FRECCIAROSA

LA PREVENZIONE VIAGGIA IN TRENO

HEALTH GUIDE

FONDAZIONE Incontra donna

OCCUPIAMOCI DI SALUTE

FERROVIE DELLO STATO ITALIANE

Ministero della Salute

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Online Guide

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October 2024 Edition

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3. IN-DEPTH ANALYSIS

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SICP Società Italiana di Cure Palliative Patrocinio SICP n. 35 del 18/07/2024

SICPCV Società Italiana di Colposcopia e Patologia Cervico Vaginale

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GISCi GISMa GISCoR

Dear travellers,

I am pleased to contribute to the 14th edition of the Frecciarosa campaign, a project promoted by the IncontraDonna Foundation in collaboration with FS Group, and with the sponsorship of the Ministry of Health and the Presidency of the Council of Ministers.

Each year, this initiative makes its way across Italy, and thanks to the doctors and volunteers involved, it reaches thousands of people offering free consultations and exams, reinforcing the culture of cancer prevention journey after journey, particularly breast cancer.

As the Health Handbook that you're reading reminds us, there are many things that each of us can do to stay healthy and prevent the onset and progression of disease.

It is essential to promote primary prevention, starting with proper nutrition and physical activity, as well as to bolster screening campaigns for earlier and timelier diagnoses.

These are activities to which we are highly committed, even through the National Oncology Plan and the National Prevention Plan, which includes specific regional actions.

By establishing synergies with all stakeholders in the health system and making greater use of associations and non-profit organisations, we aim to raise awareness of the importance of prevention as a main pillar of healthy living.

This commitment goes hand-in-hand with a global vision of health and a "One Health" approach, which is more crucial than ever to the well-being of the future generations.

Enjoy your journey, and happy reading.

Orazio Schillaci

The Minister of Health

ITS TIME TO LAUNCH FRECCIAROSA 2024!

The 14th edition of the Frecciarosa project has begun. The month of October is dedicated to the prevention of breast cancer and other major cancers, and raising awareness of healthy lifestyles and environmental protection.

And we mustn't lose sight of the **Global Health** (One Health) perspective. Our future and that of the next generations depend on it. The IncontraDonna Foundation is highly committed to promoting health, prevention, and care at the national level, and will offer **free consultations** to men and women who travel on FS Group trains all throughout the month of October. People who fall into certain age groups can also undergo **breast exams and ultrasounds**, based on the assessment of the on-board physician.

The Frecciarosa project covers all of Italy, including its major islands, disseminating important health messages, and reinforcing the value of our **National Health System**, to which we make constant reference. The Health Guide is one of the communication tools that we use to help people take better care of themselves. It's available free of charge during the month of October on trains and in various Freccia Lounges, and can even be downloaded for free from the website **www.frecciarosa.it**. We therefore invite you to share it among friends, family members, and acquaintances, and to leave copies at the workplace. Don't miss the opportunity to dedicate a few minutes of your time to your health and to learn about all the latest innovations brought about by scientific research. I would like to thank all the tireless IncontraDonna Volunteers, who will be travelling on the trains alongside you, the doctors who, with professionalism and empathy, will be offering free consultations this month, the experts who contributed to the creation of the Health Handbook, and the staff of the IncontraDonna Foundation.

A special thanks goes out to FS Group for participating in the project for 14 years, and to the Ministry of Health, which has been an active partner in the project.

Adriana Bonifacino

President of the IncontraDonna Foundation

1.

BEHAVIOURAL FACTORS AND HEALTH

One Health
A vision for making informed choices for a healthy lifestyle

GIOVANNI LEONARDI AND DENISE GIACOMINI

Coined in 2004 at the Manhattan Conference, up until 2020 the One Health concept was exclusively considered for the connection between human and animal health, for issues related to food safety, zoonotic disease, and antibiotic resistance. With the outbreak of COVID 19, we began to expand the horizons of the One Health approach to include the pollution of natural resources, the destruction of biodiversity, and urban, production, and transport design, in order to safeguard the integrity of the planet, ultimately defining the concept of health in all policies.

Today, in order to fully grasp the One Health concept, it is necessary to understand the concept of **circular health**, and to recognise the clear correlation between human health and the health of the planet, and the relationships between climate, environment, animal health, and food safety, with the awareness that a *threat to just a single component of the system can have significant impacts on the others*.

In terms of both prevention and the health systems' organisation, every public health strategy must be based on a One Health vision. With regard to these issues, at the level of health planning, the One Health outlook encompasses the measures of the **2020-2025 National Prevention Plan** and (in keeping with the UN 2030 AGENDA for sustainable development) guides the National Plan's new projects for additional NRP investments.

An innovative One Health vision allows us to take action on disease prevention and health promotion through public health policies: in fact, we know how important the **exposome** is, or rather exposure to external factors that affect the risk of various non-communicable systemic diseases (*allergies, cancers, neurodegenerative diseases, diabetes, etc.*).

Living according to **"a One Health approach"** means being informed and engaging in healthy conduct, through specific food choices (*think, for example, of the fight against domestic waste*), adopting healthy lifestyles, and respecting the environment, with the responsible use of antibiotics and the sustainable use of water, which can help **reduce pollution**.

With the One Health vision, institutions (Ministries and Local Health Authorities) work in an interdisciplinary manner to promote food hygiene, and to monitor endocrine disruptors, chemical contaminants, and the use of plant protection products so that the health of ecosystems, animals, and human beings is protected. In fact, the One Health vision is an outlook that completes the circle of **the unified health concept, in which environmental conditions and human well-being are closely interconnected**.

The time has come to be more responsible: we need to think about the health of our Planet as a whole, and the One Health vision will allow us to tackle global challenges with a holistic and systemic approach. In fact, life prospects are not only influenced by genetic factors, but also by environmental factors (respecting biodiversity and sustainability), social factors (integration, sharing, solidarity, and activism), and healthy lifestyle choices (moderate and "local" eating habits, based on traditions and outdoor life).

We need to inform all our citizens on these issues, and give them **"transformative opportunities"** to improve health conditions at all ages with greener and more liveable cities, and Mediterranean diets and lifestyles, according to a strategic One Health vision.

Nutrition
An apple a day isn't enough

SALVATORE ARTALE, ROBERTO COPPARONI, AND GIUSEPPE PLUTINO

There is no single food that can protect us from every metabolic disease, such as cardiovascular disease, diabetes, or cancer.

We are constantly being bombarded with contradictory information from the media, social media and, unfortunately, even from experts or pseudo-experts who boast miracle diets with no underlying scientific rationale. The purpose of this short chapter is **to suggest eating habits and lifestyles based on scientific evidence**. In particular, we will refer to the recommendations of the *World Cancer Research Fund* (WCRF), which has set out ten golden rules of healthy eating, based on scientific evidence from dose-response studies: taking into account three different levels of exposure to cancer risk, the organisation has established three levels of evidence showing that a food can contribute to preventing or causing a certain type of cancer. The strongest level of evidence is convincing, followed by probable and limited.

Based on this evidence, Italy's Ministry of Health has drawn up clear and specific indications for good dietary habits.

Which dietary model should we use as a reference?

The dietary model recommended by the Ministry of Health refers to the Mediterranean Diet. The salient features of the Mediterranean diet include constant presence of cereals and processed cereal products (bread, pasta, etc.), an abundance of fruits and vegeta-

bles, the use of extra virgin olive oil, and the consumption of meat and seafood, as well as proteins of plant origin, from legumes. The consumption of the foods in various combinations, which are nevertheless always nutritionally complete (cereals and legumes, cereals and foods of animal origin, meat or seafood with vegetables), is also extremely important.

Thanks to its healthy fat profile, low carbohydrate percentage, low glycaemic index, and high levels of dietary fibre, antioxidant compounds, and anti-inflammatory effects, the Mediterranean diet reduces the risk of certain diseases, such as cardiovascular disease and cancer.

The most solidly demonstrated factors are overweight and obesity (especially abdominal obesity): in fact, people with a BMI above 25 or a waistline above 80 cm (for women) and 94 cm (for men) have an increased risk of breast (post-menopausal), uterus, kidney, oesophagus, intestine, pancreas, and gallbladder cancer. The cancers most affected by the quantity and quality of foods are obviously those of the gastrointestinal tract, especially those of the **oesophagus**, **stomach**, and **colon/rectum**: it is estimated that up to three quarters of these cancers could be prevented with better dietary habits. In order to prevent the onset of neoplastic diseases, it is important to reduce the daily intake of all high-calorie foods, or rather foods high in fat and sugar, which can lead to obesity.

Consumption of fruit and vegetables is also important. Here's a brief guide.

THE GUIDE TO EATING FRUITS AND VEGETABLES

1. **Five portions:** eat "at least" 5 portions of fruit and vegetables every day, including ready-to-eat ones with no added salt and/or sugar; vary your choice of colours, and opt for seasonal ones.
2. **Never go without!** Always keep fruit and vegetables on hand so that you always have some within view in the fridge or freezer.
3. **Who says vegetables should only be "side dishes"?** Try eating fennel, carrots, celery, cherry tomatoes, and lots of other vegetables as snacks: it's good for you, and will stave off hunger!
4. **Studying or working?** Have some fresh fruit for a real energy boost!
5. **What are you eating today?** A nice first course with plenty of vegetables: this will give you a delicious opportunity to enjoy one of your 2 or 3 daily vegetable portions.
6. **Craving something sweet?** Sure, every now and then... but fruit can always be added to your home-made sweets to make them even tastier and more satiating.
7. **Nothing goes to waste!** Use every part of your vegetables: make broths and soups with the vegetable stalks, and use a blender or juicer recover the fruit's pulp "residue" and add it to the drinks that you prepare. Vitamins and fibre together!
8. **Hit the mark with a nice one-pot meal! 2-3 times a week:** a delicious soup with grains (e.g. pasta, rice, spelt, wholemeal bread, etc.) and legumes, for a guaranteed nutritious meal.
9. **Vegetables give their best when they're "crisp".** Try not to overcook them: they'll retain their nutrients better, and you'll feel fuller.
10. **Set a good example!** Start eating fruit and vegetables yourself in front of your children, and you'll entice them to do the same.

Doctor, how much dairy should a person consume?

The Ministry of Health has drawn up a useful guide for **the proper inclusion of milk & yoghurt** in the daily diet:

1. Consume **3 portions of milk and yoghurt every day**. One portion corresponds to 125 g, or rather a small glass, a 1/2 cup, or a single-serving container of yoghurt.
2. **Milk and yoghurt are good breakfast foods**. With a full cup of milk (2 portions) for breakfast, and a single-serving container of yoghurt as a snack, you can reach the 3 recommended daily portions.
3. In addition to being good **sources of calcium**, milk and yoghurt also contain **vitamin A**, and **B vitamins**, as well as other minerals, like phosphorus, magnesium, zinc, and selenium.
4. From a nutritional standpoint, milk and white yoghurt with no added sugar are very similar. Thanks to the presence of milk enzymes, yoghurt promotes the **balance of intestinal flora**.
5. You can choose between fresh pasteurised, high quality fresh pasteurised, pasteurised, microfiltered, and long-life (UHT) milk. If, however, you choose to use raw milk, always remember that it must be boiled prior to consumption.
6. Yoghurt is obtained by fermenting milk with specific microorganisms. When the milk's fermentation is not due to the action of yoghurt micro-organisms, fermented milks are obtained. An example is a typical Eastern European beverage, called **kefir**.
7. Milk and yoghurt can be whole, skimmed, or partly skimmed, depending on the fat percentage. Skimmed or semi-skimmed milk and yoghurt have a reduced fat and calorie content, with no reduction in calcium and protein.
8. **Milk can be drunk at any age**. Lactase, an enzyme necessary for the digestion of lactose (milk sugar), is present in the human intestine. This makes milk an appropriate food for children, adults, and the elderly, with the exception of those who suffer from lactose intolerance, who have a documented lactase deficiency.
9. Yoghurt is well tolerated by most people who suffer from lactose intolerance. In addition, many products with reduced or no lactose content, such as lactose-free milks, are also available.
10. **The calcium and phosphorous present in milk and yoghurt** are easily absorbed by the body. Their consumption helps reduce the risk of developing osteoporosis.

For more information: visit the nutrition area on the Ministry of Health website at:
https://www.salute.gov.it/portale/nutrizione/homeNutrizione.jsp

What more is there to say?

To answer this question, it is necessary to introduce a topic that represents the cutting edge in the field of oncology, namely the study of the microenvironment, or, more simply, the **microbiota**. The microbiota is the *microbial community (including bacteria) of the human body*. In particular, this chapter we make reference to the **gut microbial** community, which, when in balance, regulates digestion, metabolism, and the immune system, thus preventing the invasion of pathogens and inflammatory processes.

How can we maintain this balance?

To maintain the right balance we must preserve the health of our bacteria by **including soluble fibres** (legumes, nuts, onions, garlic, rye, etc.), insoluble fibres (whole grains, quinoa, certain fruits and vegetables), and probiotics (low-fat yoghurt, kefir, etc.) within our diet. Some of these foods may contain both types of fibre, and can also be an excellent **source of protein**. The introduction of fibre into our diet promotes the formation of short-chain fatty acids (e.g. butyric acid), through a fermentation process carried out by the microbiota. These fatty acids are able to regulate the immune system, protect the intestinal barrier against attacks by pathogens, and even promote **immunotherapy response**. Fibre may also be helpful in reducing cholesterol levels and slowing the absorption of sugars.

What should you not do?

Don't follow restrictive diets or adopt do-it-yourself methods. Seek the advice of experienced nutritionists, and only from centres with adequate experience in the field.

From theory to practice

In order to make things easier for our patients and their family care-givers, we invite them to visit the Oncology and Cooking website, where they can find easy-to-make recipes for preventing the side effects of cancer treatments, all prepared in accordance with the principles of the Mediterranean diet.

www.oncologiaecucina.org - Instagram: @oncologiaecucina

Smoking and alcohol

SMOKING

DANIELA GALEONE AND MARIA GIULIA MARINO

Why is smoking bad for our health?

According to the World Health Organisation (WHO), **more than 8 million people die each year from tobacco use**. In Italy, the estimated avoidable deaths amount to more than **94,000** per year. One cigarette contains about **600** ingredients, and it creates more than **7,000** chemical substances when it burns.
At least 69 of these chemicals are known to cause cancer, and many are toxic. 20 cigarettes a day reduces the average life span of a young person who starts smoking at the age of 25 by about 4.6 years, which is **equivalent to losing one day of life for every week of consumption**.
The nicotine contained in tobacco is the neuro-psychotropic substance responsible for addiction, and causes behavioural changes related to memory and emotions.

What are the most common risks?

Smoking increases the risk of many types of cancer: lung and respiratory tract, oesophagus, stomach, liver, colon/rectum, pancreas, kidney, ureter, bladder, ovary, cervix, and myeloid leukaemia. In addition, **second-hand smoke is a recognised risk factor for breast cancer**.

Smoking is also the main risk factor for non-neoplastic respiratory diseases, including chronic obstructive pulmonary disease (COPD), and is one of the most significant cardiovascular risk factors: nicotine (*also contained in heated tobacco products, many e-cigarettes and "nicotine pouches*) causes an increase in heart rate and contractility, increases blood pressure, can promote the formation

of atheromas; it also reduces insulin sensitivity and can aggravate diabetes. Smoking adversely affects the female reproductive system by altering hormone production, causes menopause about 2 years earlier than in non-smokers, and affects fertility. Pregnant women who smoke has an increased risk of miscarriages, stillbirths, and underweight babies. In addition, smoking also has **undesirable aesthetic effects**, such as white gums, yellow teeth, older-looking skin, and increased facial hirsutism.

Why quit smoking?

Quitting smoking is an investment in health, as it reduces the risk of developing many diseases, and protects others against the risks associated with **second-hand smoke**, thus reducing the risk of many diseases in children caused by exposure to smoke, such as respiratory diseases, like asthma, and ear infections (otitis).

When quitting smoking: within a short time blood circulation and lung function improve, and within 1 year the risk of heart attack becomes half that of a smoker; after 10 years the risk of lung cancer decreases to half, and within 15 years the risk of chronic disease becomes equal to that of a non-smoker. **Quitting smoking is also good for those who have already developed smoking-related diseases**.

How to quit?

You can try to quit on your own, but the chances of success are greatly increased with the help of a doctor or a specialist. If necessary, the doctor may recommend drug therapy with pharmaceutical nicotine substitutes (NRT), Bupropion, or Citisin, which alleviate withdrawal symptoms and help you quit.

Are there other products to watch out for?

In addition to cigarettes and other conventional tobacco products, new products have also been on the market for several years, such as **heated tobacco products, or electronic cigarettes with or without nicotine** and, more recently, oral pouches containing nicotine salts.

It is not yet clear what effects they may have on the health of consumers. An **electronic cigarette** (e-cig) is a device for inhaling vapour, usually flavoured, most frequently containing nicotine in varying amounts (usually between 6 and 20 mg), in a mixture made up of water, propylene glycol, glycerol, and other substances, mainly flavourings.

Unlike e-cigarettes, **Heated Tobacco Products (HTPs)** are devices that actually contain tobacco sticks, which are heated to a high temperature (around 350°), creating a smoke-like emission. These products contain nicotine and other chemicals, and there is currently no evidence to show that they are less harmful than traditional cigarettes. And while it is known that they may expose users to lower levels of certain toxic substances contained in cigarettes, they also expose consumers to higher levels of other potentially toxic and harmful chemicals not contained in traditional cigarettes.

Due to their attractive designs and flavourings, these products encourage experimentation on the part of young people.

For more information:
https://www.salute.gov.it/portale/fumo/homeFumo.jsp
https://smettodifumare.iss.it/it

ALCOHOL

MARIA ASSUNTA GIANNINI AND MARIA MIGLIORE

Alcohol use

Along with the elderly and young people, the World Health Organisation lists women among the **population groups most susceptible** to alcohol exposure. Women are more susceptible to harm from alcohol intake because they have a lower body mass than men and a lower concentration of water in the body; for this reason, their ability to metabolise alcohol is lower than that of men, and therefore the same amount of consumption **results in a higher blood alcohol level**. In fact, women who consume alcoholic beverages are more likely to develop a number of diseases, including several types of cancer (*particularly breast cancer*), osteoporosis, reduced fertility, and pregnancy-related complications, such as miscarriage and the risk of giving birth to babies suffering from foetal alcohol syndrome (FAS/FASD).

Lower risk consumption

In order to avoid health problems, the guidelines of the Council for Research in Agriculture and Analysis of Agricultural Economics (CREA) advise women **not to consume a daily amount of alcohol exceeding 12 grams** (equivalent to 1 Alcoholic Unit, approximately 330 mL of beer, 125 mL of wine or 40 mL of a spirits), regardless of the type of drink consumed.

