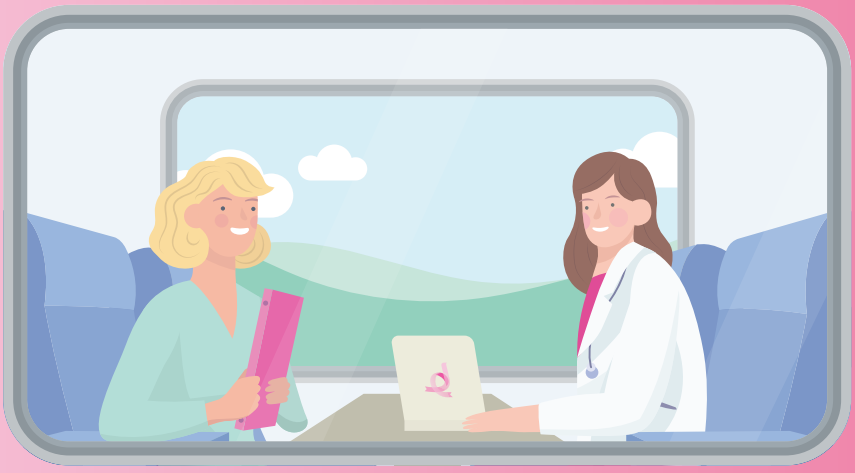
FRECCIAROSA

LA PREVENZIONE VIAGGIA IN TRENO

HEALTH GUIDE



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FRECCIAROSA

LA PREVENZIONE VIAGGIA IN TRENO

HEALTH GUIDE

October 2023 edition

FONDAZIONE Incontra donna

OCCUPIAMOCI DI SALUTE

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Dear travellers,

As both a doctor and as the Minister of Health, I take particular pride in presenting the latest edition of the valuable Health Guide produced each year as part of the Frecciarosa breast cancer prevention project, which is promoted by the IncontraDonna Foundation in collaboration with Ferrovie Dello Stato Italiane Group, and with the sponsorship of the Ministry of Health.

Throughout the years, this initiative has reached thousands of people aboard our nation's trains, providing free medical examinations and useful information, and helping to disseminate the culture of prevention and healthy lifestyles.

I firmly believe that the fight against cancer can only be won through major investments in prevention activities. Since the early days of my term, I placed the promotion of healthy lifestyles at the top of my agenda, and immediately re-launched the awareness-raising activities regarding the available screening programmes, also to make up for the waiting times accumulated during the pandemic.

Now more than ever, we understand that investing in prevention and health education is the key to building healthier societies and improving everyone's lives.

I am confident that, with everyone's cooperation, we will get a lot done, and will achieve the goals that we have set for ourselves.

Happy travels

Orazio Schillaci
The Minister of Health

Welcome back to the 2023 Frecciarosa project!

The entire month of October is dedicated to breast cancer prevention. For the IncontraDonna Foundation, it's an opportunity to inform, engage with, and offer free advice to the people travelling on Ferrovie dello Stato Italiane trains.

We've been by your side for 13 years. 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 FrecciaLounges, and can even be downloaded free of charge from our website (www.incontradonna.it). We therefore invite you to share it with friends and acquaintances, and to leave copies at the workplace. Let's not miss out on this opportunity!

I would like to thank the tireless IncontraDonna Volunteers who will be accompanying you on your train journey, as well as the doctors who, with the utmost professionalism and empathy, will be offering free consultations this month.

Now for a few words about the new Guide.

Being Healthy. That's the purpose of this Guide. How to deal with prevention, and, in the case of an existing oncological condition, how to stay healthy and get more insight, in order to better cope with the various treatment pathways.

The Guide has been broken down into various sections: Primary Prevention, Secondary Prevention in Oncology, Treatment in Oncology, and Support.

