal recessive fashion. They occur primarily in siblings and are usually absent in preceding generations.

The most common syndromes include hereditary forms of breast, ovarian, colorectal and uterine cancer. Each type of cancer can be either sporadic or inherited. To date, more than 200 hereditary cancer syndromes have been reported, however, there is still a number of tumours, in which high-risk genes are yet to be identified.

### Diagnostics

Genetic testing is relevant only in the case of high-risk genes, while screening of low and moderate-risk genes, is of limited clinical significance. Patients with an increased personal and familial risk of cancer should be referred to a genetic specialist for further assessment. Based on thorough risk evaluation, the geneticist determines susceptible genetic changes and decides on family members who are to be tested. He interprets the results and suggests further investigations or preventative measures. Patient's informed consent is always required prior to genetic testing. Genomic DNA testing is performed by accredited molecular genetic laboratories. Specific mutations are identified by Sanger sequencing or next-generation sequencing (NGS) and every positive result has to be confirmed by another independent genomic DNA testing.

### Hereditary syndrome of breast and ovarian cancer (HBOC)

This syndrome is an autosomal dominant disorder caused by germline mutations of **BRCA1** (locus 17q21-q24, 24 exons) and **BRCA2** (locus 13q12-q13, 27 exons) genes. It is estimated that approximately one in 300-800 people carry either mutation.

BRCA (breast cancer susceptibility genes) are tumour suppressor genes involved in the regulation of cell cycle and apoptosis, **homologous recombination** (HR) and associated DNA reparative mechanisms. The BRCA2 gene is essential for transporting the RAD51 protein into the cellular nucleus. It is a part of the Fanconi anaemia pathway, which is involved in the reparation of DNA interstrand cross-links.

There are also other gene mutations associated with breast cancer susceptibility (CHEK2, ATM, PALB2, NBN, BRIP1). A higher risk of breast cancer is associated with Li-Fraumeni syndrome, neurofibromatosis type 1, Peutz-Jeghers syndrome, and diffuse gastric cancer syndrome.

Several factors play a role in determining one's cancer risk including age, type of cancer, and whether the mutation affects BRCA1 or BRCA2. On average, however, the risk that someone with HBOC will develop several types of cancer by age 70 is as follows:

- Breast cancer – The lifetime risk of breast cancer among women in the U.S. is around 12%. The risk rises to 55-70% for women with BRCA1 mutations and 45-70% for BRCA2.
- Ovarian cancer – The lifetime risk of ovarian cancer is approximately 1%. For carriers of BRCA1, however, the risk is around 40% and for carriers BRCA2, approximately 15%.
- Prostate cancer – Male carriers of BRCA1 have around a 15-20% risk of prostate cancer, while the risk for those with BRCA2 is about 30-40%. By contrast, in the general population the risk ranges from around 14–19%.
- Breast cancer in men – On average, men in the U.S. have about a 0.1% risk of breast cancer. Men with BRCA1 and BRCA2 mutations, however, have a 1% and 8% risk, respectively.
- Pancreatic cancer – The average lifetime risk for pancreatic cancer in the U.S. is 1.5%. For BRCA1 carriers the risk rises to 2-4%, while those with a BRCA2 mutation have a 5% risk.

HBOC also increases the risk of melanoma (skin cancer) and, in women, cancer of the fallopian tubes, though the extent to which the risk is increased for these cancers is not yet well defined.