Over the past ten years, the number of women who consume alcohol outside meals has steadily increased, and that upward trend does not seem to be slowing down.

Drinking alcohol outside meals, an extremely common behaviour among women, even in combination with other types of risky be-

haviour such as smoking, **increases the risk and exposes you to a greater likelihood of developing diseases, namely cancer**.

Zero alcohol during pregnancy

Alcohol consumption during pregnancy is associated with a wide range of pregnancy issues, such as miscarriage, stillbirth, sudden infant death syndrome, premature birth, certain congenital malformations, low birth weight, intrauterine developmental delay, and a number of other disorders covered by the term "**Foetal Alcohol Spectrum Disorders** (FASD)", starting with the most severe manifestation, *Foetal Alcohol Syndrome* (FAS), which consist of a series of structural and neurodevelopmental abnormalities leading to severe behavioural and neuro-cognitive disabilities.

All alcohol consumed by the mother during pregnancy ends up in the bloodstream of the foetus, so even the smallest amount of alcohol can cause damage and compromise its health. In addition, all stages of embryonic development are vulnerable to the teratogenic effects of alcohol, which is why alcohol consumption during pregnancy is contraindicated according to clinical guidelines in most countries of the world, and the public health message is **"don't drink during pregnancy (zero alcohol) and don't drink when you decide to have a child."** Foetal alcohol disorders can be 100% prevented if alcohol is avoided during pregnancy.

A brief guide:

1. Drinking alcoholic during pregnancy increases the risk of harming your child's health
2. There is no amount of alcohol that can be considered safe or risk-free for the foetus during pregnancy
3. Consuming any alcoholic beverage during pregnancy harms the foetus, regardless of the type or strength
4. Alcohol is a toxic substance capable of passing through the placenta and reaching the foetus at the same concentrations present in the mother

5. The foetus does not have the ability to metabolise the alcohol, which therefore directly harms the brain cells and the tissues of the organs being formed
6. Alcohol is especially harmful to the foetus during the first few weeks and the last trimester of pregnancy
7. If you are planning to become pregnant, you should avoid drinking alcohol. If already pregnant, it is better to stop drinking until the child has been born. Damage caused to the child by prenatal exposure to alcohol is irreversible and cannot be cured
8. It is also recommended to avoid consuming alcoholic beverages while breastfeeding
9. All damage and defects caused by alcohol consumption during pregnancy can be prevented by avoiding alcoholic beverages
10. Stopping alcohol consumption is a gesture of responsibility and love towards your unborn child.

Cancer rates among women in relation to alcohol intake

The International Agency for Research on Cancer (IARC) has estimated more than 3200 new cases of cancer among women in Italy, including 2300 new cases of breast cancer.

One of the ways in which alcohol (ethanol) causes cancer is through damage caused to cellular DNA.

Alcohol can cause at least 7 types of cancer:

 Oral cavity (mouth)	 Oropharynx (throat)	 Oesophagus	 Liver
 Larynx	 Colon (large intestine and rectum)	 breast	

The most common types of cancer caused by alcohol are breast cancer in women and colon cancer in men. People who smoke tobacco and drink alcohol have a 5 times greater risk of developing cancer of the oral cavity, oropharynx, larynx, and oesophagus compared to people who only use alcohol or tobacco.

The International Scientific Community (IARC) has clearly expressed the notion **that there is no safe level of alcohol consumption with respect to cancer risk**, so the WHO has intended to urge caution, supporting the statement **"Less is better"**.

Useful numbers: Alcohol Toll-Free Number (NHS) 800632000
Websites: www.salute.gov.it
www.epicentro.iss.it/alcol/osservatorio-nazionale-alcol

Physical activity

FLAVIO SINISCALCHI

What is physical activity?

Physical activity is considered one of the most effective behaviours for leading a healthy life. The World Health Organisation (WHO) defines it as *"any bodily movement produced by skeletal muscles that involves energy expenditure"*. Therefore, this definition includes athletic activity, as well as activities performed daily during work, leisure, housework, and moving from one place to another, including walking and cycling.

Why is it important?

Numerous scientific studies have shown that regular physical activity has multiple **mental and physical benefits**: it improves cardiovascular health, combats obesity and sedentariness, improves cognitive function, and reduces anxiety and depression. Moreover, regular physical activity has been shown to be associated with a reduced risk of developing several types of cancer, including breast cancer. And let's not forget that. after surgery, adapted physical activity (AFA) and structured exercise play a key role in patient rehabilitation, especially when performed under the supervision of qualified professionals, even in non-health facilities, such as health gyms. In short, engaging in sports and regular physical activity - as Minister Abodi often reminds us - constitutes a true social "immune defence".

How much physical activity should you actually do?

Aware of the importance of physical exercise in promoting health, the WHO has issued specific guidelines to provide detailed recommendations broken down by age group, with **the aim of preserving and improving the general health of the population**.

They suggest that children and adolescents should engage in an average of **60 minutes** of moderate- to vigorous-intensity, predominantly aerobic, **physical activity per day** during the week, combined with musculoskeletal strengthening exercises at least 3 times per week. Adults and elderly people, on the other hand, are advised to engage in 150 to 300 minutes of moderate-intensity physical activity per week or 75 to 150 minutes if vigorous-intensity, accompanied by muscle-strengthening exercises at least two days per week, and balance training to increase functional capacity and reduce the risk of accidental falls.

No matter which type of physical activity one chooses, the important thing is to maintain a constant and active approach. Incorporating these practices into everyday life contributes significantly to the prevention of chronic disease and definitely improves quality of life.

2.

INTRODUCTION TO CANCER PREVENTION AND CARE

Foreword

Cancer is not a single disease that only affects certain people who are considered to be at risk. It is a heterogeneous group of over 200 different diseases, each of which has its own particular characteristics.

In Italy, there are over **3.6 million** people living with cancer, or 5.7% of the population. **In 2006 that number was "only" 2 and half million**. The most widespread cancers in 2022 were breast, colorectal, lung, prostate, bladder, stomach, pancreatic, non-Hodgkin's lymphoma, melanoma, kidney, thyroid, liver, endometrial, and leukaemia. The absolute annual number of new cancer diagnoses in Italy is expected to increase in the coming decades. An average increase of 1.3% per year in men and 0.6% per year in women has been calculated. *The main reason for this increase is the increase in the average age of the population* on the "Old Continent". **Although it can affect adults, young people, and even children, cancer is a disease that's most typically associated with old age**.

Healthy lifestyles are a very powerful weapon against cancer. Just think that 40% of cancer cases could be avoided by eliminating or modifying so-called risk factors.

Various cancers can also be treated nowadays with extremely effective therapeutic weapons. In fact, we are seeing very encouraging results, and this is also due to the early diagnoses that we're often able to obtain. However, there are still some very harmful cancers for which survival rates remain low. Primary prevention (healthy lifestyle) and secondary prevention are therefore both essential.

In Italy, the total observed number of deaths in both men and women caused by cancer from 2007 to 2019 was lower than expected: 268,000 fewer deaths. On the following pages you will find information on the most common forms of cancer in Italy and, above all, **the importance of contacting your doctor and having appropriate checks carried out for early diagnosis**.

Public health models: cancer screening

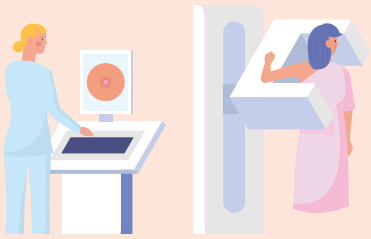
MARIA ROSARIA CAMPITIELLO, GIUSEPPE GAMBALE, AND ROSARIO ANDREA COCCHIARA

Secondary cancer prevention is aimed at detecting cancer at an early stage.

In fact, identifying the tumour at an early stage ensures timely treatment, and improves the chances of preventing the disease's progression. Secondary prevention can be aimed at recognising the earliest manifestations of the disease, or even highlight an increased risk of developing it in the future, in asymptomatic (and therefore apparently healthy) individuals.

Given their high impact in terms of health for the population, cancer screening programmes are included among the Essential Levels of Care (ELC), or rather the services and facilities guaranteed by the national health system to all citizens (either free of charge or with a co-pay ticket).

Three different screening programmes are active nationwide in Italy:



- **Breast cancer screening:** for women 50 to 69 years of age, consisting of a mammogram offered every 2 years. For an accurate diagnosis, the results of the examination must be evaluated separately by two radiologists. If cancer is suspected, further investigations will follow, such as a breast ultrasound or biopsy for histological examination. Once the investigations have been completed, the patient will be referred to either the normal two-year timetable for the general population, a follow-up examination, or, in the event of

diagnostic confirmation, the necessary treatment.

- **Cervical cancer screening:**
  for women 25 to 64 years of age, carried out by means of either a Pap test (every three years for women 25 to 30 years of age) or an HPV-DNA test (every five years for women 30 to 64 years of age).
  If the results of these first-level investigations are positive, the patient may be referred for a colposcopy and, if necessary, an in-depth examination with a biopsy. In this case, depending on the whether the final diagnosis is positive or negative, the doctor will either refer the patient to treatment or else continued monitoring according to the normal screening schedule.

- **Colorectal cancer screening:**
  for both men and women 50 to 69 years of age. The programme involves testing for faecal occult blood every two years. The relevant local heath office will organise the screening campaign and invite people in the age group concerned, and will communicate the results of the test once it has been carried out.
  The stool specimen container can be easily collected from and returned to a pharmacy or other nearby facility, with no need for an appointment. In the event of a dubious or positive result of the screening test, an in-depth colonoscopy will be necessary. This is not only diagnostic, but also therapeutic, as any polyps present in the intestinal lumen can be removed during the examination.

In addition to the nationally guaranteed screening programmes, individual regions may also choose to extend the range of tests offered to their own populations, for example by expanding the age groups covered by the prevention campaigns.

The scientific evidence shows the health benefit that screening programmes provide to citizens, and highlights the importance of broad population adherence and the consistent and regular performance of these tests, in order to allow for the early detection of cancers and better prognoses.

Oncofertility

FRANCESCA POGGIO AND LUCIA DEL MASTRO

There are approximately 50,000 new breast cancer diagnoses in Italy each year, and more than 3,000 women are affected while still of childbearing age.

The issue of **possible infertility** at the time of a cancer diagnosis is increasing, both because the number of cancer diagnoses at fertile age is on the rise, and because the age of first pregnancy is becoming increasingly advanced.
The course of treatment following diagnosis may affect the possibility of having future pregnancies: in fact the side effects of chemotherapy agents can include impaired fertility, and even early menopause, with all of the relative consequences. **Cancer treatments can temporarily or permanently impair fertility**. The infertility risk depends on several factors, including the type of treatment received, and the patient's age (the risk is greater for women whose age at diagnosis is close to the age of physiological menopause).

Today, the goal of treating early-stage cancer patients is not limited to recovery, but also to safeguarding their future goals, including future family planning. For this reason, before starting chemotherapy, it is essential for patients to be made aware of these possible consequences, and for possible strategies aimed at reducing these risks to be explained and offered to them.

Strategies available for preserving fertility prior to undergoing cancer treatment are the following:

- **embryo cryopreservation:** this technique, currently prohibited in Italy by law no. 40/2004, is the most effective for preserving female fertility.
- **oocyte cryopreservation:** this technique involves ovarian stimulation, and is recommended for patients who are able to postpone

chemotherapy treatment by about 2-3 weeks and who have an adequate ovarian reserve. It consists of pharmacological hormonal stimulation, with subsequent oocyte retrieval under ultrasound guidance by means of an invasive procedure lasting about 10 minutes, followed by evaluation, selection and cryopreservation of the oocytes. The likelihood of success depends on various factors, primarily the patient's age and the number of oocytes retrieved. *This technique's success rates are steadily increasing.*

- **Ovarian tissue cryopreservation:** this technique is still considered experimental, but can be applied in cases where the previous techniques cannot be used due to age or the timing of the cancer treatment. This technique consists of a laparoscopic surgical procedure aimed at harvesting fragments of ovarian tissue, which are then cryopreserved and subsequently re-implanted if necessary. It does not require hormonal stimulation, and can be performed at any stage of the menstrual cycle, thus avoiding any delay in the start of chemotherapy treatment.
- **pharmacological protection of the ovaries** with a class of drugs (synthetic human sex hormone analogues, GnRH analogues) that can "turn off" the ovaries during chemotherapy, protecting them from harmful effects. In this manner, it is possible to reduce the percentage of women who experience early menopause following chemotherapy, and **increase the likelihood of pregnancy after the treatment**. In 2016, the drug was approved by AIFA and provided to all women who are candidates for chemotherapy and expressed an interest in preserving ovarian function and fertility, and its use was adopted into the national and international guidelines. Ovarian suppression using GnRH analogues during chemotherapy and cryopreservation strategies are not mutually exclusive, and can be used in combination to increase the chances of preserving ovarian function and fertility in young women with cancer who are candidates for chemotherapy.

Ageing and senescence

IGNAZIO UGO CARRECA AND ANNA PAOLA CARRECA

What is ageing?

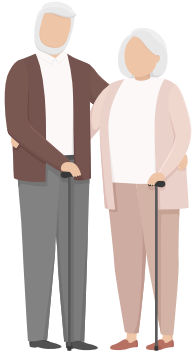
It is a complex phenomenon resulting from a progressive maladaptation to changes at the organic, cognitive, and environmental levels. Ageing is a natural mutation process that begins in early adulthood. According to many recent studies, this process starts around the third to fourth decade of life, in which the body's organs and apparatuses begin a phase of gradual functional decline, which progresses with age until the moment when the general functioning of the various organs and apparatuses and their underlying cellular systems reach a critical threshold of degradation.

In 2014, the scientific community established the threshold for entering old age at 65 years. This figure was subsequently raised to 75 years in light of the high number of perfectly active 65-year-olds, but this left the parameters for precisely determining the condition of being "elderly" unspecified, and they have remained so to this day.

What are the parameters of ageing and senescence?

Age (documented or chronological): primary indicator attainable from the subject's official documents. The older we get, the greater the likelihood of developing chronic or degenerative diseases affecting major organs (such as cancer). Our body's proper functioning is based on two principles: **homeostatic cellular balance and functional organic reserve**. The efficiency of this mechanism allows each organ of the human body to renew all of its cells while maintaining the same total number of cells and its functionality. It is also capable of repairing the damage and failures induced by serious or persistent "insults" that may affect the entire organism or an individual organ during the course of an individual's life, restoring basal conditions. This perfect mechanism loses its effectiveness over time, as it can no longer cope with the constant

demands for action that the body is almost always sending out. Cell renewal is slowly reduced until it comes to a complete halt. It is important to point out that cell renewal is due to various factors, including a particular type of functional organelles located on the ends of human chromosomes, called “telomeres”. These shrink with each cellular repair until they are too small to function, thus triggering the onset of **cellular senescence** in all the organs of the body.



Age (biological or physiological): this refers to the age that can be attributed to an individual based on his or her morphological and functional conditions, in relation to the reference standards. This should typically coincide with the individual’s documented age, but many other prevailing factors must often be taken into consideration, such as genetic, behavioural (lifestyle, diet), and environmental factors (climate, pollution). In this case, the biological age can appear to be much higher than the chronological age due to the effects of various long-lasting morbid events that engage and either partially or fully exhaust the body’s overall functional response, leading to frailty.

Types of ageing

In 2014, the **WHO** (**World Health Organisation**) defined two basic types of ageing: **successful** ageing and **frailty**.

The former is a process that optimises age progression with good health, while the latter is a typical condition of ageing characterised by increased vulnerability to morbid events.

However, ageing is an inevitable process. Understanding how **we can age in a healthy manner** and the main risk factors to be monitored in order to prevent the onset and spread of cancer has become a priority in terms of health protection and management. **Lifestyle plays a key role in successful ageing**.

Types of cancer and treatments for the elderly

With 28% of its population over the age of 65, Italy now ranks second worldwide in terms of among countries with the highest percentages of elderly people (Japan is ranked first with 30.5 %). These data also show a parallel increase in chronic degenerative diseases that impair personal health, above all cancer.

The ageing process is the basis for high rate of cancer among people aged 65-70 years worldwide. In Italy, out of approximately 385,000 new cases that arise each year, over 65% affect people over 65. Among the elderly population, the risk of developing malignant cancer increases with age. Cancers are the second leading cause of death and disability after cardiovascular disease. This is also one of the main reasons why neoplasms are on the rise worldwide, as is the increase in the average life expectancy and the number of people over 70 years of age.

Walking speed test

Taking more than **5 minutes** to walk **4 metres** is indicative of:

- Disability
- Long-term care needs
- High risk of falls
- Early mortality

Among the latter, the risk of developing cancer is about forty times greater than among those aged 40-50, and ten times greater than in those aged 60-65. Moreover, between the ages of 60 and 69, the odds of being diagnosed with cancer are 1 in 5 for men, and 1 in 8 for women.

The most frequent types of neoplasms among the elderly of both sexes are similar to those found among younger people: prostate, lung, breast, colorectal, bladder, stomach, and pancreatic.

Treatment strategies

The treatment strategies for elderly people with cancer must be determined considering that, among people over the age of 65, age and

pre-existing illnesses can affect the outcomes of the cancer treatments. Moreover, up until now it has been assumed that treating an elderly person was the same as treating an **aged adult**, thus using the same treatment protocols used for young people. This preconception often has led, and continues to lead, to unsatisfactory results, resulting in errors in patient management, with high toxicity, and increased mortality rates.

The **WHO** has already divided the elderly into two categories, based on their physical and mental status: those "in (good) health" physically and mentally, defined as **fit** and the frail ones, defined as **unfit**.

Recent studies have shown that, during cancer treatment, **fit** subjects are able to withstand the toxicity and side effects of the treatments like younger subjects, with similar therapeutic results. Conversely, **the unfit develop severe multi-organ and multi-apparatus toxicities, often with very serious consequences.** For these subjects, the disadvantages outweigh the advantages, and attempting treatment becomes a dangerous pathway, with only modest benefits. In these cases, the treatment choices must be made with caution, taking into account the problems associated with the therapy and the cost-benefit ratio.

An oncologist treating an elderly person with cancer should know how to carry out personalised treatments for **unfit** individuals, with minimal toxicity and side effects, or palliative care only. There are currently very few such experts out there. Those with decision-making power should make this a priority issue. Certain assessment tests can help better determine the characteristics of the patient to be treated.