Primary Prevention

This consists of the various activities, interventions, and measures taken to prevent the onset of diseases in healthy individuals

Secondary Prevention in Oncology

This consists of the various activities and interventions aimed at recognising a condition (in this case an oncological condition) before symptoms arise. The goal is for the condition to be identified at a very early stage so that it can be treated, in order to avoid the least favourable outcomes. The most common and frequently encountered oncological conditions will be examined, categorised by the organ affected. Leading national experts will illustrate the various diagnostic possibilities, with the supervision and intervention of the Ministry of Health. There is also Tertiary Prevention, which is not covered in the Guide, and consists of actions and activities aimed at limiting the complex effects of these conditions.

Treatment in Oncology

There is a great deal of Science and Research taking place in the field of Oncology. Over the past 10 to 15 years, we have witnessed a true revolution in cancer treatment. Advancements include personalised medicine, immunotherapy, genomics, molecular investigations, and increasingly specific pharmacological cancer fighting treatments, even with excellent results and maintaining the patient's quality of life. There are still various critical issues to be tackled, as well as inequities with respect to the availability of the most innovative drugs, and there remains a cultural resistance within Italy to enrolling patients in clinical trials. Our goal is to work with patients through education and engagement in order to achieve increasingly effective results in terms of controlling these diseases.

Support

Doctor-patient communication and the involvement of caregivers (those who assist the patient throughout their cancer journey) are key aspects of effective treatment. And the rights of cancer patients are equally important. It is important for cancer patients to be made aware of the most important regulations to which they can refer. Happy reading!

Adriana Bonifacino, President of the IncontraDonna Foundation

Nutrition

ANTONIO MOSCHETTA

Despite the fact that the link between food and health has been studied since ancient times, the fact that a healthy lifestyle is essential for prolonging and improving quality of life is a concept that has only arisen in the modern era.

Generally speaking, healthy lifestyles and a varied diet that provides the body with different nutrients allow the body to prevent the onset of chronic degenerative diseases.

In 2010, UNESCO recognised the Mediterranean Diet as a protected asset, and included it among its Masterpieces of the Oral and Intangible Heritage of Humanity, where it is defined as a model inspired by dietary patterns that were widespread in certain Mediterranean countries in the 1950s (such as southern Italy, Spain and Greece). This diet is characterised by conviviality, and the regular consumption of specific foods, such as grains, fruit, vegetables, seeds, extra virgin olive oil, the rare use of red meat and animal fats, and moderate consumption of fish, white meat (poultry), legumes, eggs, dairy products, red wine and sweets.

Due to its high content of unsaturated fats, fibre, vitamins and trace elements, the Mediterranean diet has a significant anti-inflammatory and anti-oxidant effect, which can help balance the intestinal bacterial flora, thus preserving the metabolism of the entire organism. In the 1990s, the European Prospective Investigation into Cancer and nutrition (the EPIC study) established the importance of the Mediterranean

Diet, showing how greater adherence to this lifestyle reduced the risk of developing cancer. In addition, a 2016 Spanish study analysed the breast cancer rate among women 60 to 80 years of age, and showed that adherence to the Mediterranean diet reduced the number of breast cancer cases. It is therefore extremely important to understand whether and the extent to which we are really adhering to the Mediterranean Diet. By filling out a questionnaire that assesses adherence to the Mediterranean Diet, such as the Chrono med diet score (www.chronomeddiet.org), it is currently possible to associate the consumption parameters of the various food groups with the subject's lifestyle, allowing the individual's cardiovascular risk factor to be calculated in a matter of minutes. This score also takes into account eating schedules, nutrient quantity and quality, and personal care through exercise, thus allowing for an effective assessment of the individual, and the possibility of identifying tailored pathways based on the patient's specific needs and metabolic characteristics.

It is therefore fundamentally important for people to understand how a diet that is consistent with the Mediterranean model, based on predominantly daytime food intake (daytime chronotype), and avoiding excessive food consumption at night (night-time chronotype), can help prevent the onset of numerous conditions, by maintaining both the body and the intestinal bacterial flora in a good state of health.