### **Basic criteria for BRCA genetic testing**

In patients with sporadic occurrence of cancer:

- bilateral breast cancer, first before the age of 50 years, or both before 60 years of age
- unilateral breast cancer before 45 years (or before 50 years if family history is not known)
- all patients with epithelial ovarian carcinomas, fallopian tube carcinomas and peritoneal carcinomas irrespective of age
- breast and ovarian cancer duplicity at any age
- breast tumour in a male
- ovarian cancer, medullar carcinoma or triple-negative breast cancer at any age
- breast and pancreatic cancer duplicity at any age

3 relatives (including the proband = an individual affected with a disorder who is the first subject in a study) with breast cancer at any age

2 relatives (including proband) with breast cancer – at least one diagnosed under the age of 50, or both under the age of 60



Proband with breast cancer and direct relative with:

- ovarian cancer
- medullar carcinoma or triple-negative breast cancer
- breast cancer (male)
- pancreatic cancer
- high-grade or primarily metastatic prostate cancer

Proband with lobular breast cancer and with personal or family history of diffuse gastric cancer.

In case the proband is not alive, the testing is possible by first-degree relative, from father's side second-degree relatives.

## Central venous catheters (CVCs)

Intravenous infusion is the principal modality of administration of anti-cancer drugs for most types of malignant disorders. Chemotherapy administration carries safety concerns for both patients and the medical team. These concerns include extravasation of chemotherapy, which is defined as the accidental infiltration of chemotherapy into the subcutaneous or sub-dermal tissue at the injection site, and can result in tissue necrosis.

Intravenously administered drugs can be classified into five categories according to their damage potential: Vesicant, Exfoliants, Irritants, Inflammittants, and Neutrals. The drug damage from extravasation can range from skin erythema to soft tissue necrosis.

Consideration of the appropriate vascular access is crucial for the prevention of chemotherapy extravasation. Chemotherapy infusion can be either through a central venous access or through an adequate peripheral vein. Patients who do not have adequate peripheral venous access should have a central venous catheter placed.

Long-term central venous access devices are essential in the management of oncology patients, as they minimise the discomfort of frequent venipuncture and cannulation. There are four main classifications of CVCs:

- Non-tunnelled catheters, which are indicated for short-term use when peripheral venous access is unachievable.
- Tunnelled central catheters, used when long-term access (> 30 days) is required for the administration of chemotherapy, antibiotics, parenteral feeding and blood products.
- Fully implantable or surgically implantable catheters (ports or port-a-caths), also provided for long-term use and associated with a low risk of infection. The device, which consists of a chamber (completely metallic, plastic or both) connected to a catheter, is placed under the skin. The catheter is threaded into the subclavian, jugular or femoral vein. The subcutaneous reservoir is placed in a pocket created in front of the pectoralis major muscle, in the sub-clavicular region. The reservoir is accessed via a specific needle through intact skin.
- PICCs (peripherally inserted central catheters) are placed via a peripheral vein (i.e., basilica vein, brachial vein or less frequently cephalic vein) of the arm into the superior vena cava (SVC). Their main limitation is shorter longevity, due to a higher risk of thrombosis.

To maintain the patency of subcutaneous ports that are not in active use, a four-weekly flush is recommended. For tunnelled cuffed catheters and PICC lines, a weekly flush is also recommended. Flushing with 0.9% normal saline is recommended. Extensive, routine prophylaxis with anticoagulants to prevent CRT (catheter-related thrombosis) is not recommended. The use of thrombolytic agents (e.g., urokinase) shows inconclusive results in different trials, and there is insufficient data for it to be recommended.



## Resources

- KISS, Igor, Radim NĚMEČEK, Michael DOUBEK a Rostislav VYZULA. Klinická onkologie pro mediky. Solidní nádory, nádory dětského věku a hematologické malignity. 3., přepr. a dopl. elektron. Brno: Masarykova univerzita, 2021. ISBN 978-80-210-9908-1.
  - Chapter Prevention and screening of cancer diseases – p. 10 – 12 written by Jiří Žaloudík
  - Chapter Breast cancer – p. 296 – 302 written by Katarína Petránková and Miloš Holánek
  - Chapter Hereditary cancer diseases – p. 361 – 367 written by Lenka Foretová
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More information about cancer screening programs in the Czech Republic:

<https://nsc.uzis.cz/cs/populacni-screeningove-programy/>