Charlson Comorbidity Index (1) and (2)

Comorbidity	Score		
Mild liver disease	1	Myocardial infarction	1
Diabetes	1	Congestive heart failure	1
Hemiplegia	2	Peripheral vascular disease	1
Moderate or severe renal disease	2	Cerebrovascular disease	1
Malignant cancer (any)	2	Dementia	1
Leukaemia	2	Chronic bronchopneumopathy	1
Malignant lymphoma	2	Connective tissue disease	1
Moderate or severe liver disease	3	Ulcerative gastritis	1
Metastatic malignant cancer	6		
Aids	6		

+6 indicates a 40% lower survival rate in 5 years

Elderly people, obesity, and cancer risk

The World Health Organisation (WHO) considers **obesity** to be a true planetary disease, which is spreading rapidly wherever the dietary model of industrial civilisation prevails, with over-processed and high-calorie foods that do not conform to the principles of proper and high-quality nutrition. Moreover, obesity affects both the affluent and the poorer classes, and excess weight is a condition characterised by excessive accumulation of body fat, almost always due to a poor diet and a sedentary lifestyle. Obesity may also have a genetic component, which is multi-factorial, and several recent studies have found that this hinders the ability to lose and maintain a low body weight, or even to gain weight.

What seems to have been ascertained at this point is that all current scientific data **indicate overweight and obesity as risk factors for a multitude of human diseases**, such as heart disease, type 2 diabetes, insulin resistance, hypertension, and cancers of the *breast (postmenopausal), colon, uterus, oesophagus, gallbladder, kidney, liver, ovaries, pancreas, stomach, thyroid, meningioma, and multiple myeloma.*

All this is caused by **subcutaneous fat** and **visceral fat**, which accumulate with obesity in both sexes and at all ages, but especially in people over 65.

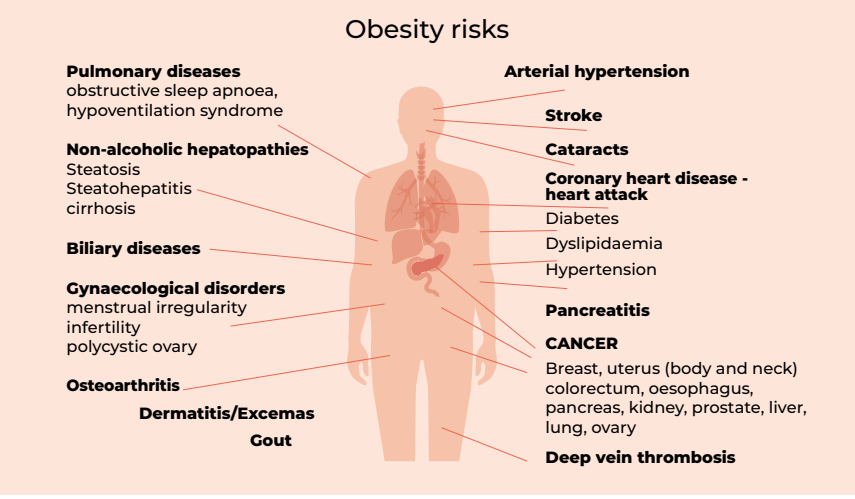
Subcutaneous fat is typically found in the abdominal area (waist) in both men and women, and in the buttocks and thigh areas in women. Visceral fat, on the other hand, is fat located around the central organs of the body, such as the liver, the gastrointestinal system, and the cardiovascular system.

To reduce visceral fat, it is important to maintain a healthy lifestyle and to engage in regular physical activity.

1. Mental Health:
- Reduces stress and improves mood;
- Relieves symptoms of anxiety and depression Promotes self-esteem and self-confidence;
- Stimulates the production of endorphins, known as "happy hormones".

2. Cardiovascular Health:
- Strengthens the heart and blood vessels;
- Lowers blood pressure;
- Improves blood circulation;
- Reduces the risk of heart disease and stroke.

3. Muscular and Skeletal Health:
- Maintains muscle strength and flexibility;
- Reduces the risk of osteoporosis and fractures.



Latest news

4 March 2024 marked World Obesity Day, established in 2015 by the **World Obesity Federation**, with the aim of raising awareness among citizens and institutions of the impact that obesity has on health and promoting its prevention at the societal level.

A month earlier, the world-renowned journal Lancet had published a report on a study conducted by the NCD Risk Factor Group and the WHO on people of various ages, from 190 countries, which showed that the total number of obese children, adolescents, adults, and elderly exceeded one billion. The same paper reported that the total number of normal or underweight people has progressively and significantly decreased since 1990.

Obesity is currently the most common form of malnutrition in most countries worldwide, and the phenomenon is considered to be one of the greatest threats to global public health. (WHO-2024)

Hereditary and familial cancer risk

MARIA PIANE AND SIMONA PETRUCCI

Genetics is the study of how hereditary traits are passed down from one generation to the next, and the alterations in individual genes that can cause or predispose individuals to genetic diseases. This is done by studying genomic DNA, usually obtained from venous blood samples.
Genomics, on the other hand, deals with groups of genes expressed in a specific tissue, their functions, and how they interact with each other. **Both play a role in the development and treatment of numerous forms of cancer.** Cancer is a disease with a multifactorial aetiology, which is influenced by hormonal, metabolic, environmental, immune, and genetic factors.

Where can cancers originate?

Cancers can be sporadic, familial, and hereditary. Sporadic cancers occur with only one case being present within a family, and are generally caused by genetic variants, called "somatic" variants, which originate in one or more cells of the body. *These acquired variants are not passed on to offspring*. Familial cancers involve more than two collaterals (relatives) in the same family line, and may result from several genetic factors or shared environmental exposures.

Hereditary cancers, on the other hand, are associated with a specific genetic predisposition, related to the presence of so-called "constitutional" or "germline" variants, present in all cells of the body, and transmissible to offspring. These are variants that give the carrier an increased risk of cancer with respect to the general population. **In other words, one does not inherit the cancer itself, but rather the risk of potentially developing it**.

It is important to note that both sexes can inherit deleterious variants, and in turn pass them on to their offspring.

According to the latest data (source: AIOM 2023), it is estimated that at least 31,000 patients in Italy who carry a pathogenic variant fall ill with cancer every year. The most frequent cases include breast cancer (5,514), colorectal cancer (2,886), lung cancer (2,200), prostate cancer (2,118) and pancreatic cancer (2,045).

Over the past 30 years, over 150 genes have been identified (Cancer Predisposition Genes, see the table on pages 44 and 45), whose pathogenic variants give their carriers a moderate to high risk of cancer (2 to 20-fold). The most common include deleterious variants in the ***BRCA1/BRCA2* genes, which increase the risk of developing breast and ovarian cancer.** However, mutations in these genes do not exclusively affect women. **Me can also inherit deleterious variants, and in turn pass them on to their offspring.** Male carriers are more prone to male breast cancer or prostate cancer. The risk that a pathogenic variant in *BRCA1 or BRCA2* will be transmitted from the carrier parent to their offspring is 50%.

What should be done if there have been certain types of cancer in one's family?

Members of families in which there have been one or more cases of the aforementioned types of cancer should consider seeking cancer genetic counselling *(especially if the cancers arose at a young age)*. Within the family unit, there is the possibility of identifying healthy persons with genetic alterations that predispose them to certain types of cancer. Family members at risk can be assessed during genetic counselling (usually first-degree relatives at risk of having inherited or transmitted the deleterious variant) in order to discuss their likelihood of being carriers, illustrate the advantages and limitations of genetic testing, and, finally, sign a dedicated informed consent. This makes it possible to identify prevention strategies, or else active surveillance with frequent examinations for **early cancer detection**.

Syndrome	Genes	Inheritance	Related cancer (% risk of falling ill)	Surgical primary prevention strategies
Hereditary breast and ovarian carcinoma/ Fanconi anaemia	*BRCA1*	AD/AR	breast (women): >60% breast (men): 0.2%-1.2% ovary: 39%-58% pancreas: ≤5% prostate: 7%-26%	bilateral mastectomy, optional; salpingo-oophorectomy at 35-40 years recommended
Hereditary breast and ovarian carcinoma/ Fanconi anaemia	*BRCA2*	AD/AR	breast (women) >60% breast men: 1.8%-7.1% ovary: 13%-29% pancreas 5%-10% prostate: 19%-61%	bilateral mastectomy, optional; salpingo-oophorectomy at 40-45 years recommended
Li-Fraumeni Syndrome	*TP53*	AD	breast: >60% pancreas: 5%-10% brain: 14% sarcomas: 15%	bilateral mastectomy, optional
Peutz-Jeghers syndrome	*STK11*	AD	breast: 32% -54% ovary (non-epithelial): ≥20% uterus: 9% cervix: 10% pancreas: 11%-36% colon: 39% stomach: 29% lung: 7%-17% testicle: 9%	hysterectomy, optional
Cowden syndrome	*PTEN*	AD	breast: >60% endometrial: 28% thyroid: 35% colon: 11-20% kidney: 34% Melanomas 6%	bilateral mastectomy, case-specific; optional hysterectomy
Hereditary diffuse gastric cancer	*CDH1*	AD	breast: 41%–60% diffuse gastric: 56%	bilateral mastectomy, optional; gastrectomy at 18-40 years, recommended
Susceptibility to breast and pancreatic cancer	*PALB2*	AD	breast (women): 41%–60% breast (men) 0.9% in men; ovary: 3%-5% pancreas: 5%-10%	bilateral mastectomy, optional; salpingo-oophorectomy after 45 years, optional
Familial breast and ovarian cancer susceptibility/ Fanconi Anaemia	*RAD51C*	AD/AR	breast: 20-40% ovary: 10%-15%	Salpingo-oophorectomy at 45-50 years, recommended
Familial breast and ovarian cancer susceptibility	*RAD51D*	AD	breast: 20-40% ovary: 10%-20%	Salpingo-oophorectomy at 45-50 years, recommended
Susceptibility to breast cancer / Ataxia Telangiectasia/	*ATM*	AD/AR	breast: 20%-40% ovary: 2%-3% pancreas: 3%-5% prostate: > compared to gen. pop. Colon: 5%-10% stomach: 2%-3%	–

Syndrome	Genes	Inheritance	Related cancer (% risk of falling ill)	Surgical primary prevention strategies
Susceptibility to breast cancer	*BARD1*	AD	breast: 20%-40%	–
Breast, prostate and non-polyposis colon cancer susceptibility	*CHEK2*	AD	breast: 20%40% colon: 5-10%	-
Lynch syndrome (HNPCC)	*MLH1, MSH2, MSH6, PMS2, EPCAM*	AD	breast: <15% **ovary: <38%** pancreas: <6.2%; biliary tract <3.7% prostate: <24% **endometrium: ≤57%** colon: ≤61% stomach: ≤9% small intestine: ≤11% kidney, pelvis, ureter: ≤28% bladder: ≤12% brain: ≤7.7%	hystero-adnexectomy, optional
Familial Adenomatous Polyposis	*APC*	AD	colon: 100% duodenum/ periampullary: <1%-10% intra-abdominal desmoid: 10%-24% thyroid: 1.2%-12% stomach: 0.1%-7.1% small intestine: <1% haepatoblastoma: 0.4%-1.5% brain: 1%	colectomy, only if the excessive number of polyposis does not allow for sufficient endoscopic control
Attenuated Familial Adenomatous Polyposis	*MUTYH* (biallelic variants)	AR	colon: 70%-90% duodenum: 4% ovary: 14.7% bladder/urinary tract: 8%	colectomy, only if the excessive number of polyposis does not allow for sufficient endoscopic control
Juvenile gastrointestinal polyposis	*SMAD4*	AD	colon: ≤50% stomach: ≤21%	-
MEN1/MEN4	Menin/ CDKN2B	AD	pituitary gland (adenomas): 50% parathyroids (adenomas): 95% pancreas/duodenum (NET): 30%-70% NET in other locations: >3%	–
MEN2	RET	AD	thyroid (medullary carcinoma): 90% pheochromocytoma: 57% parathyroids (adenomas): 20-30%	thyroidectomy, recommended
Hereditary melanoma syndrome	CDKN2A/ CDK4	AD	melanoma: 28-76% pancreas: >15%	–

AR: Autosomal recessive inheritance (the normal gene is dominant over the mutated gene)
AD: Autosomal dominant inheritance (the altered gene is dominant over the normal one)

Table: Main “Cancer predisposition genes” commonly investigated in diagnostics when suspecting hereditary forms of cancer.

SOURCES: NCCN Guidelines version 3, February 2024"; https://www.omim.org/

Cervix, endometrium, and ovaries

CERVIX

DOMENICA LORUSSO, MARIACHIARA PADERNO, GIOVANNI FUCÀ, AND ILARIA SABATUCCI

Cervical cancer is a malignant neoplasm that originates in the cervix, the lower part of the uterus that opens into the vagina. It is one of the most common gynaecological cancers in developing countries, and is a significant public health concern. It is the fourth most common cancer among women globally.

EPIDEMIOLOGICAL DATA

Approximately 570,000 new cases are diagnosed and an estimated 311,000 women die from the disease each year. Incidence and mortality rates in developed countries are significantly reduced thanks to vaccination and screening programmes. In developing countries, however, incidence and mortality rates remain high due to limited access to such programmes.

What is the main risk factor?

The main risk factor for cervical cancer is persistent human **papilloma virus** (**HPV**) infection, particularly the high-risk strains such as HPV-16 and HPV-18. HPV infection is mainly transmitted through sexual contact. Although HPV infection is very common, only a small percentage of infections persist and can lead to precancerous lesions and, eventually, cervical cancer. HPV can cause cancer in other parts of the body such as the vulva, vagina, penis, anus, mouth and pharynx. **Men are therefore also at risk.**

Is prevention possible?

Cervical cancer prevention is based on two main strategies: HPV vaccination and regular screening.

Why is HPV vaccination important?

Vaccination against HPV is one of the greatest achievements in cervical cancer prevention. **In Italy, the HPV vaccination is recommended and offered free of charge to girls and boys starting at age 11**, and is administered in two doses 6 months apart. If the vaccination cycle begins after the age of 15, there are three doses. Vaccination is recommended before the patient becomes sexually active. A catch-up programme has been established for women up to 26 years of age and for men up to and including 18 years of age, and remains free of charge for all doses of the vaccination cycle if they have not been previously vaccinated or have not completed the vaccination cycle. **However, vaccination is also effective and recommended for sexually active men and women up to the age of 45**. The HPV vaccines used today protect against the 9 most dangerous HPV serotypes, and are extremely safe and effective: they can prevent over 90% of HPV-associated cancers, and have been safely administered to millions of girls and boys worldwide.

What is a Pap test?

A Pap test, or Papanicolaou test, is an effective screening method for early detection of any cellular changes in the cervix that could develop into cancer. During the Pap test, a sample of cells is taken from the cervix and analysed under a microscope to check for any abnormalities. **The guidelines recommend that women start having Pap tests at the age of 25 and continue every three years up until the age of 65.** Women over the age of 30 can opt for co-testing,

which combines the Pap test with the HPV test, every five years.

What is the HPV test and what is it used for?

The HPV test detects the presence of human papillomavirus DNA in the cervix. This test is particularly useful for **identifying infections with high-risk strains of HPV that can lead to cervical cancer**. Studies have shown that the HPV test is more effective at detecting precancerous lesions than the Pap test. It can be used as a primary screening tool or in combination with the Pap test (co-testing).

How is cervical cancer treated?

The treatment of cervical cancer depends on the stage of the cancer at the time of diagnosis, the patient's general health conditions, and other individual factors. The main treatment options include surgery, radiotherapy, chemotherapy, and immunotherapy.

Surgical procedures vary depending on the extent to which the cancer has spread, and may include:

- **Conisation:** removal of a conical portion of the cervix containing the cancer. It is used for precancerous lesions and very small tumours.
- **Trachelectomy:** removal of the cervix, keeping the uterus intact. This procedure is an option for women who want to preserve fertility.
- **Hysterectomy:** removal of the uterus and cervix. This procedure can be either total (with removal of the uterus and cervix), or radical (which also includes removal of part of the vagina and pelvic lymph nodes).

How does radiotherapy work?

Radiotherapy uses high-energy radiation to kill cancer cells. It can be used as a primary treatment or in combination with surgery and chemotherapy. There are two main types of radiotherapy:

- **External radiotherapy**: radiation is administered from outside the body.
- **Brachytherapy:** radiation is administered directly into the cervix through a vaginal device.

What role does chemotherapy play?

Chemotherapy uses anti-cancer drugs to destroy cancer cells. It can be administered alone, in combination with radiotherapy (*chemoradiation therapy*) to treat locally advanced cervical cancer, or together with immunotherapy for certain types of metastatic or recurrent cervical cancer.

What are the future prospects for cervical cancer?

Thanks to advances in prevention and treatment, cervical cancer incidence and mortality rates can be significantly reduced. Prevention through regular screening with Pap tests and HPV tests, together with vaccination against HPV, is essential to reduce the incidence of this cancer.

Promoting education, access to prevention programmes, and appropriate treatment is crucial to continue fighting this disease and improving the health of women worldwide.

Finally, it is important to support research in order to develop new therapies and improve the survival rates of women suffering from cervical cancer.

ENDOMETRIUM

Endometrial cancer, also known as endometrial carcinoma, is a malignant neoplasm that originates in the inner lining of the uterus, called the endometrium. It is the most common type of cancer of the uterus, and primarily affects post-menopausal women, although it can occur at any age. In terms of frequency, it is the fourth most common cancer among women in developed countries, and is the most common gynaecological cancer in these regions.

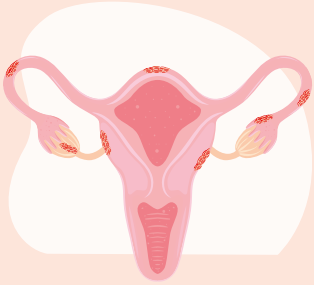
EPIDEMIOLOGICAL DATA

Each year, approximately 382,000 new cases of endometrial cancer are diagnosed globally, with higher rates in developed countries than in developing countries. The five-year survival rate is relatively high if the cancer is diagnosed at an early stage, but decreases significantly with advanced diagnosis.

What are the main risk factors for endometrial cancer?

Several risk factors have been identified for endometrial cancer. The most significant include:

- **Age:** the risk increases with age, with most cases being diagnosed in women over 50.
- **Obesity:** excess fatty tissue can lead to higher levels of oestrogen, which stimulates endometrial growth.
- **Reproductive history:** the risk is increased among women who have never had children (nulliparity) and those who have entered menarche early or menopause late.
- **Hormone replacement therapy**: the use of oestrogen not balanced by pro-



gesterone after menopause may increase the risk.
- **Polycystic ovary syndrome (PCOS):** women with PCOS often have higher oestrogen levels.
- **Personal or family history of cancer:** a history of breast, ovarian or colon cancer may increase the risk due to possible genetic mutations.
- **Lynch syndrome:** an inherited genetic condition that increases the risk of various types of cancer, including colon and endometrial cancer.