The "Guide" is intended to provide families and consumers with practical tips for increasing their fruit and vegetable consumption.

Metabolic syndrome

GIUSEPPE PUGLIESE

Metabolic syndrome is not a disease, but rather a series of symptoms and signs indicative of high metabolic and cardiovascular risk.

How is metabolic syndrome defined?

Metabolic syndrome is defined as the presence of at least 3 of the following conditions:

- Central obesity, or rather an accumulation of fat at the abdominal level, which is diagnosed by measuring the circumference of the waist at the navel. This measurement should generally be less than 102 cm for men, and 88 cm for women.
- High blood pressure, or rather blood pressure values above 130 mmHg for systolic and 80 mmHg for diastolic, or ongoing treatment with anti-hypertensive drugs.
- Elevated triglycerides, or rather blood triglyceride levels above 150 mg/dl, or related ongoing treatment.
- Low HDL cholesterol levels, below 40 mg/dl in mean, and below 50 mg/dl in women.
- Prediabetes, or rather impaired fasting blood glucose or impaired glucose tolerance, or else manifest diabetes, or specific related ongoing treatment.

How can metabolic syndrome be prevented?

The prevention of metabolic syndrome, as well as that of type 2 diabetes, requires 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.

What are the risks associated with metabolic syndrome?

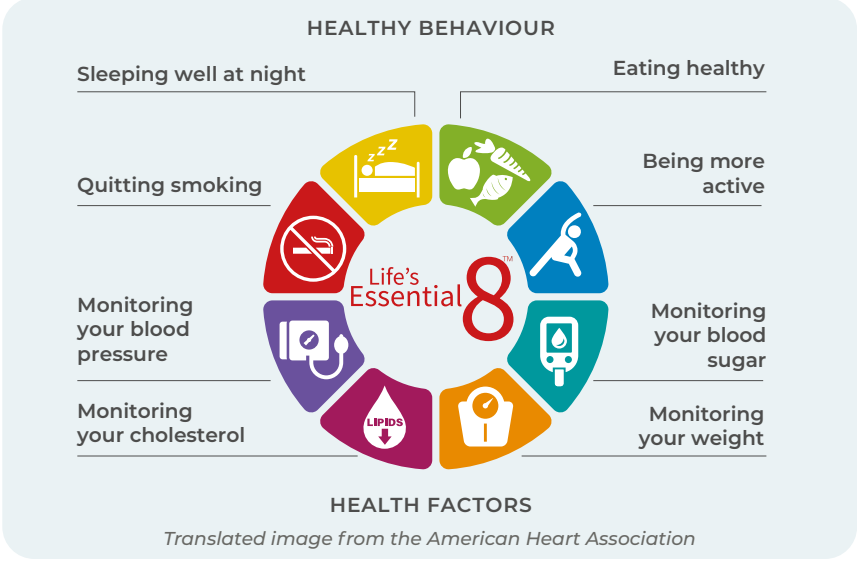
Obesity, diabetes, high blood pressure, and dyslipidaemia are all cardiovascular risk factors, meaning that each of them increases the like-

lihood of a major cardiovascular event, such as a myocardial infarction or stroke. Consequently, the risk is multiplied when more than one of these conditions are combined, as is the case with the metabolic syndrome. If diabetes is not already present, pre-diabetic conditions and the other components of metabolic syndrome carry a high risk of developing this disease. Finally, metabolic syndrome and, above all, obesity, are also risk factors for the development of certain cancers.

How is metabolic syndrome treated?

The treatment of metabolic syndrome is based on the same measures indicated for its prevention, or rather changes in diet and physical activity. If this is not sufficient, drugs will need to be prescribed to lower the blood pressure or blood sugar, and to correct any changes in the lipid profile. In cases of severe or even moderate obesity with associated complications, bariatric surgery (obesity surgery involving several types of interventions, to be evaluated by highly specialised professionals) may even be required.