Are there any preventive measures that can be taken for endometrial cancer?

Although there is no specific method to prevent endometrial cancer, several strategies can help reduce the risk:

- **Healthy diet:** obesity is a significant risk factor. A diet rich in fruit, vegetables and whole grains can help maintain a healthy weight and reduce the risk of cancer.
- **Regular physical activity:** exercise can help maintain a healthy weight and balance hormone levels.
- **Oral contraception:** the use of combined oral contraceptives (oestrogen and progesterone) for several years can reduce the risk.
- **Management of hormone therapy:** women who require hormone replacement therapy after menopause should discuss with their doctor whether to use progesterone together with oestrogen to reduce the risk.
- **Medical monitoring:** women with significant risk factors, such as Lynch syndrome or a family history of cancer, should be monitored regularly by a medical specialist.
- **Limit alcohol use:** moderate or no alcohol consumption can reduce the risk of many types of cancer, including gynaecological cancers.
- **Avoid smoking:** cigarette smoking is associated with an increased risk of many cancers, so avoiding smoking can help prevent their onset.

What are the most common symptoms?

Symptoms of endometrial cancer can vary, but the most common include:

- **Abnormal vaginal bleeding:** this is the most common symptom and is often the first sign. It includes bleeding between menstrual cycles, bleeding after menopause, or unusually heavy menstrual flows.
- **Pelvic pain:** pain may occur in the pelvic area or during sexual intercourse.
- **Abnormal vaginal discharge:** discharge unrelated to the menstrual cycle, which may be watery or bloody.
- **Unexplained weight loss:** unintentional weight loss can be a symptom of advanced cancer.

How is endometrial cancer diagnosed?

Early diagnosis of endometrial cancer is crucial to improve the chances of successful treatment. The main diagnostic techniques include:

- **Pelvic examination:** during a pelvic examination, the doctor may detect abnormalities in the cervix or uterus.
- **Transvaginal ultrasound:** this examination uses sound waves to create images of the uterus and can help identify abnormalities in the structure of the endometrium.
- **Endometrial biopsy:** a small sample of endometrial tissue is taken and analysed under a microscope to detect the presence of cancerous cells.
- **Hysteroscopy:** a procedure in which a small instrument equipped with a camera (hysteroscope) is inserted into the uterus to examine the endometrium and take tissue samples.
- **Magnetic resonance imaging (MRI) or computed tomography (CT):** these advanced imaging examinations can be used to assess the spread of the tumour and plan treatment.

How is endometrial cancer treated?

Treatment of endometrial cancer depends on the stage of the tumour and the patient's general health conditions. The main treatment options include:

- **Surgery:** surgical removal of the uterus (hysterectomy) is the main treatment for endometrial cancer. It may also include removal of the ovaries and fallopian tubes, and pelvic lymph nodes.
- **Radiotherapy**: uses high-energy radiation to destroy cancer cells. It can be used after surgery to reduce the risk of recurrence, or as a primary treatment for women who cannot undergo surgery.
- **Chemotherapy:** uses anti-cancer drugs to destroy cancer cells. It can be administered alone or in combination with radiotherapy, especially in cases of advanced or recurring cancer.
- **Hormone therapy:**for cancers that are sensitive to hormones, progesterone therapy may be an option. This treatment option is particularly useful for women with early-stage tumours who wish to preserve fertility.

What role does immunotherapy play in the treatment of endometrial cancer?

Immunotherapy is an option recently introduced into clinical practice for the treatment of endometrial cancer, especially in cases of advanced or recurrent cancer. Immunotherapy uses the patient's immune system to recognise and destroy cancer cells. One of the main forms of immunotherapy consists of immune checkpoint inhibitors, such as anti-PD-1 and anti-PD-L1 antibodies, which help to unlock the immune response against the cancer. Clinical studies have shown encouraging results, especially in patients with cancers characterised by *mismatch repair system (dMMR) deficiency or high microsatellite instability (MSI-H)*.

OVARIES

Ovarian cancer is a type of cancer that originates from the ovaries, the female reproductive organs that produce egg cells and hormones, such as oestrogen and progesterone. This cancer may develop from the epithelial (superficial) cells of the ovaries, germ cells (which produce oocytes), or stromal tissue (which produces hormones).

EPIDEMIOLOGICAL DATA

Ovarian epithelial cancer is the fifth most common cancer among women, and the leading cause of death from gynaecological cancer. Worldwide, it is estimated that more than 310,000 new cases are diagnosed and more than 207,000 women die from the disease each year. The rates varies from region to region, with higher rates in developed countries than in developing countries.

What are the risk factors associated with ovarian cancer?

The main risk factors for ovarian cancer include:

1. **Advanced age:** most cases of ovarian cancer are diagnosed in women over 50, with the rates peaking between the ages of 60 and 70.
2. **Family history:** having first-degree relatives (mother, sister, daughter) with ovarian or breast cancer significantly increases the risk. This is often due to inherited genetic mutations.
3. **Genetic mutations:** mutations in the BRCA1 and BRCA2 genes significantly increase the risk of developing ovarian and breast cancer. Other genetic syndromes, such as Lynch syndrome, can also increase the risk.
4. **Endometriosis:** women with endometriosis, a condition in

which the tissue lining the uterus grows outside of it, have an increased risk of developing certain types of ovarian cancer.

5. **Post-menopausal hormone therapies**: the use of oestrogen without progesterone after menopause has been associated with an increased risk of ovarian cancer.
6. **Reproductive and hormonal factors:** women who have never been pregnant (nulliparity) have an increased risk of developing ovarian cancer. Prolonged use of oral contraceptives, on the other hand, seems to reduce the risk.
7. **Personal history of cancer:** having had breast, uterine, or colon cancer may increase the risk of developing ovarian cancer.
8. **Lifestyle and environmental factors:** several studies suggest that obesity and a diet high in saturated fat may can increase the risk of ovarian cancer.

How is ovarian cancer diagnosed?

Early diagnosis of ovarian cancer is difficult because the initial symptoms are often common and non-specific, and therefore *can be confused* with other conditions. These symptoms include swelling, pelvic pain, difficulty eating or feeling full quickly, and the need to urinate frequently and urgently.

1. **Gynaecological examination:** the doctor looks for masses or irregularities in the ovaries and surrounding organs.
2. **Transvaginal ultrasound:** uses sound waves to examine the uterus and ovaries.
3. **Computed tomography (CT) or magnetic resonance imaging (MRI):** provides detailed images of the abdomen and pelvis.
4. **Blood test:** the CA-125 cancer antigen test can be used, although it is not specific and may be elevated with other conditions.
5. **Biopsy:** a definitive confirmation of the diagnosis is obtained through the analysis of a sample of ovarian tissue.

What treatments are available for ovarian cancer?

Ovarian cancer treatment depends on the stage of the cancer at the time of diagnosis, and may include a combination of surgery, chemotherapy and, in some cases, radiotherapy, or targeted therapies.

1. **Surgery:** surgery is often the first step, and the aim is to remove all visible cancer without leaving any residue.
2. **Chemotherapy:** a systemic treatment, using intravenous drugs, that acts throughout the body to kill existing cancer cells and prevent the spread of the disease. Chemotherapy may be administered either prior to surgery (neoadjuvant) in order to reduce the tumour mass, after surgery (adjuvant) to eliminate any residual cancer cells, or as the main treatment if surgery is not possible.
3. **Targeted therapies:** these treatments use drugs designed to act specifically against a "target" in the cancer cells. One example is PARP inhibitors, which are used as maintenance therapy after chemotherapy.
4. **Immunotherapy:** several studies are exploring the use of immunotherapy, which stimulates the immune system, to recognise and combat cancer cells.

If ovarian cancer is suspected, it is important to contact a centre that's specialised in the treatment of this disease.

Are there genetic mutations that increase the risk of ovarian cancer?

Mutations in the BRCA1 and BRCA2 genes are among the most significant genetic factors associated with ovarian cancer. These mutations are hereditary and have a significant impact on the risk of developing this type of cancer. **Scientific studies have revealed that approximately 15-20% of epithelial ovarian tumours are due to mutations in the BRCA1 and BRCA2 genes.** This finding is crucial, as it indicates that a substantial percentage of ovarian cancer cases can be attributed to known and identifiable genetic factors. Women carrying mutations in the BRCA1 gene have an extremely high risk of developing ovarian cancer during their lifetime, with a probability ranging from 39% to 46%. Although associated with a slightly lower risk, mutations in the BRCA2 gene still carry a significant probability of between 10% and 27%. **These percentages highlight the importance of genetic testing for women who may be at high risk, allowing closer surveillance and targeted preventive interventions.**

In addition to BRCA mutations, another inherited condition that increases the risk of ovarian cancer is **Lynch syndrome**. This syndrome is caused by mutations in DNA repair genes, and carries a high risk of various types of cancer, including colon, endometrial, and ovarian cancer. Women with Lynch syndrome have a risk of developing ovarian cancer ranging from 10% to 12%, depending on the specific mutated gene.

Is there any way to prevent ovarian cancer?

A yearly gynaecological examination with transvaginal ultrasound can facilitate early diagnosis. However, there are currently no scientifically reliable screening programmes for ovarian cancer prevention. The only type of prevention available is for women at increased familial risk and with established genetic mutations, such as BRCA1/2 gene mutation and Lynch Syndrome. *Surgical removal of the fallopian tubes and ovaries can prevent almost all genetic/inherited ovarian cancers.*

In general, maintaining a healthy lifestyle can play an important role in reducing the risk of ovarian cancer. A balanced diet rich in fruit, vegetables, and whole grains, regular exercise, and maintaining a healthy body weight can have positive effects. Long-term use of oral contraception has also been associated with a reduced risk of ovarian cancer.

What have been the latest developments in the field of ovarian cancer treatment?

Ovarian cancer research is constantly evolving. Current studies are examining new drug combinations, the role of immunotherapies, and personalised therapies based on the genetic and molecular profile of the cancer. Research studies regarding new **biological markers** that could improve early diagnosis and the assessment of the treatment response are also ongoing.

Colon/rectum

EMILIO DI GIULIO

Most colorectal cancers are caused by the malignant transformation of polyps. These consist of small benign growths caused by the uncontrolled reproduction of cells within the intestinal mucosa.

EPIDEMIOLOGICAL DATA

The new diagnoses recorded in 2023 amounted to **50,500** (26,800 among men, and 23,700 among women). The five-year survival rates are 65% and 66% respectively. In total, there are over 513,500 patients in our country living with this type of cancer.

What are the risk factors?

The recognised risk factors are the following: environmental, behavioural (smoking, sedentary lifestyle, obesity), and dietary. One so-called "generic" risk associated with **age**: starting at age 50, the risk for both men and women increases. The risk also increases in the presence of certain conditions (such as diabetes or metabolic syndrome), chronic inflammatory bowel diseases (such as Crohn's disease, ulcerative recto-colitis), or genetic syndromes (such as familial adenomatous polyposis or Lynch syndrome). Physical activity, regular consumption of fruit and vegetables, and healthy lifestyles, on the other hand, play a preventive role.

The main red flags that should be reported to a doctor

The presence of blood in the stool, even if mixed with mucus, changes in bowel behaviour due to the appearance of diarrhoea or constipation, anaemia, fever, feeling of exhaustion, incomplete evacuation or rectal pain, unexplained weight. All of these symptoms are non-specific, but should be reported to a doctor.

What tests can be used to diagnose the disease?

The most accurate and widely used diagnosis method is colonoscopy, which also allows for histological confirmation through tissue samples (biopsies). In some special cases, a so-called "virtual colonoscopy" can be used as an alternative. Colorectal cancer has a high incidence, especially from the age of 50, which is why regional screening is required. Men and women receive invitations from their local health offices to undergo regular faecal occult blood tests (or in some regions rectosigmoidoscopy). In fact, the early diagnosis of this type of cancer is crucial to the survival and quality of life of patients. **Occult blood testing is not a diagnostic test, as it does not provide sure proof of cancer, but is rather a screening tool used to identify the subjects most at risk, to who should subsequently undergo a complete colonoscopy**.

Skin

MIRELLA D'ANDREA AND PAOLO ANTONIO ASCIERTO

Skin cancers are traditionally broken down into melanomas and epithelial non-melanoma skin cancer.

Melanoma

A malignant tumour that originates from melanocytes, cells that contain the *pigment melanin* responsible for skin colouration. It can develop in the skin anywhere on the body, although in rare cases it can also develop in the mucous membranes (e.g. mouth, genital intestinal tract, or eyes), or may even have unknown origins. Melanoma can develop on a pre-existing newly formed mole. The most common type of skin melanoma, which accounts for about 70% of all cases, is **superficial melanoma**, which appears as a flat or slightly raised lesion, often with irregular borders and colour variations.

These lesions mainly appear on the torso for men, on the legs for women, and on the upper back for both sexes. About one third of these melanomas originate from a pre-existing nevus.

EPIDEMIOLOGICAL DATA

The incidence of this tumour is constantly increasing. Approximately 85% of skin melanomas that arise annually worldwide affect the populations of North America, Europe, and Oceania. It is one of the main cancers that can develop at a *young age*, and is currently the third most common cancer in Italy in both sexes under the age of 50. Despite the increase in the incidence rate, the mortality rate has remained more or less stable in recent years.

Who is at risk

The main risk factor for cutaneous melanoma is **excessive and repeated exposure to ultraviolet (UV) light**, which reaches us in the form of **UVA and UVB** rays, and is mainly carried by the sun's rays. Too much sun exposure, especially at an early age, is a potential hazard, as it can damage the DNA of skin cells and trigger cancerous transformation, which can lead to melanoma many years down the road. It's important to remember that **sunlamps and sunbeds** are also sources of ultraviolet radiation and should therefore be used as little as possible, preferably never. Suffice it to say that, years ago, the IARC (the World Health Organisation's cancer research agency) conducted a study that showed that exposure to even one tanning lamp under the age of 30 increases the risk of developing melanoma by 75%.

The risk is greater among Caucasian (white) individuals, and increases among people with **freckles** or many **moles**, with **light-coloured eyes, hair**, and **skin**, and those who have suffered numerous sunburns, especially during childhood. Other major risk factors include: having a **close relative who has had this type of cancer** or having had a **previous cutaneous melanoma** or a different type of skin cancer, such as squamous cell carcinoma and basal cell carcinoma.

Types

Cutaneous melanomas originate from either undamaged skin or pre-existing nevi, or rather those which have been present since birth (congenital) or early childhood, or else from nevi that appear during the course of one's lifetime (acquired). The risk of melanoma developing from a congenital nevus is very low, with the exception of giant congenital nevi (greater than 20 cm), for which the risk is greater.

From a clinical standpoint, there are 4 types of cutaneous melanoma: **superficial spreading melanoma** (the most common, accounting for about 70% of all cutaneous melanomas), **lentigo maligna melanoma, acral lentiginous melanoma, and nodular melanoma** (the most aggressive, accounting for about 10-15% of all cutaneous melanomas). Unlike the first 3 types, which initially grow superficially, nodular melanoma invades the underlying tissue from the outset.

Signs and symptoms

The main sign of cutaneous melanoma is a **change in a mole's appearance, or the development of new mole**. The characteristics of a mole that may indicate melanoma are summarised with the acronym ABCDE:

- **A** for **Asymmetric** in shape (a benign mole is generally circular or otherwise roundish, while a melanoma is more irregular);
- **B** for irregular and indistinct **Borders**;
- **C** for variable **Colour** (i.e. different shades within the mole itself);
- **D** for increasing **Dimensions**, both in width and thickness, although melanomas may also be just a few millimetres wide;
- **E** for **Evolution** of the mole, which will tend to undergo changes in appearance (size, shape, colour) in a rather short time frame.

Other red flags that should be assessed by a doctor include any **mole that bleeds (even minimally)**, that **itches**, or that is totally different from the others (ugly duckling sign).

Non-melanoma epithelial skin cancers

Basal cell carcinoma is the most common type of non-melanoma skin cancer, and mainly affects the more superficial layers of the skin. This type of skin cancer is often caused by excessive exposure to UV radiation from the sun. Symptoms include translucent or red nodules on the skin, ulcers that do not heal, and discolouration of the skin.

Basal cell carcinoma is usually diagnosed by taking a *biopsy of the*

lesion. The most common treatment for this type of skin cancer is surgery to remove the tumour. Other treatments may include radiotherapy, cryotherapy, and topical drugs.

Squamous cell carcinoma is another common type of non-melanoma skin cancer that develops in the squamous cells of the epidermis. This type of skin cancer is often caused by excessive exposure to UV radiation from the sun, but can also be caused by genetic and environmental factors. Symptoms include rough, scaly, nodular skin lesions prone to bleeding.

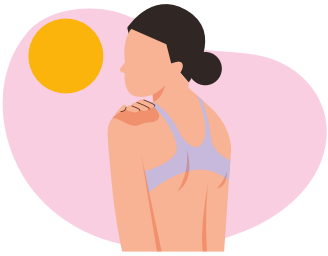
Squamous cell carcinoma is usually diagnosed by taking a biopsy of the lesion. Treatment for this type of skin cancer varies depending on the size and location of the tumour, and may include surgery, radiotherapy, and loco-regional therapies.

Merkel cell carcinoma is a rare and aggressive form of skin cancer with a high risk of recurrence and metastasisation, often within two to three years after the initial diagnosis. It usually manifests as a hard, shiny, flesh-coloured or bluish-red swelling. It tends to grow rapidly without pain or tenderness. Although Merkel cell carcinoma can develop on any part of the skin, it is most commonly found on areas that are frequently exposed to sunlight (e.g. the face and arms).

Prevention

Certain behaviours can reduce the risk of developing skin cancer. First of all, it is essential to **limit one's sun exposure** from an early age, avoiding sunburns. **In general, it is recommended to protect the skin by avoiding direct exposure to sunlight during the hottest hours of the day, and by avoiding the use of tanning lamps or sunbeds**. When exposed to the sun, it is recommended to wear clothing that protects against ultraviolet rays, including hats and sunglasses, and to use sunscreen with a high sun protection factor (SPF) to protect against UVA and UVB rays, to be applied in the rec-

ommended quantity, and reapplied at regular intervals, also after getting wet, so as to ensure continuous coverage.



These precautions are particularly important for children, who are highly prone to sunburn: **the cancerous transformation process is very long, and can often result from an alteration that occurred in childhood.**

It is also necessary to **periodically check the appearance of one's moles**, either by consulting a dermatologist, or independently, by looking in the mirror or having a family member look at them in places that cannot be observed with one's own eyes.

Diagnosis

Early diagnosis of skin cancer does not exclusively require a doctor: in many cases, periodic **self-examinations** allow for any changes in moles to be identified and for a dermatologist to be promptly contacted.

The specialist will initially carry out a **comprehensive examination**, in which he or she will assess the patient's family history and the presence of any typical signs and symptoms of melanoma. A more thorough visual examination of the skin is carried out using a special technique for magnifying and illuminating the skin, called **epiluminescence**. However, a final diagnosis of cutaneous melanoma requires a **biopsy**, in which the suspected lesion is removed and analysed under a microscope.

How it is treated

The treatment of choice for melanoma is surgery, which often succeeds in eliminating the disease definitively at an early stage. With the advent of new immunotherapeutic agents, in some cases capable of restoring the body's immune response against cancer cells (such as ipilimumab, pembrolizumab, and nivolumab), and molecular targeted therapy (such as vemurafenib, dabrafenib, trametinib, cobimetinib, encorafenib and binimetinib), the approach to patients with advanced melanoma has changed radically with respect to the use of traditional chemotherapy.

In clinical practice, the choice of treatment depends on the extent of the disease, whether a rapid response is required, the possibility of achieving a long-lasting result, any concomitant diseases, and the patients' health status.

Radiotherapy is used in some specific cases (for example when symptomatic bone or brain metastases are present), as well as for therapeutic purposes, combined with other treatments, or as palliative care.

What does melanoma prevention consist of? What are the main steps that need to be taken?

The prevention measures are divided into primary and secondary measures. The former concern **lifestyle aspects: sunburns must be avoided**, because sunburn is a first degree burn that creates damage to the melanocytes, the mole cells from which melanoma can originate.

Young people and children are the most susceptible. In the summertime, intense sunlight between 12 noon and 3 pm should always be avoided. During the rest of the day, a high-SPF sunscreen (**above 50**) must always be applied, and **should always be reapplied** every two hours, or after getting wet (unless it is of a water-resistant type). If a sunscreen cannot be applied, a UV-resistant shirt should be worn. Even in the mountains, where the rays have a higher incidence, and the reflective effect of the snow makes sun-

burn an even greater risk during a ski holidays.

How to recognise a suspicious mole?

Now let's talk about secondary prevention, or rather early diagnosis. Let's begin with two key methods: the first is the **ABCDE** method, where A stands for Asymmetry; or rather a lesion that is not symmetrical; B stands for irregular, map-like Borders; C stands for changing Colour; D stands for Dimensions greater than 6 millimetres; and E stands for Evolution within a short time, such as weeks or months. **If even just two of these letters apply the mole under observation, it is recommended to seek an urgent visit with a specialist.** The other is the "ugly duckling" method, according to which **if one mole among a large group is uglier than the rest, it should be seen immediately**.

What does mole mapping consist of?

Mole mapping is a simple and painless examination performed by a dermatologist, whereby potentially dangerous moles can be identified based on their characteristics.

Can I undergo mole mapping during pregnancy or breastfeeding?

Yes. Mole mapping has no contraindications for pregnant or breastfeeding women.

How often should a skin cancer screening be carried out?

Every 12 months, or in some cases every 6 months if recommended by a specialist.

How should sunscreen be applied?

Sunscreen should be applied to dry skin 30 minutes prior to exposure. Reapply the same amount of sunscreen every 2 hours.

In addition to melanoma, there is also another common form of skin cancer: basalioma. What type of cancer is it, and how can it be recognised?

Basalioma, or basal cell carcinoma, is a neoplasm originating from basal cells, which are located in the deepest layer of the epider-

mis, in contact with the dermis. This type of skin cancer generally manifests clinically as red bumps, ulcerations, reddish plaques, nodules, erosions, or inflamed scars that do not tend to heal. A dermatologist will easily recognise this type of lesion, and **diagnosis is histological**.

Which areas of the body are most affected by basal cell carcinoma, and what are its symptoms?

This type of cancer usually develops as a result of chronic damage due to sun exposure. The parts of the body most commonly affected are therefore areas exposed to sunlight, such as the head, neck, shoulders and back. A lesion that tends to enlarge, become inflamed, and ulcerate repeatedly in one of these areas should arouse suspicion.

Liver and bile ducts

LORENZA RIMASSA

One the most common forms of primary liver and bile duct cancer in adults is hepatocarcinoma, which originates in the hepatocytes (the organ's main cell type). It can begin as a single nodule or in a multifocal form (simultaneous onset of multiple nodules in various parts of the liver). In up to 20% of cases, however, the cancer affects the bile ducts, which carry bile to the gallbladder, and are called cholangiocarcinomas.

EPIDEMIOLOGICAL DATA

In 2023 there were a total of **12,200** new cases in Italy, and the incidence is twice as high among men as it is among women. The five-year survival rate is 22% for both genders. In total, there over **33,800** diagnosed patients currently living with this type of cancer.
5,400 people per year are diagnosed with bile duct carcinoma, and the five-year survival rate is 17% in men and 15% in women. In total, there are currently more than **12,700** patients.

Do hepatitis viruses increase the risk of disease?

Most cases of hepatocarcinoma arise in patients with **liver cirrhosis**. More than 70% of cases of primary liver cancers are caused by **hepatitis C virus (HCV)** infection, and are almost always associated with liver cirrhosis. The hepatitis B virus (HBV) also increases the risk, even in the absence of cirrhosis. Patients considered to be at high risk (liver cirrhosis, chronic HBV or HCV infec-

tion) should undergo regular (half-yearly) liver ultrasound scans to check for malignancy.

What are the most common symptoms?

Liver cancer is manifested by the appearance of abdominal pain and tightness, weight loss, fatigue, and decreased appetite.
For bile duct cancer, symptoms are weight loss, physical emaciation, jaundice, dark urine (reddish brown) and pale (hypopigmented) stools.

How is the disease diagnosed?

For liver cancer, certain radiological examinations are used. In order to reach a reliable diagnosis of bile duct cancer, examinations such as a CT scan, MRI (which can also be a cholangio resonance imaging) or endoscopic retrograde cholangio-pancreatography (CPRE) are required.

Breast

ADRIANA BONIFACINO

Breast cancer is a formation of tissue consisting of cells that grow in an uncontrolled and abnormal manner within the mammary gland. The various stages of the disease (I to IV) concern the involvement of the mammary gland alone, the surrounding tissues, and tissues from other parts of the body.

Early diagnosis is the most effective method of breast cancer prevention.

EPIDEMIOLOGICAL DATA

In 2023, there were an estimated **55,900** new diagnoses in women, making it by far the most frequent cancer in women. In fact, it accounts for 30% of all cancers in women.
There are currently **834,200** women in Italy living with a breast cancer diagnosis, with 6-7% being cases that have already metastasised. 45% of breast cancer diagnoses are in women aged 45-74, 35% in women >74 years of age, and 20% in those <45 years of age. 1-2% of breast cancers affect men.
It's a type of cancer that can be linked to family history, and in some cases (around 10%) to a genetic mutation (BRCa1 and 2), which can lead to ovarian, prostate, or pancreatic cancer, or melanoma.
The prevention and early diagnosis procedures are examined below.

Lifestyle!

There are two fundamental and effective ways to stay healthy: a healthy diet and physical activity. Numerous scientific studies have

shown that these should be considered as "medicines" to be used for prevention, as well as during and after treatment.

Mammogram

The public health Mammogram Screening model envisages a free mammogram every two years for women aged 45/50 through 69/74, at the invitation of their local Public Health Office (in some regions, like Emilia Romagna and Tuscany, mammograms are offered one a year for women between the ages of 45 and 49). If these investigations should reveal a significant and/or suspicious alteration, the patient will be called back for further investigation at a Level II public centre.

Law no. 388 of 23 December 2000 (The Veronesi Law) provides for mammograms every two years for all women between 45 and 69 years of age, with no out-of-pocket payment.

Adherence to the screening programme is an excellent tool for early breast cancer detection.

What can you do if you are outside the screening age?

There is no current scientific evidence showing that mammogram screening is effective as a public health model for women aged 40-45. However, if personal and/or family risk factors or symptoms are present, women of any age are encouraged to consult their doctor to determine whether a personalised prevention programme may be advisable.

Is breast self-examination useful?

Self-examination is NOT a means of self-diagnosis. This is a form of education designed to help patients familiarise themselves with and have confidence in their own breasts, rather than fear. Periodically observing and palpating your breasts can facilitate the detection of any changes, which in turn should be referred to your

doctor for evaluation and/or advice. There's absolutely no clinical or scientific basis for the statement, "I can't feel anything in my breast, so there's no need for me to have a mammogram." Early diagnosis is based on instrumental investigations carried out in accordance with the public health models outlined above.

Can breast cancer be hereditary?

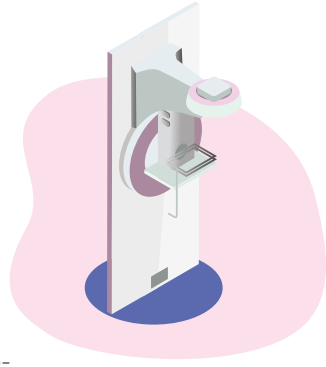
About 10-12% of all breast cancers are hereditary. In cases of heredity/family history, mutations can be found on 2 main genes (BRCa1 and BRCa2). Individuals with family histories that include multiple cases of malignant breast, ovarian, prostate, pancreatic and/or stomach cancer (carcinoma), on the side of either the mother or father, may way to consider genetic counselling order assess the likelihood of a genetic mutation. In order to be proactive and take fewer risks, gathering information about your own family history (oncological, autoimmune, neurological, vascular diseases) can be a useful way to come up with a more personalised prevention pathway with your doctor.

What are the programmes to be followed in the case of family history, BRCa1 and 2 genetic mutation, or very dense breast tissue?

The Ministry of Health and the Regions are aware of the need for prevention programmes dedicated to women who fall into these categories. Some regions already have personalised programmes dedicated to the highest risk groups, with admissions open to the public. It is recommended to visit the your Region's website and consult with your doctor to find out whether any such programmes are already available. However, there is an urgent need for a national programme that will put an end to local inequalities, and will be able to guarantee appropriate and effective public treatment programmes for all women. Associations dedicated to patients and citizens, like the IncontraDonna Foundation, are in constant contact with the institutions in order to assert these rights and ensure the presence of adequate and coherent public health programmes within every local area and region.

What kinds of instrumental investigations are carried out?

Attention! Each examination should be kept on file and brought to the subsequent check-ups.



Mammogram: a radiological examination that uses an extremely low dosage of radiation. The breast is compressed between two surfaces, thus allowing for any changes in tissue density, nodules, microcalcifications, distortions, or glandular asymmetries to be detected. Different technologies are available: digital and tomosynthesis. Tomosynthesis involves a three-dimensional (3D) reconstruction of the mammary gland. There is not yet enough scientific evidence to propose tomosynthesis for level I mammogram screening, but there are study groups currently working on this prospect. It is currently only used if further investigation (Level II) is deemed necessary. BI-RADS is a radiological classification system for lesions that consists of 5 categories: 1 to 3 (benign), 4 (suspicious), 5 (carcinoma). It also provides for 4 categories of breast density (A to D). Classes C and D are those which indicate the greatest density. Thanks to scientific research, we now know that greater radiological density entails a higher risk of developing breast cancer. The early diagnostic methods used for these higher categories include ultrasound combined with mammography, and in some cases MRI with a contrast medium (if requested by the specialist).

CESM: digital mammography with an iodinated contrast medium (fasting and a recent creatinine test required), which, in some cases, can be considered a substitute for MRI (Magnetic Resonance Imaging) with contrast medium. This is recommended by the specialist in specific cases. It is not a routine examination.

Ultrasound imaging: uses ultrasound waves (not radiation) to detect changes in the mammary gland. This method can also provide information regarding vascularisation (colour and power Doppler) and tissue elasticity (Elastosonography). It can be performed at any point of the menstrual cycle. Mainly used in young women, and those with dense breasts, regardless of age. Mammography and ultrasound are complementary, and one does not exclude the other.

Magnetic resonance imaging (MRI with contrast medium): uses a magnetic field (not radiation). It is only recommended by the specialist as an in-depth examination or to supplement the investigations, in specific cases where detailed tissue vascularisation imaging is required. A renal function test (creatininemia) is required. It is neither a substitute for mammography nor ultrasound imaging. For women of childbearing age, this exam should be performed between days 7 and 14 of the menstrual cycle.

What kinds of cell or tissue samples can be taken?

The need for sample collection is determined by the breast specialist (radiologist, clinician, surgeon, oncologist, radiotherapist) based on that which is revealed by the mammogram/ultrasound. In many cases, unnecessary surgery can be avoided. In the case of breast cancer, however, this allows the surgery itself to be planned in detail. In addition, thanks to recent technological and scientific advances, the examined tissue is able to be classified with increasing precision, with the possibility of adopting extremely effective and personalised treatments (hormone receptors, c-erb b2, Ki67 cell proliferation index, testing for particular genes in the tumour tissue). **Today, thanks to early diagnosis and innovation, the net survival rate 5 years after diagnosis is 88%. The likelihood of surviving for additional years is 91% (Aiom. Cancer Figures in Italy 2023)**. No type of cell or tissue collection causes the cells to spread; they are collected when it is necessary to determine the nature of a lesion detected by mammography, ultrasound, or magnetic resonance imaging. For over 20 years, the surgical removal of a lesion has only been considered after the cells or tissues have been examined.

- **Fine needle aspiration:** this method of cell collection (cytological examination) is performed by inserting a simple syringe needle, often guided by ultrasound, but also by stereotactic (mammographic guidance) or MRI technology at specific facilities, into a nodule or area of gland that requires further investigation. This method is minimally invasive, does not require local anaesthesia, and, in the case of breast cancer, has a reliability rate of up to 97%.
- **Biopsy:** this tissue collection method (histological examination) is performed using a 1-2 mm calibre needle designed to remove small fragments of tissue, called a tru-cut, and is performed under local anaesthesia. This type of tissue collection is also mainly performed with ultrasound guidance (but, like with fine needle aspiration, also with mammography or MRI), and is always conducted on an outpatient basis.
- **VABB (Vacuum Assisted Breast Biopsy):** this method of tissue collection (histological examination) is performed by inserting a needle of just over 2 mm (probe) into a very small incision in the skin (2-3 mm). It is performed under local anaesthesia, and requires specific, technologically advanced equipment capable of precisely centring nodules and microcalcifications using both ultrasound and radiological (stereotactic) guidance.

What are the selection criteria, and who should undergo counselling?

General criteria: multiple cases of breast cancer in the family (at least 2 or 3) especially if arising at a young age (2 cases if < 50 years; even just one case if < 35 years); family history of male breast cancer, ovarian cancer, pancreatic cancer, coexistence of breast and ovarian cancer within the same family or in the same individual, or bilateral breast cancer. The genetic/molecular mutation test, which may be recommended by a specialist after a thorough assessment, should be carried out on those who have or have already had the cancer; if this first test leads to the identification of a genetic mutation, the analysis will be proposed to all healthy family members (both female and male), and those who are found to be carriers of the mutation, and are therefore at “genetic risk” of cancer, for whom

specific prevention pathways and possible preventive (prophylactic) surgeries are available. Under some circumstances, (e.g. when there is a clear indication for the genetic-molecular test, and the family members with cancer are all deceased, or living relatives who do not agree to undergo the test) genetic counselling and the performance of the test on the healthy subject are also considered.

Where can one go for genetic counselling?

There are many dedicated public centres in Italy. It is always best to contact a large hospital or university that has a centre specifically dedicated to medical genetics or hereditary cancers.

For more information, see the sections of the Health Guide entitled "Family History, Heredity and Genetics".

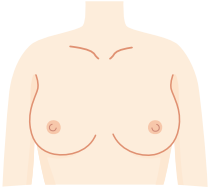
Who should I contact if I am diagnosed with breast cancer?

Each region has dedicated Breast Units, which are identified by the Regions according to criteria established by the Ministry of Health. The Breast Unit is public, and consists of a multidisciplinary team that takes care of the cancer patient throughout her journey. From diagnosis to treatment and support. The Breast Unit must begin treatment, whether surgical or pharmacological (time needed to plan and carry out all the preliminary investigations), within 30-40 days of diagnosis. Statistics have shown that being cared for by an interdisciplinary public Breast Cancer Treatment Centre can result in up to a 20% greater chance of recovery and survival 5 years after the event. To find out more about the Breast Units in your region, visit the regional website.

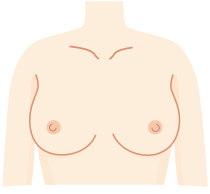
Breast self-examination

Self-examination is not a substitute for mammography or ultrasound scanning. Every woman is advised to examine her breasts periodically. The time of least breast tension should be chosen, or rather the week following the menstrual cycle (or simply once a month if you are menopausal or pregnant).

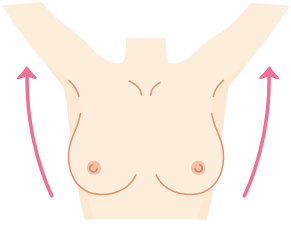
WHAT TO CHECK FOR



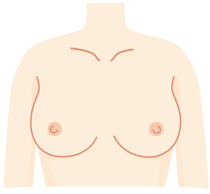
Stand in front of the mirror, with your arms at your sides. Observe and carefully compare the shape and volume your breasts and nipples. You will likely notice that they are not exactly the same. This is perfectly natural. Check whether any changes occur over time.



Next, carefully observe the profile of each breast as well. Check that there aren't any unusual changes in shape. Pay particular attention to any lump-like protrusions. Also examine the appearance of the skin: watch for any wrinkled or sunken areas.



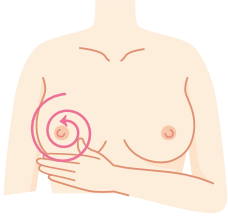
Next, face the mirror again raise both arms. Check the appearance of both breasts again, comparing them. Having your arms raised further highlights the characteristics of the nipple. Observe the profile of your breasts in this position as well.



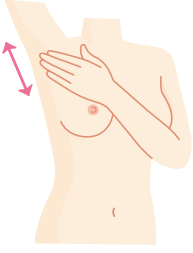
Last position. Stand in front of the mirror with your arms at your sides. Take a deep breath. Once again, observe the characteristics of your breasts. In this case, with the skin more taut, you can more easily note any skin alterations. Check the regularity of the profile again.

WHAT TO FEEL FOR

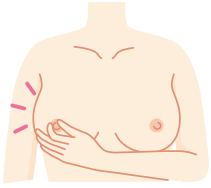
Lie down, placing a pillow under your back. This will help lift the breast and make it easier to examine. Raise your arm on the side of the breast to be examined, with your hand under your head. Perform the palpation with the other hand.