8 ESSENTIAL FACTORS FOR LONGEVITY AND QUALITY OF LIFE



Translated image from the American Heart Association

Physical activity

MARIA CHIARA VULPIANI

What is physical activity?

The World Health Organisation (WHO) defines physical activity as "any bodily movement produced by skeletal muscles that requires energy expenditure." This definition therefore not only includes athletic activities, but also any normal movements carried out during daily life, such as walking, cycling, dancing, playing, housework, gardening, and recreational activities. Anyone, of any age and ability level can be physically active, and "every kind of movement counts." Even just a small amount of physical activity is better than none at all.

Why is it important?

Regular physical activity has proven clinical health benefits: it has a positive effect on the immune system, improves cardiovascular efficiency and exercise tolerance, combats weight gain and obesity, increases willpower and self-esteem, and reduces anxiety and depression. Last but not least, it also plays a significant preventive role against cancer, namely breast, colorectal, endometrial, bladder, kidney, oesophageal. and stomach cancers. It has been shown that more physically active women have a reduced risk of developing breast cancer compared to less active women. In a major 2020 study involving 8002 adults, the replacement of 30 minutes of sedentary activity with 30 minutes of moderate-intensity physical activity was shown to decrease in the risk of cancer mortality by 8%, and by 31% if the physical activity was of moderate to vigorous intensity.

How much physical activity should you actually do?

According to the current WHO recommendations, adults should do at least 150 minutes of moderate-intensity aerobic physical activity per week (this also includes small tasks like housework, gardening, brisk walking, swimming, dancing, or cycling), or at least 75 minutes of intense aerobic physical activity (such as walking uphill, running, fast swimming, or jogging), combined with twice-weekly strengthening of the main muscle groups. For example, we recommend doing at least 30 minutes of aerobic physical activity (such as walking, cycling, or swimming) five days a week. Children and adolescents 5 to 17 years of age should engage in at least 60 minutes of moderate-intensity aerobic physical activity per day, and muscle-strengthening exercises at least three times a week.

However, people should not forego engaging in physical activity just because they think they won't reach the recommended goals. Even doing just a little bit of physical activity every day is better than being completely sedentary!

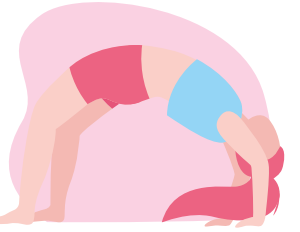
Children: the adults of tomorrow

ROBERTO FARNÈ

The World Health Organisation (WHO) recommends that children 0 to 5 years of age be active at least three hours a day, preferably outdoors.

This promotes physical and cognitive development, and sows the seeds for healthy future adults, who are less at risk of chronic diseases, such as obesity, type 2 diabetes, metabolic syndrome, and cardiovascular problems. The other pillar of childhood health recommended by the WHO is an adequate amount of daily sleep, never less than ten hours. However, the statistics show widespread increasing sedentariness among children and youths in Italy, a problem that was exacerbated by the pandemic. Not surprisingly, Italian youths are also among the most obese in Europe.

- **Engage in outdoor activities as much as possible;**
- **Spend as little time as possible indoors, looking at screens;**
- **Sleep well, and for long periods of time.**



These are three of the main recommendations that the World Health Organisation (WHO) has issued for parents of children under the age of five, so that, starting at a very young age, the seeds will already be sown for them to grow into physically and mentally healthy adults. During the first few years of their lives, children are athletic by their very nature! They run, jump, roll, crawl, and climb... they never want to keep still, and nobody should ever stop them. But the Italian National Institute of Statistics (ISTAT) has revealed a very different picture of our increasingly sedentary children, even starting at a very young age: over the past twenty years, the number of