The palpation follows a spiral movement, from the outside inward, or rather towards the nipple. Bring your fingertips together and gently press deep down, proceeding slowly with the rotary movement towards the nipple. Check for changes in consistency (lumps or hard areas).



Next, it is important to carefully check, starting from the groove under the breast, the area between the breast and the armpit as well. Perform the check with your arm raised, and then with your arm lowered, perhaps while sitting. In this latter position it is easier to detect any nodules at the base of the armpit (lymph nodes).



Next, take the nipple between your fingers and press gently. Check that there are no secretions. You can also check for this while pressing on the breast. If any liquid comes out, check the colour with a handkerchief and tell your doctor.

Consult a doctor if you notice any of these symptoms:

- Unusual breast shape
- Unusual nipple appearance
- Change in breast profile
- Skin changes: wrinkled or sunken areas
- Any lumps in the breast or armpit
- Any irregularity in the nipple's appearance (for example, retroflexion: retracted nipple)
- Secretions from the nipple
- Eczema (rash) of the breast

Breast implants and the risk of lymphoma

ARIANNA DI NAPOLI

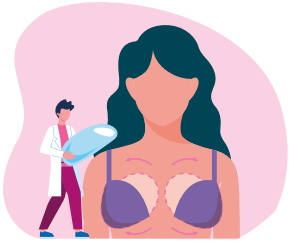
Breast implants are medical devices regulated in Italy by Legislative Decree no. 46/1997, implementing European Directive 93/42/EEC, which lays out the criteria for their design and manufacture. Since they are considered class III devices (the highest risk class), their placement on the market requires a CE certificate to be issued by a relevant certification body. Implants are currently used for cosmetic reasons, as well as for reconstructive purposes in patients who have undergone mastectomies for breast cancer.

How many types of breast implants are there?

There are various types of implants. In particular, they are available in a rounded shape, with either a smooth or rough surface (macro- or micro-textured), or else in a teardrop shape (anatomical) to mimic the natural shape of the breast, but only with a textured surface. Both are available in a wide range of sizes to suit the needs of each patient. Their contents can consist of either silicone or saline solution, and there are even dual chamber implants with a silicone core surrounded by saline solution. **Most of the implants utilised in Europe over the past 20 years have been the textured type**, while those utilised in the United States have mainly been the smooth type.

What is breast implant-associated anaplastic large cell lymphoma (BIA-ALCL)?

Breast Implant Associated Anaplastic Large Cell Lymphoma BIA-ALCL) is a rare form of malignant cancer that develops around breast implants placed for both cosmetic and reconstructive purposes. The cancer originates from T lymphocytes, a type of immune cell, which, about 9 years after implantation on average, transforms into a lymphomatous cell that multiplies, creating a build-up of fluid (seroma) between the implant and the fibrous peri-prosthetic



capsule (a kind of scar tissue surrounding the implant). In a minority of patients, the neoplasm manifests itself as a solid mass that grows within the tissues surrounding the implant and/or with an enlargement of the axillary lymph nodes, or with an erythema (pathological reddening) of the skin on the breast.

BIA-ALCL must be distinguished from another form of lymphoma that can occur in patients with medical implants, including breast implants: Fibrin-associated Large B cell Lymphoma (FLA) in which the neoplastic cells show signs of Epstein Barr virus infection. To date, 16 cases have been described in the international literature, including one case in Italy.

Another rare form of cancer that can arise in association with breast implants is squamous cell carcinoma (BIA-SCC), of which the US Food and Drug Administration (FDA) had reported 19 cases as of 8 March 2023. No cases have been reported in Italy.

How is the diagnosis made, and what is the clinical course of BIA-ALCL?

Diagnosis is carried out by cytological examination of the aspirated seroma under ultrasound guidance, or by histological examination of a fragment of the tumour mass or enlarged lymph node collected by surgical biopsy. The prognosis is generally excellent when a timely diagnosis is followed by the removal of the implant, the peri-prosthetic capsule, and all the tumour tissue.

What have the competent authorities done with regard to BIA-ALCL?

- In 2011, following the initial reports, the FDA set up a BIA-ALCL registry in order to monitor and understand whether there was a correlation between the medical devices themselves and the occurrence of neoplasia. Similarly, in 2014, the Italian Ministry of Health established a Task Force in collaboration with the other competent European authorities in order to continuously monitor the number of new cases in Europe.

- In 2016 the World Health Organisation (WHO) recognised BIA-ALCL as a new lymphoma entity, and included it within its updated classification of neoplasms of lymphoid organs.
- In November of 2018, an international workshop chaired by the European Task-Force, and attended by the various Competent EU Authorities, breast implant manufacturers, and Medical Scientific Societies, showed that a predominance of BIA-ALCL cases emerged in patients with textured surface implants. Despite the fact that there was no scientific evidence to support a direct causal link between the occurrence of BIA-ALCL and the type of implant surface, the French Health Agency for the Safety of Medicines and Medical Devices (GMED) decided not to renew the CE marking for 13 types of textured surface breast implants.
- In April of 2019, the company Allergan Limited, whose implants were found to be associated with several cases of BIA-ALCL, withdrew its macro-textured prostheses from the European market, and later also from the global market in July of 2019.
- On 24 April 2021, the Scientific Committee on Health Environmental and Emerging Risks (SCHEER) having been asked about the safety of breast implants concluded that there was moderate epidemiological scientific evidence linking the occurrence of BIA-ALCL to the use of textured implants. However, the SCHEER emphasised the need for further scientific studies in order to better clarify the aetiology and pathogenesis of the disease, which to date has been attributed to chronic inflammation of the peri-prosthetic breast tissue, which, in genetically predisposed patients, would favour the development of cancer over the years.

What is the incidence of BIA-ALCL?

As of 30 June 2023, the FDA reported a total of 1264 BIA-ALCL cases, 64 of which resulted in death, while in Italy, as of April 2023, there were 111 cases reported, with two resulting deaths. Lymphoma develops equally in patients who have received implants for reconstructive purposes (16% of cases) and for cosmetic purposes (15% of cases), while in 69% of cases the reason is unknown. Bilateral involvement was reported in just 8 patients. Although the incidence varies from country to country, and based on the type of implant,

it is nevertheless low; in Italy, as of June 2019, the incidence was estimated at 3 cases per 100,000 implant patients. However, the use of registers to monitor both BIA-ALCL diagnoses and the numbers and types of implants received is considered to be the most appropriate tool to obtain a better risk estimate. To this end, the Italian Ministry of Health established its BIA-ALCL Register in 2015, and established a National Register of Breast Implants, the relevant regulations for which entered into force on 2 February 2023, and were published in the Official Gazette on 18 January 2023. As of 1 August 2023, this register will be populated with mandatory data from the regional registers to which the surgeons or businesses that distribute such devices are required to transmit the data regarding each individual breast prosthesis implanted, explanted, or marketed in Italy for either cosmetic or reconstructive purposes.

What should women with textured implants do?

While the SCHEER has not recommended the preventive removal of textured implants in asymptomatic patients, it nevertheless noted **the importance of clinical follow-ups for patients who have received breast implants for both cosmetic and reconstructive purposes, in order to facilitate early diagnosis and timely treatment of BIA-ALCL, which is largely treatable in this manner.** Italy's Ministry of Health is actively monitoring the clinical cases on the ground, also thanks to the various educational and awareness-raising activities carried out by healthcare professionals through the dissemination of specific memoranda, complete with the guidelines for the diagnostic and treatment pathway and the informed consent to be submitted to patients prior to implantation, both of which were drafted by the Permanent Technical Working Group on BIA-ALCL established by the Ministry in 2019. Moreover, the Ministerial Circular of 5 June 2024 recently limited the implantation of breast implants for cosmetic purposes to people who have reached the age of majority, with the exception of individuals with severe congenital malformations certified by a doctor affiliated with the National Health Service or a public health facility.

Onco-haematology

LUIGI CAVANNA

Blood cancers are based on an irregular and uncontrolled growth of cells. They are diseases that often arise in the bone marrow and lymphatic system.

EPIDEMIOLOGICAL DATA

They account for an estimated 10% of all cancers in Italy, and **35,000** new cases are diagnosed each year. Seven out of ten patients manage to beat the odds and go on living normal lives.

Like with solid tumours, blood cancers have recognised risk factors, which can make them more likely to arise. The most important are the following:

- **unhealthy lifestyles** (namely obesity and smoking)
- **environmental factors** (prolonged exposure to certain chemicals or radiation)
- **side effects** of certain anti-cancer treatments
- **age** (two thirds of cases involve people over 65)
- **particular diseases or genetic factors**
- **infections** with certain viruses

Blood cancers manifest with non-specific symptoms that are often mistaken for trivial health problems (fatigue, weakness, fever, aches, weight loss, minor bleeding, excessive night sweats, or itching). But signs such as these should always be reported to a doctor, who can then prescribe more in-depth examinations.

Onco-haematological diseases are detected through specific blood tests or through a bone marrow biopsy (or biopsy of an enlarged lymph node).

They are divided into three macro-groups:

- **Acute and chronic leukaemias:** caused by the uncontrolled proliferation of cells in the bone marrow, which produces red and white blood cells and platelets
- **Lymphomas:** these affect the lymphatic system, especially B and T lymphocytes, or rather the cells used to fight infections
- **Myelomas:** these affect the immune system cells originating in the bone marrow (plasma cells). They derive from B lymphocytes which, together with T lymphocytes, are among the main cells involved in the immune response

Pancreas

MASSIMO FALCONI

The pancreas is a gland about 15 centimetres long located in the upper abdomen, and is divided into three parts: head (right), body (middle) and tail (left). Pancreatic cancer occurs when certain cells that make up the organ multiply out of control. The portion of the organ that produces pancreatic juices is called the "exocrine pancreas". About 90-95% of all cancers originate here. The part that generates hormones, on the other hand, is the "endocrine" part, and can account for the remaining 5-10% of all malignancies.

EPIDEMIOLOGICAL DATA

14,800 new cases were diagnosed in Italy in 2023 (6,800 among men and **8,000** among women). The five-year survival rates are 11% and 12% respectively. In total, there are currently more than 21,200 men and women living with this type of cancer.

How does the disease manifest itself?

At the onset, it usually causes pain, jaundice (yellowing of the skin), and weight loss. There may also be less specific symptoms, such as acute or chronic diarrhoea and depression. Symptomatology depends on the location and extent of the carcinoma. Pain is present in 75-90% of cases, is continuous, and is often accentuated after meals and at night: it is also localised mainly in the upper abdomen radiating to the back. Weight loss is consistent, progressive, and associated with aversion to food. Diabetes is also associated in over 25% of patients.

Is it linked to certain hereditary genetic diseases?

There are proven links with multiple atypical familial melanoma syndrome, Peutz-Jeghers syndrome, hereditary pancreatitis, hereditary non-polyposis colorectal cancer, familial breast and ovarian carcinoma syndrome (BRCA), familial cystic fibrosis adenomatous polyposis, ataxia telangiectasia and Fanconi anaemia.

What examinations should be carried out?

For a correct diagnosis, ultrasound, abdominal CT scan, endoscopic ultrasound. and sometimes MRI are used. A positive diagnosis of the disease, however, is obtained with a biopsy.

Lung

MASSIMO DI MAIO

Lung cancer can develop from the cells that make up the bronchi, bronchioles, and alveoli, and can form a mass that obstructs the proper flow of air, or else can cause bleeding, or symptoms such as coughing or chest pain. A distinction is made between non-small cell lung cancer (the most common form) and small cell lung cancer (less frequent but more likely to have a clinically aggressive and rapid course).

EPIDEMIOLOGICAL DATA

The new diagnoses recorded in Italy in 2023 amounted to **44,000** (30,000 among men, and 14,000 among women). The 5-year survival rates amount to 16% and 23% respectively, but are naturally better in cases diagnosed at an early stage and worse in cases diagnosed at an advanced stage. In total, there are over 117,800 patients in our country living with lung cancer.

What are the symptoms?

The most frequent and common symptoms are a dry cough with phlegm (sometimes streaked with blood), difficulty breathing, minor bleeding with coughing, chest pain, weight loss, and fatigue. These symptoms are non-specific, meaning that they are not always indicative of lung cancer.

However, people considered to be at risk (such as heavy smokers) should not underestimate the symptoms.

What diagnostic tests are necessary?

The most advanced test for detecting the disease is the 3D spiral CT scan. In order to diagnose the disease by taking a piece of tissue, it is necessary to perform a bronchoscopy (which allows for a direct view of the bronchi) or percutaneous needle biopsy under CT guidance (which allows a few cells from the suspected lesion to be removed via a needle introduced from outside the chest wall).

Are there screening programmes for early diagnosis?

Clinical studies have shown that the use of low-dose spiral CT can reduce mortality in heavy smokers by about 20%. While there is still no public screening programme in Italy (like there is for breast and colorectal cancer), there is a ministerial programme, called the Italian Lung Screening Network (RISP – Rete Italiana Screening Polmonare), dedicated to men and women considered to be at risk (people between 55 and 75 years of age, who smoked at least one pack of cigarettes per day for more than 30 years, or heavy smokers who have quit within the last 15 years).

Prostate, kidneys, testicles, bladder

Genitourinary cancers account for about 20% of all cancers recorded in Italy.

Prostate cancer is the most frequent among the Italian male population, and usually does not manifest through specific signs or symptoms. It is often diagnosed in patients who undergo specialist urological examinations for urinary disorders associated with benign prostatic hyperplasia. **Testicular cancer is considered a "juvenile" form of cancer,** as it typically occurs between the ages of 14 and 45. It is a curable disease in the vast majority of cases, but can have **a strong negative impact on fertility**.

Kidney cancer is the fifth most common form of cancer in males. Several risk factors have been identified, related to either lifestyle (including smoking and obesity) or chronic disease (such as diabetes or hypertension). Certain chronic kidney diseases may also increase the risk of occurrence.

With bladder cancer, the main symptom is haematuria, or the presence of blood in the urine. The persistence or recurrence of this phenomenon is a red flag that should not be underestimated. This is especially true for men who are considered to be at risk, e.g. those over 50 or heavy smokers.

Nowadays medical specialists have various effective methods available for treating urological cancers. The traditional therapies, which have long been used, include surgery, radiotherapy, and chemotherapy. These have more recently been joined by immunotherapy

and targeted therapies.

Finally, **primary and secondary prevention is fundamental**. Therefore, in addition to a healthy lifestyle, it is also extremely important to undergo check-ups and medical examinations aimed at detecting genitourinary cancers early on.

For further insights and to learn more about the subject, scan the following QR code to view the Health Guide entitled “Dedicated to you - Male Cancer Prevention”, created by the IncontraDonna Foundation and the Italian State Railways Group for the new initiative aimed at the male population.

Stomach

EMILIO DI GIULIO

Cancer is caused by the formation of tissue consisting of cells that grow in an uncontrolled manner. 90% of cases of stomach cancer form in the inner wall of the stomach, and are called adenocarcinomas.

EPIDEMIOLOGICAL DATA

15,000 new cases were recorded last year (9,000 among men and 6,000 among women). The five-year survival rates are 30% and 35% respectively. It is estimated that there are currently 82,400 people in Italy living with a gastric cancer diagnosis.

Are the symptoms generic?

They can be mistaken for those of much less serious diseases, such as gastritis or ulcers. The most common symptoms experienced by patients are digestive problems, lack of appetite, feelings of nausea and vomiting, feelings of heaviness, pain or heartburn, difficulty swallowing, presence of blood in the stool or black stools, fatigue due to anaemia, and significant weight loss.

What is Helicobacter pylori?

It is a bacterium that can colonise the stomach lining (or gastric mucosa). It is a very common microorganism, and is responsible for ulcers and gastritis. Chronic infection can lead to stomach cancer in some cases, if left untreated. In fact, it is classified by the International Agency for Research on Cancer (IARC) as a type I carcinogen.

For this reason, the bacterium must be eradicated with antibiotics, to be prescribed by a physician. The cancer risk is reduced by eradication and endoscopic surveillance of any precancerous lesions that may have already developed.

How can the disease be detected?

Through gastroscopy and biopsy, which allow cancerous lesions to be definitively diagnosed through the collection and analysis of cells, or with a CT scan, which also allows the extent of the cancer to be assessed.

Thyroid

LAURA LOCATI

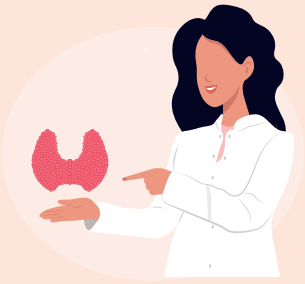
The thyroid is a gland located in the neck and, based on the type of cells from which it originates, thyroid cancer can be of two types. The first and most common is differentiated thyroid cancer, with its subtypes (papillary, follicular, etc.), which originates from the follicular cells (which synthesise the hormones thyroxine and triiodothyronine). The second, and much more rare form, is medullary thyroid cancer, which arises from the parafollicular cells that produce the hormone calcitonin.

EPIDEMIOLOGICAL DATA

The new diagnoses in 2023 amounted to approximately **12,200** (3,500 among men, and 8,700 among women). The five-year survival rates are 92% and 96% respectively. There are currently **212,900** people in Italy living with a thyroid cancer diagnosis.

What is the most common and widespread symptom?

Thyroid cancer manifests as an isolated lump inside the gland. It can be felt with the fingers when touching the neck in the area of the organ. However, not all thyroid nodules are forms of cancer. They are often just a sign of **thyroid hyperplasia**, a benign form of glandular growth. Moreover, thyroid functions are never altered by the presence of nodules, therefore the patient almost never complains of any specific disorder.



What are the main tests that allow a diagnosis to be made?

These include blood tests, ultrasound, fine-needle biopsy, and lymph node biopsy.

Are women at greater risk than men?

The disease if 4 times more likely to occur in women than in men. One of the various risk factors is iodine deficiency, which is also the main cause of goitre. This consists of a marked increase in the volume of the thyroid, characterised by numerous benign nodules in the gland. Another risk factor is exposure to ionising radiation. This type of cancer is more common among people who have undergone radiotherapy treatments on the neck, or have accidentally been exposed to high doses of ionising radiation (as was the case with the Chernobyl nuclear power plant disaster).

3.

In-depth analysis

Metabolic syndrome, diabetes, and obesity

GIUSEPPE PUGLIESE AND ANDREA LENZI

How common are diabetes and obesity?

Diabetes, especially type 2, is a rapidly spreading disease, especially in developing countries; in Italy, it is estimated that 6-7% of the population suffers from it. And this type 2 diabetes "pandemic" is linked to another "pandemic": that of obesity. In Italy, **about 36% of the population is overweight, and 12% is frankly obese**, with a worrisome increase in the number of overweight children, especially in the south.

How are diabetes, obesity, and metabolic syndrome defined?

Diabetes is a metabolic disorder caused by a defect in the secretion or peripheral action of insulin, and characterised by glucose levels of 126 mg/dl or more. Obesity, on the other hand, is a chronic condition characterised by excess fat mass, defined by a Body Mass Index (BMI) of 30 or greater (25 for overweight). BMI is determined by the dividing the subject's weight in kilograms (kg) by the square of their height in meters. Central obesity is an accumulation of fat at the abdominal level, defined by a waist circumference, measured at the navel, greater than 102 cm in males and 88 cm in females. It represents the lowest common denominator of metabolic syndrome, in which it is associated with type 2 diabetes or prediabetic condition, high blood pressure, and so-called atherogenic dyslipidaemia, or rather triglyceride levels above 150 mg/dl and HDL cholesterol levels below 40 mg/dl in males and 50 mg/dl in females.

What are these conditions caused by?

These conditions depend on multiple factors, and occur with genetic predisposition, combined with environmental factors and, in particular, unhealthy lifestyles, especially poor diet and sedentary habits.

How can they be prevented and treated?

Prevention is based on the adoption of a healthy lifestyle from childhood onwards, or, if this is not the case, changes in diet and physical activity as early as possible during adulthood. Such changes are of fundamental importance, even after these conditions have manifested themselves, together with the possible use of medications prescribed by a doctor.

Prevention is therefore essential, but the proper management of the condition once diagnosed is also extremely important to avoid potentially serious complications.

Healthy behaviour

8 ESSENTIAL FACTORS FOR LONGEVITY AND QUALITY OF LIFE

FOCUS: Obesity should not be considered "an individual's responsibility"

Obesity is not just a matter of individual choice or a consequence of their lifestyle.

Obesity is a chronic, progressive, and relapsing disease caused by a complex series of factors, including genetics, psychosocial factors, and environmental factors, and should be treated like any other disease. Citizens should be aware that it can be prevented with information, training, and education, and must therefore be recognised early on (both in themselves and in their children). In fact, many patients with obesity do not view themselves as such, and there are just as many parents who do realise that their children are obese. Society repudiates and invalidates obese people with social stigma and discrimination, and "blames" them for their condition.

Obesity, is also a risk factor for the development of numerous other diseases such as type 2 diabetes, cardio-cerebrovascular disease, respiratory disease, and cancer, and thus increases the risk of premature death.

In order to avert the spread of this disease, whose growth projections according to the WHO are worrisome for global health, we must to establish a multidisciplinary alliance, adopt a "one health" approach, and, **at the NHS level, include obesity in the National Chronicity Plan, which guarantees adequate and standardised care throughout the various regions**.

Watch the video interview on **"A silent pandemic: obesity"** with **ANDREA LENZI**, Professor Emeritus of Endocrinology at La Sapienza University of Rome.

Vaccinations

According to the World Health Organisation, **vaccinations are able to prevent between 2 and 3 million deaths each year** from the most well-known vaccine-preventable diseases, which, until about a century ago, were the main causes of death worldwide, even in the most developed countries.

Vaccination and immunisation programmes are therefore recognised as a **fundamental preventive health protection strategy** for protecting both the **individual** (before the infectious disease manifests itself) as well as the **public**, when vaccination is carried out on a large scale.

In fact, by reducing the number of people who are able to contract the infection and multiplying the protective effect thanks to what is known as **"herd immunity"**, vaccinations make it more difficult for the microbes responsible to spread and reproduce.

Vaccination is ageless!

As far as **children's health** is concerned, prophylactic vaccinations (a set of rules and methods for avoiding or preventing the spread of diseases) have led to a significant reduction in the number of serious illnesses, deaths, and disabilities among children worldwide.
For adolescents, the introduction of the Human Papilloma Virus (HPV) vaccine has significantly reduced cases of HPV-related cancers. However, despite these findings, there is still much to be done.
From the perspective of healthy ageing, **adult** vaccination is a key element in a society where people are enjoying increasing longevity, with a consequent increase in the prevalence of chronic diseases.
A major focus must be placed on **groups that are at-risk** due to age, illness, occupational exposure, or other conditions, for which a specific vaccination calendar is provided.

Vaccination fatigue and “fake news”

Despite the evidence, knowledge of the benefits of vaccinations among the population (especially those at risk) and **adherence to these preventive strategies is still too low** due to several factors, including the impact of the pandemic and so-called “vaccination fatigue”, and increasing access to misleading information.

Healthcare misinformation poses a serious risk to individuals and society as a whole. It is therefore **fundamentally important to increase trust between civil society and healthcare professionals**, through wide-reaching and authoritative information campaigns that make reference to official sources.

The IncontraDonna Foundation, which has always been on the side of patients and the public, **collaborates with the Ministry of Health to promote health communication and information campaigns**, and to encourage more accessible and effective protection and immunisation measures.

A good example of this synergy is the **Vaccine Calendar Disc**, a convenient reference tool to support the **#VaccinationHasNoAge** awareness campaign and in line with the 2023-2025 National Vaccine Prevention Plan.

The Vaccine Disc is distributed in conjunction with the Frecciarosa 2024 event and during other public activities promoted by the IncontraDonna Foundation, and can be viewed digitally on the Incontradonna.it website

RISK CATEGORIES BY AGE AND DISEASE

When associated with frequent concurrent diseases, an age-related decline in immune response can lead to increased susceptibility to infection and a greater risk of infectious disease severity in the elderly. Faced with an ageing population, this phenomenon poses and increasingly serious public health challenge.

In fact, diseases in the elderly tend to be more severe, and have a greater impact in terms of disability, reduced quality of life, and mortality.

Therefore, in order to guarantee the general population's continued good health into old age, as far as possible, and to prevent serious complications from infectious diseases in the chronically ill, the 2023–2025 NVPP promotes an expansion of the vaccines offered, and a progressive increase in vaccination coverage, with a particular focus on caring for the most vulnerable members of society.

Prevention is one of the most appropriate and cost-effective responses to the challenge of ensuring the best living conditions for everybody, as it helps to improve the health of an ageing population in a sustainable manner.

People ≥ 60 years of age

Flu vaccination: offered free of charge starting at the age of 60, in accordance with the annual indications contained in the Ministry of Health Memorandum.

Anti-pneumococcal vaccination: offered as a priority people 65 years of age, even together with or independently of the flu vaccination, and at any time of year.

Herpes Zoster vaccination: 1 or 2 doses depending on the age and condition of the patient, and the vaccine used, to be offered annually to those over 65 years of age and at-risk individuals over 18 years of age (2 doses). This vaccination can very effectively re-

duce the risk of developing herpes zoster (also known as Shingles) and post-herpetic neuralgia (one of the most frequent and debilitating complications of the disease).

People at risk of disease

In addition to age-based vaccination strategies, the 2023-2025 NVPP also provides for the recommended free vaccinations to be offered to people of all ages considered to be at risk of disease (e.g. people with cardiovascular, respiratory, onco-haematological, metabolic, or chronic kidney disease, as well as immunological disorders and HIV). This category of people is at increased risk of contracting invasive infectious diseases, and developing serious complications.

LET'S DISPEL A FEW DOUBTS

Which vaccinations are free?

In general, all those recommended based on age, pathological conditions, certain behaviours, or other conditions are actively offered free of charge, as indicated in the 2023-2025 National Vaccine Prevention Plan. There may be regional differences, with some regions having an expanded offering.

Can cancer patients get vaccinated?

Yes! Certain vaccinations are highly recommended for cancer patients and all those with whom they come into close contact. The recommended vaccinations are the following: flu, pneumococcal, SARS-CoV-2, and Shingles.

How do I book a vaccination?

Contact your doctor and/or the Public Health and Hygiene Service in your region.

For further information:
visit the Ministry of Health website (www.salute.gov.it)

MANIFESTO FOR THE ELIMINATION OF CANCERS CAUSED BY HUMAN PAPILLOMAVIRUS

Italy could be the first European country to completely eliminate all cancers caused by Human Papillomavirus by 2030.

For this reason, in March 2021, a group of Associations, including IncontraDonna, decided to lay out the critical issues that have emerged in the fight against HPV-related cancers (and which have been amplified by the Covid-19 pandemic) in a Manifesto, and launched an appeal to the Institutions and the public to improve our primary and secondary prevention activities, which are the only true weapons we have against cancers caused by Human Papillomavirus.

Watch the video interview on **"The importance of vaccinations in frail patients"** with **ROBERTO IERACI**, Infectologist, Lazio Region Vaccination Strategies.

Research and scientific innovation

LUCIA DEL MASTRO AND DAVIDE SOLDATO

Research and scientific innovation in female oncology

Research and scientific innovation play a fundamental role in improving the prognosis and quality of life in women diagnosed with cancer.

Among women, breast cancer is the type of cancer most frequently diagnosed. In Italy, the latest epidemiological data, published in "The Cancer Figures in Italy 2023", estimate 55,900 new cases diagnosed in 2023. The same report states that approximately 37,000 women in Italy are living with a diagnosis of metastatic breast cancer. Recent advances in cancer research and the availability of new drugs have led to a dramatic improvement in terms of prognoses. Today, over 90% of women are still ALIVE 10 years after being diagnosed with breast cancer, and the 5-year survival rate for women with metastatic cancer has increased by 16% over the past 20 years. Unfortunately, breast cancer is still the **leading cause of cancer death** among women, and it is therefore essential to continue to promote and support research aimed at further improving these results.

In recent years, thanks to scientific research and a better understanding of cancer, drugs have been able to be introduced that have revolutionised the treatment of women's cancers, and breast cancer in particular.

A better understanding of how cancer cells multiply has led to the development of "Cyclin-dependent kinase (CDK) inhibitors" for the treatment of women with breast cancer expressing receptors for female hormones. These drugs act in an intelligent manner to block cancer cell multiplication, and their use has dramatically improved survival for women with metastatic breast cancer, and has significantly reduced the *risk of recurrence for women with*

early-stage breast cancer.

Another important innovation has to do with the way in which cancer cells are targeted by drugs, for example thanks to the use of **"antibody-drug conjugates"**. These are drugs that selectively target cancer cells, releasing a chemotherapeutic agent into them, thus reducing their action on the body's normal cells and therefore limiting side effects. These drugs are now used to treat all forms of metastatic breast cancer, and have been shown to improve survival rates with respect to conventional chemotherapy drugs.

Thanks to scientific research, it has been possible to develop strategies to reduce the use of certain treatments without increasing the risk of recurrence, for example **through the use of genomic tests.** These tests make it possible to analyse tumour tissue in greater depth, and to determine whether or not chemotherapy should be administered as a preventive measure after the surgical removal of the breast cancer expressing receptors for female hormones.

Finally, scientific research has led to numerous achievements in terms of improving quality of life for women suffering from breast cancer. These include, for example, the introduction of new drugs to reduce side effects, the use of new strategies to preserve ovarian function and maintain fertility in young women, and an increased focus on integrated strategies aimed at preserving women's physical well-being both during and after treatment.

Similar results have been obtained with other cancers affecting women. Examples include the use of innovative drugs for the treatment of ovarian cancer in the presence of specific gene alterations, the introduction of immunotherapy for the treatment of endometrial and cervical cancer, and the introduction of HPV vaccination campaigns for the latter as well.

Metastatic: main innovations

GIACOMO BARCHIESI AND GABRIELE PIESCO

What are metastases?

Metastases are aggregates of cancer cells that acquire the ability to migrate from the primary tumour that has arisen in a given organ (breast, lung, colon, ovary, etc.) and to multiply at a distance through lymphatic and blood vessels, without responding to any of the body's defence mechanisms.
Only the cells of malignant tumours, and not those of benign tumours, are able to metastasise.
In most cases, metastatic diseases are cannot be cured, but they certainly can be treated, or rather controlled and made chronic with drugs.

Where are metastases mainly located?

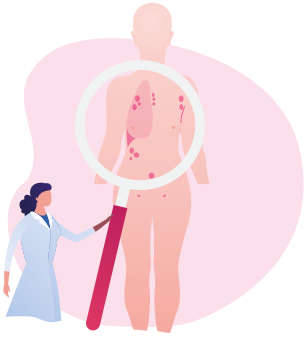
Although a malignant tumour can potentially form metastases in any organ, some types of cancer tend to metastasise to specific areas. For example, breast cancer mainly metastasises to *the bones, lungs, liver, and brain*, while ovarian tumours tend to metastasise in the peritoneal cavity. The site of metastasis is influenced by the ease with which the cancer cells are able to reach it, and by the presence of molecules that facilitate their rooting and proliferation.

How can metastases manifest themselves?

Not all tumours have the same propensity to metastasise. In some cases metastases form after a long time. In others, there's a rapid evolution, and metastases are already present at the time of diagnosis. Sometimes the tumour is discovered after symptoms specifically related to the metastases have manifested. For example, liver metastases can cause **jaundice** (yellowing of the skin and the whites of the eyes), abdominal pain, and changes in digestion; bone metastases can cause pain and potential fractures; lung metastases can create breathing difficulties; brain metastases can cause headaches and neurological symptoms.

What are the treatments for metastatic tumours?

There are numerous pharmacological options for successfully dealing with this condition, and they vary depending on the type of tumour: chemotherapy, molecular-targeted therapies, immunotherapy, and hormone therapy, often used in combination.



The goal in modern oncology is **increasingly personalised and precision medicine, aimed at finding specific genetic mutations based on which increasingly selective drugs can be chosen**, thus increasing the likelihood of prolonged disease control. Such precision (molecular-targeted) drugs are often better tolerated than chemotherapy, because they specifically target cancer cells without damaging the body's healthy cells.

In general, however, the treatments offered today (including chemotherapy) are well tolerated, guaranteeing good quality of life for working, family, and intimate relationships.

The use of many of these drugs requires molecular assessments to be performed either on the tumour tissue sample (immunohistochemistry, FISH and NGS) or by taking blood samples (genetic tests and liquid biopsies).

Liquid biopsy is an extremely valuable and non-invasive diagnostic test: it consists of a **simple blood sample with which circulating tumour DNA is intercepted, allowing the DNA mutations to be identified**, thus enabling the oncologist to determine the most suitable type of therapy for the individual patient with greater precision.

Personalised medicine

PAOLO MARCHETTI AND ANDREA BOTTICELLI

What is Personalised Medicine?

Personalised Medicine (PM) consists of identifying the genetic, clinical, environmental, and behavioural characteristics specific to each patient, in order to identify the most appropriate preventive and/or treatment strategies for that individual, with the highest probability of clinical success, and the lowest probability of adverse effects or ineffectiveness.

With Personalised Medicine, the medical strategies focus on the patient, and not just the disease.

Precision Medicine is thus transformed into Personalised Medicine through modern technologies aimed at identifying the unique characteristics of the patient and the disease. **Since each of us metabolises drugs differently, the effects of those drugs and their toxicity is unique to each individual**. Today, we are able to study the alterations in the genes involved in drug metabolism, and can know ahead of time whether the drug will be more or less effective, or will have adverse effects on the patient. This is one of the pillars upon which treatment personalisation is based.
The assessment of any interactions between all the drugs being taken is also a factor that will determine the success or failure of a given drug.

On average, individuals over the age of 65 take 1 to 3 drugs, those over 70 take over 5 different drugs, and hospitalised patients take up to 8 different drugs. Different drugs can interact with each other, and this can increase or decrease the effectiveness of the drugs themselves. The effect that **drug interactions** have on the effectiveness of treatments in patients with oestrogen-positive breast

cancer treated with molecularly targeted drugs (the “cyclins”) has been demonstrated and published. **Today, we are able to study drug interactions, personalise the treatments, and create personal identity cards for each patient.**

The treatment is personalised based on the characteristics of the cancer. Every cancer is different. By studying the mutations, or rather the alterations in the DNA of the cancer cells, is its now possible to determine the prognosis (or rather the course) of the disease, **as well as the drugs to which the cancer is most likely to respond. Another frontier is liquid biopsy, or rather the study of mutations with a simple blood sample.** While it is not possible to diagnose the presence of breast cancer through liquid biopsy, it is possible to obtain very important information that allows for a more accurate, and above all personalised, treatment selection. For example, this type of test, which is capable of detecting ESR1 mutations, is crucial for the selection of treatment with oral drugs, such as Elacestrant, in HR+ breast cancer patients.

For example, breast cancers with an overexpression of the HER-2 protein (meaning that the histological examination returns a positive result for this protein, called c-erb) are sensitive to molecularly targeted drugs (smart drugs, targeted drugs, etc.) like Trastuzumab, Pertuzumab, Lapatinib, and TD-M1. Likewise, lung cancers characterised by EGFR gene mutations are sensitive to molecularly targeted drugs like Osimertinib, Gefitinib, Erlotinib, and Afatinib. These are just a small sample of the currently available treatment options.

What are antibody-drug conjugates?

The real new frontier in cancer treatment is the introduction of Antibody-drug conjugates (ADCs). ADCs are smart drugs that use monoclonal antibodies as a sort of Trojan horse to transport chemotherapeutics into cancer cells only. **These new drugs combine the precision of monoclonal antibodies with the action of chemotherapy**, increasing their efficacy and decreasing their side effects. The most important include Trastuzumab deruxtecan for patients

with both HER2+ and HER2 low breast cancer. and sacituzumab govitecan for patients with Triple Negative breast cancer.

Mutational oncology and genomic testing for treatment determination

Multi-gene, molecular, and NGS (next generation sequencing) testing involve the analysis of 50, 300, even up to more than 500 genes in the neoplasm. This makes it possible to identify gene mutations, or rather **information that is essential for understanding sensitivity to molecularly targeted drugs, as well as for determining resistance**. A new pathway of precision medicine, of personalised oncology, is emerging, which does not only consist of molecular testing, but rather focuses on mutation. This new pathway involves a number of fundamental steps aimed at determining **the right drug, for the right patient, at the right time**.

The fundamental steps are the following:

1. The right indication for the test, and the right time for testing
2. The interpretation of the test result (very often difficult to interpret)
3. The choice of the right treatment
4. The possibility of creating a network among professionals (not only oncologists) in order to guarantee access to the most innovative drugs.

This pathway must be regulated and controlled by the **Molecular Tumour Board (MTB)**, a group of specialists (including an oncologist, a molecular biologist, and an anatomopathologist) who will be present throughout each stage of the pathway. The challenge in the coming years will be to guarantee this pathway to all patients.

Genomic testing for determining risk of recurrence

Another possible application of multigenic testing is to determine the risk of the cancer recurring in patients who have undergone breast cancer surgery. These types of tests (such as

Oncotype, Mammaprint, Prosigna, etc.) provide a recurrence **risk score**, which **can help oncologists determine which patients require adjuvant/preventive chemotherapy treatment** (i.e. after surgery), and which patients **only require anti-hormonal therapy.**

The combination of the information obtained from studying the patient, the cancer, the drugs administered, and the microbiota now represents a major opportunity, and is the ultimate expression of Personalised Medicine.

Watch the video interview on **"Innovative and treatment in breast cancer: what point are we at?"** with **GIUSEPPE CURIGLIANO**, Oncologist, European Institute of Oncology and University of Milan, Presidect-elect ESMO.

Immunotherapy

PAOLO MARCHETTI AND ANDREA BOTTICELLI

Thus far, the weapons at our disposal in the fight against cancer have been surgery, chemotherapy, hormone therapy, molecular targeted therapy, and radiotherapy. Yet our bodies possess another extremely effective weapon, which not only protects us against infection, but also against cancer.

In fact, the purpose of our immune system is to recognise anything that is foreign, and therefore potentially harmful, to the body, and to destroy it.
In the early stages of a cancer's development, the immune system is able to recognise and destroy it. At later stages, cancer cells are able to hide from the immune system, block it, and grow into a clinically evident tumour.

Immunotherapy is specifically aimed at educating the immune system to once again recognise cancer cells and destroy them. The immunotherapy revolution has initially focused on metastatic melanoma, increasing our patients' survival rates and quality of life. Immunotherapy is now used daily to treat melanoma, lung cancer, kidney cancer, gynaecological cancers, and head and neck cancers, and, in recent months, has also been used to treat both triple-negative and metastatic breast cancer. The latest innovation in the field of immunotherapy has been its use in the neoadjuvant phase for patients with triple-negative breast cancer. In this phase, it allows for the complete eradication of the disease in about 60% of patients. The indication of this treatment and the control and prevention of the side effects are guaranteed within the Breast Units thanks to the collaboration of the various specialists involved in the pathway.

Doctor-patient-caregiver communication

ANNA COSTANTINI

A recent Italian multi-centre study conducted among patients with advanced stage cancer showed that 49% lack correct information about their prognosis, 60% believe that their family is shielding them from bad news, and 56% would like to talk more about their disease with their relatives.

Systematic surveys have shown that cancer patients would like to receive more information about their disease, future symptoms and how to manage them, treatment options, and life expectancy, in ways that differ from person to person. In general, they would like to dialogue with a doctor who is empathetic and asks them questions. But talking about cancer isn't easy for anybody. Cancer is still something that instils a great deal of fear in the general population. It can strike at any age, it can change our outlook on life, and can alter our roles both inside and outside the family. Previous experiences interfere in our relationships with people who have fallen ill, by influencing the words we choose, in most cases not always in a conscientious manner. It is important to pay attention to how we communicate, for various reasons: first, because words have a psychological effect; second, because we cannot avoid communicating, and we must therefore choose whether to communicate what we really want to, or something else. While there are no absolute right or wrong things to say, when dealing with a person suffering from an illness there are certain general indications that can help facilitate communication, convey the right information, and offer support to the patient:

1. **Communicate conscientiously:** saying things like, “Everything is going to be fine”, “Everything will work out”, “You’ve been cured, take it easy”, or “Don’t worry, the scan will be fine”, might offer premature reassurance and provide a degree of immediate relief, but can cause greater disappointment afterwards if they turn out to have been a source of false hope. Saying “Don't worry” can also convey the idea that we are unwilling to listen to the person’s fears. Another thing that people often say is: “You’re strong, you have to fight this”, which, in a certain sense, implies that it is not good to show weakness or to express anxiety, thus impeding the possibility of sharing negative thoughts.
2. **Be careful not to draw comparisons:** don’t say things like, “If I were in your place”, of “If it were my father going through this.” You are not the patient, and the patient is not your father. People have different life stories, personality traits, and ways of coping with stressful events.
3. **The importance of non-verbal communication:** communication is not only verbal. Your tone of voice, expression, and posture are immediately grasped, long before any words are stated. Using a solemn or awkward tone, avoiding eye contact, or expressing exaggerated optimism when not appropriate for the situation can communicate that something is wrong and that you’re trying to hide it.
4. **Remember that cancer can lead to depression or anxiety, even in those who have never suffered from these conditions.** Seeing a loved one demoralised or depressed is painful. It can make us feel powerless, and reacting by saying things like, “Cheer up! It’ll be worse if you let it get you down”, “You shouldn’t even be thinking about certain things,” or “You have to stay positive to help the recovery process”, which aren't even based on scientific data, can lead to feelings of guilt, due to the belief that their thoughts and feelings are making things worse.
5. **Be aware that emotions can cause embarrassment,** and the fear of not knowing how to handle them can sometimes lead us to block or minimise them by changing the subject, giving unsolicited practical advice (“Try to think about other things”, “Try that supplement, it's miraculous”), or making claims like “You’ve be cured, take it easy.” Saying things like this will result in the patient feeling that they’re

not understood or that they can't freely express their emotions, prompting them to repress them in the future, thus leading to feelings of loneliness.

6. **Treating the patient like he/she always needs to be protected** and is no longer able to make decisions on his/her own is not always effective. Saying things like "Just let everybody else handle everything", "Let me talk to the doctors", or "Don't you worry about anything" is acceptable at certain stages of the treatment pathway, but helping the person maintain a sense of identity and a certain level of autonomy can also prevent them from feeling demoralised.
7. **Answering questions while first trying to understand what the person really wants to know**, and how he or she wants to be told, thus facilitating personalised communication.
8. **Helping the patient understand what is going on** restores a general sense of control, which an illness like cancer tends to take away, and prevents psychic regression, which in turn can fuel feelings of helplessness.
9. **How do you start talking?** It's not easy to overcome the speechlessness we face when attempting to engage in a personal dialogue with a loved one who has fallen ill. Nor is it easy for a doctor, who, despite having been trained in the technical aspects of the illness, has not necessarily been trained to handle difficult intimate and existential conversations. One useful suggestion is to always begin with an open question like, "How are you doing?", because the person will naturally begin talking about the thing that's most important to them. Asking "How are you feeling?" also communicates interest in the person's subjective experience, a willingness to listen, and solicits a reply. Finally, it is important to listen to the patient without interrupting them with premature reassurances or minimisation, so that the patient is able to indicate how he/she wants to continue the discourse, as well as his/her needs and limits.
10. **Each person their own individual ways** of dealing with difficult situations, and their own points of weakness. Not everyone likes to talk about it in the same way or at the same moments. There are even those who prefer not to talk about it at all, and to think about other things. The patient's personal preferences should always be respected.

11. **If an authentic channel of communication is opened up, emotions should be expected**, both on our own part, and on the part of the patient. Cancer is a trying situation for everyone. It is therefore important to be prepared, not to be frightened by the emotions, and to express your sorrow in a genuine fashion. The point is that we cannot resolve the patient's health problems or prevent their suffering, but **we can be supportive by expressing genuine interest and empathy**.
12. **Feeling one's emotional experience acknowledged** makes one feel more profoundly understood, and decreases the intensity of the emotions. Empathy is one of the most powerful support tools for modulating emotions. It consists of the ability to understand how a person is coping with difficult situation, to see it from their perspective, and to communicate that understanding to them. For example, instead of saying, "Cheer up, everything will be fine", one can say: "This treatment must have been really hard for you to cope with", or "You must have been very disappointed with the results of the CT scan."
13. **Our sources of hope can change.** While the only hope we are able to give is that of winning the war against cancer, sometimes we win it, and sometimes we lose it. It is therefore better to help the individual find difference sources of hope. For example, one can give hope by highlighting the successes achieved in the field of medicine and in clinical trials, by being there, by saying things like "I'll always be there for you", "We can talk whenever you want", "I'm here to support you in your decisions", by using appropriate terms like "chronic" rather than "incurable", or by helping to maintain a sense of worth, saying "Being brave doesn't mean not being afraid, but being able to cope", or "Being strong doesn't mean not feeling scared or discouraged."
14. **Human beings need to have a reason to live, and it is therefore important to encourage them to find meaning:** "Even if you're sick, you're still a father, a husband, and a role model", or "You can live with your illness and still maintain your dignity, your identity, and your sense of self worth." Austrian psychiatrist Viktor Frankl wrote: "If you don't like something, change it. If you can't change it, change your attitude." More recently, on the other hand, Vialli wrote: "Life is made up of 10 percent of what happens to us, and 90 percent of how we deal with it."

Patient and caregiver rights

ELISABETTA IANNELLI

Information about the rights of cancer patients and their caregivers

Life expectancy for cancer patients has improved dramatically in recent years: for many cancers, scientific research and medicine have changed the clinical course of the disease, to the point that, in many cases, complete **remission or long-term chronicity can be achieved**. Life after cancer is an increasing possibility, and is no longer a distant hope. As a result, the **extra-medical needs** of patients and their families have also changed, and these must be met by strong, concrete social, economic and, above all, labour market responses. The fragile conditions brought about by the disease are an obstacle to returning to normal life, and one must be aware of one's rights in order to be able to assert and exercise them effectively within every social and healthcare context.

It's a complex and multifaceted subject matter. The information herein is provided in summary form in order to help patients and their family members orient themselves, and is taken from the following publications by the Italian Association of Cancer Patients, Relatives and Friends (AIMaC) edited by Atty. Elisabetta Iannelli, with critical review by the INPS General Medical-Legal Coordination: **"The rights of cancer patients"** e **"The right to cancer confidentiality"**, from which the following information was taken.

Exemption from out-of-pocket payment due to illness or disability

Cancer patients are entitled to an exemption from out-of-pocket payments for illness **(code 048)** in order to obtain appropriate

drugs, examinations, and tests for the treatment of their cancer and any complications, as well as for rehabilitation and the prevention of further relapses. **Recognition of 100% civil disability entitles the patient to total exemption (cod. C01) from any out-of-pocket expenses for drugs and medical visits associated with any illness.**

Welfare protection (civil disability)

The Decree of Italy's Ministry of Health of 05/02/1992 provides for the recognition of specific percentages of civil disability for cancer patients experiencing certain levels of disease severity: 11%, 70% and 100%. Depending on the type of disability recognised, and their financial situation, patients can obtain the following benefits:

- **disability pension (100% disability);**
- **disability allowance (74% to 99% disability);**
- **accompaniment allowance;**
- **attendance allowance.**

In order to access legal and economic benefits, cancer patients must apply to INPS to have their **disability and handicap status** assessed. The procedure for submitting the application to INPS electronically consists of two stages:

1. digital medical certificate issued by a certifying doctor accredited by INPS (*general practitioner or specialist*), who must complete the required medical certificate online via the INPS website. It must be verified that the case was initiated for cancer (Law 80/2006). INPS must then summon the individual and provide the commission's response within 15 days;
2. completion and electronic submission of the administrative application (linked to the cancer certificate) by the individual concerned, either personally, through a delegate, or through an authorised intermediary (tutelage);

Handicap

It is possible that the cancer patient's health conditions could become seriously impaired due to the progression of the disease and the effects of the anti-cancer treatments; in these cases, it is recommended to apply to INPS, preferably in conjunction with the

application for civil disability, for verification of handicapped status under severe circumstances, *which may even be recognised for a limited period of time*.

A number of tax benefits and important occupational protections are associated with handicapped status under severe circumstances: **the law allows severely disabled workers and, to varying degrees, workers assisting severely disabled family members, to take leaves of absence (paid and unpaid), to choose their place of work and working hours (part-time), and to enjoy other benefits aimed at facilitating the performance of their healthcare assistance and work related duties.**

Rights at the workplace

Certain work-related benefits are determined by ascertaining specific disability percentages, others by ascertaining "handicapped status under severe circumstances," and others still by fulfilling the legal requirements for the right of disabled persons to work.

Choice of work location and opposition to transfer

A worker suffering from cancer, who is recognised as having a "severe" handicap, can ask to be transferred to the place of work closest to his/her home, and may not be transferred without his/her consent.

Change of work duties and night work

Cancer patients have the right to be assigned to duties suitable for their altered working capacity, and may be assigned to duties equivalent or even inferior to those previously performed, provided that they are compatible with their conditions, while maintaining the same remuneration associated with their previous duties. In addition, workers suffering from cancer may request not to be assigned to or to be exempted from working at night by presenting a medical certificate attesting to their unfitness for the performance of such duties.

Part-time and smart working

An employee suffering from cancer may take advantage of certain

forms of flexibility in order **to facilitate the performance of their healthcare and work related activities**, and is entitled to have his/her working hours converted from full-time to part-time, retaining the right to return to full-time once their health conditions permit. **Smart working**, or agile working, is another form of flexible working that allows workers suffering from cancer to continue working even during treatment, but without going to the workplace. The remote working or smart working agreement between the worker and the employer must be formally documented in writing, and, among other things, must specify the activities to be performed, the manner in which they are to be performed, and the *right to "disconnect"*.

Exemption from mandatory availability during illness

Since an individual's illness status justifies their absence from work and the right to receive sick pay, a sick employee is normally required to render themselves available at the domicile indicated in the event that the employer or INPS should request a follow-up visit. However, it should be noted that employees (both public and private) are expressly exempted from the obligation to render themselves available if their absence is due to a serious illnesses (such as cancer) requiring life-saving treatments, or to pathological conditions associated with a recognised disability greater than or equal to 67%.

Leaves of absence

Workers suffering from cancer, recognised as disabled or severely handicapped, are entitled to the following leaves of absence:

- **work absences** (3 days/month or 2 hours/day - law 104/92);
- **work absences for special events and reasons** (3 days/year);
- **health absences** for individuals with over 50% disability (30 working days/year).

Absence for life-saving treatment

Some collective labour agreements (CCNLs) specifically protect

workers suffering from cancer and other serious illnesses requiring life-saving treatment, by stipulating that days of hospitalisation or day hospital treatment, as well as days of absence to undergo treatment, are excluded from the standard calculation of days of sick leave, and are paid in full.

VAT-registered workers

If forced to suspend their work activity even temporarily due to cancer and related treatments, self-employed workers enrolled in the INPS separate management scheme and freelance professionals enrolled in their respective social security funds can gain access to different forms of financial aid, governed by sector regulations.

Social security protection

Regardless of civil disability status, a worker suffering from cancer and with a certain contribution seniority (5 years for INPS) can ask the social security institution to which he belongs for a medical/legal recognition of their reduced working capacity **(so-called "pensionable disability")** in order to obtain ordinary "social security" disability allowance, if it is established that their working capacity is reduced by less than one third, or, , in the case of total disability, to obtain disability pension (reversible), calculated based on their social security situation. An patient who is not hospitalised, is receiving a social security disability pension and meets the conditions for accompaniment (need for continuous assistance to walk or carry out daily activities) may apply for a monthly allowance for ongoing personal assistance (non-reversible).

Early pension

Cancer patients with a recognised civil disability of over 75% are entitled to the benefit of **2 months notional contribution**, useful for pension purposes, for each year of service actually rendered in disabled condition. The benefit is recognised up to a maximum of 5 years of notional contribution.

Free circulation and parking permit

Cancer patients undergoing treatment can apply for and obtain a

free circulation and parking permit from their municipality of residence, which is personal, and can only be used when the vehicle is at the service of the permit holder.

Cancer confidentiality

On 2 January 2024, Law no. 193/2023 "*Provisions for the prevention of discrimination and protection of the rights of persons who have suffered from cancer*", better known as the **Law on Cancer Confidentiality**, came into force.
This law enshrines the right of cancer survivors not to provide information or to be investigated with regard to their prior illness, and not to be discriminated against because of it. Any cancer survivor whose therapeutic treatment has been completed without any relapses, for more than ten years for adults or five years for cancers diagnosed before the age of 21, has the right to cancer confidentiality. The purpose of the law is to eliminate any form of prejudice or unequal treatment for cancer survivors. The protection and prevention of discrimination against cancer survivors *concerns the banking and financial sectors in general (mortgages, loans), insurance, the possibility of adopting a child, employment, and inclusion at the workplace*.

Caregivers' rights

Cancer and cancer treatments put a strain on families on an emotional level, as well as on a financial and practical level. If the caregiver is working, the law provides several instruments to protect his or her rights, in order to enable him or her to balance their work time with caring for the cancer patient, recognised as disabled or severely handicapped, including the right:

- **to choose the work place closest to the assisted person's home, without the possibility of being transferred;**
- **to make use of work absences (3 days/month - law 104/92);**
- **to take an extraordinary two-year paid leave;**
- **to have priority in switching from full-time to part-time work hours;**
- **not to be assigned to work night shifts;**
- **to make use of "solidarity" holidays and rest periods.**

Once again for this 2024 edition, the AIOM and the AIOM Foundation decided to adhere to a prevention initiative targeting the entire population. The AIOM is a Scientific Association that has represented one of our National Health System's main fields of excellence since 1973: **Medical Oncology**. The AIOM Foundation, on the other hand, was established in 2005 to bring together doctors, nurses, and patient association representatives within a single organisation. We tackle the fight against cancer across the board.

Cancers are a heterogeneous group of diseases, and in 2023 there were an estimated 395,000 new diagnoses in Italy (208,000 in men and 187,000 in women). In the post-pandemic era, we are experiencing a wave of cases. Specifically, in three years' time, the number of diagnoses increased by 18,400 (it was 376,600 in 2020).
At the same time, cancer is an increasingly treatable and curable disease. Many patients manage to overcome it, and can thus return to life *"as usual"*. **Moreover, in 13 years (2007 to 2019), more than 268,000 cancer deaths have been avoided, mainly thanks to treatment innovations.**
However, prevention remains by far one of the most effective tools at our disposal. Just following a few simple rules every day is enough to avoid extremely serious health problems. In other words, it is always better to play it safe against cancer, by maintaining a healthy lifestyle, every day. Everyone must make it an absolute priority to strengthen the culture of prevention (both primary and secondary). We must start by educating our young people, and promoting screening among the target population.
These are the reasons for which we have decided to renew our contribution to the preparation of the new Guide.

Francesco Perrone, President of the AIOM
Saverio Cinieri, President of the AIOM Foundation

The IncontraDonna Foundation is a non-profit organisation that, thanks to the authority of its Scientific Committee and the experience of its patients, is now among Italy's main associations dedicated to the national health system.

In particular, the Foundation works:

- **To actively stimulate dialogue between Institutions**, Scientific Communities, and Associations, for a health system that's increasingly based on equity, innovation, and accessibility, based on the needs of cancer patients and the public, with a particular focus on breast cancer.
- **To raise awareness of the importance of prevention and spread knowledge about healthy lifestyles**.
- **To improve the population's knowledge** of the services offered by the National Health System.
- **To support patients and their caregivers**, even by offering free mind & body, sports, and wellness activities.
- **To provide training for patients, caregivers, volunteers and healthcare personnel** (CME courses).

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