Italian children three to ten years of age who engage in any form of physical activity has decreased by almost 10% (from 26.4% to 17.4%), thus confirming their ranking as a clear minority. Not to mention the fact that the very young were among those who suffered the most during the pandemic, when participation in sports by children and youths 3 to 17 years of age plummeted from 51.3% to 36.2%, and sedentariness increased from 22.3% to 27.2%. This negative trend needs to be reversed by going back to having our little ones play in our parks, gardens, and courtyards, and encouraging them to spend large parts of their days engaging in outdoor activities. This provides undisputed benefits at this crucial stage of their growth, not only in terms of physical health, but cerebral and mental health as well, as there is extensive literature associating active children with better cognitive development, not to mention better interpersonal and social skills. However, the complex management of daily family life and the almost unconditional access to all kinds of digital resources and technological devices has now come to discourage what was once the well-established habit of "going outside to play."

Spending hour after hour engaging in outdoor activities today means that you are more likely to grow up to be a healthy adult tomorrow. This is the greatest gift that we can give to our children, by dragging them to the park to play, or walking them to school. In fact, engaging in physical activity starting at an early age wards off future chronic diseases, such as cardiovascular problems, diabetes, cancer, and high blood pressure, as well as anxiety and depression. In most cases, establishing healthy habits in early childhood helps to cultivate and preserve them over time. Through playing, the child assimilates the value of mental and physical well-being, and learns how to maintain it over time.

How active should our children be?

Regularly taking part in a sport is certainly desirable during a child's upbringing, but it often doesn't help prevent sedentariness, and there can sometimes even be a real boomerang effect. In fact, parents are often mistakenly led to believe that the two hours per week that their children spend playing tennis or at the swimming pool are sufficient to check the "physical activity" box. However, especial-

ly when they're very young, they should be spending three to four hours outdoors per day (not per week)! Children need to spend a lot of time running, jumping, falling, and climbing, often going to outdoor areas like parks and gardens, where they can engage in these types of activities. The WHO has drawn up specific recommendations in this regard (see the table).

Children and physical activity, the WHO recommendations (WHO, 2019)

Infants up to one year of age: physical activity should take place several times a day, in various ways, namely through interactive play mats. While awake, infants who are not yet mobile should spend a total of at least 30 minutes spread throughout the day in the prone position.

Children 1-2 years of age: at least three hours a day of moderate to vigorous physical activity (preferably more);

Children 3-4 years of age: at least three hours a day (preferably more), with at least one hour at vigorous intensity

Sun, vitamin D, and the immune system.

Our bodies require regular exposure to natural sunlight to produce vitamin D, and children playing outdoors produce large amounts of it. Vitamin D promotes the development of the immune system and brain, as well as bone and muscle growth. It has also been shown to play an important role in mood stabilisation and sleep regularisation.

Excerpt from the article published in issue 2 of "Infanzia" (June 2023).

Prevention of environment-related diseases

ALDO FERRARA

The Environment-Health Theorem is relevant today because the nosographic classification between ENDOGENOUS diseases that develop in the individual (degenerative, lifestyle-related, genetic alterations, etc.) is expedited, while other EXOGENOUS diseases, which are perhaps more prevalent, are the expression of clinical forms linked to the environment, and are therefore also collective. Environmental alterations that can affect human health, and thus confer exogenous diseases, have traditionally been classified as either A) natural or B) anthropogenic. But in light of Climate Change, they can be attributed to human causes. Therefore, in the 21st century, we will see environmental diseases increase by 20% with respect to all diagnosable diseases (WHO, 2022). A distinction must be drawn between the following:

A. Traumatic or accidental diseases, directly dependent upon climatic and meteorological phenomena. These usually consist of environmental disasters (floods, hurricanes, etc.), which cause about 700,000 deaths per year worldwide;

B. Diseases directly related to climate change. The latter are further broken down into:

- dysfunctional diseases, usually of a cardiovascular nature due to increased environmental temperatures, and quantifiable in about another 600,000 subjects.
- ***infectious community diseases***, caused by climate change, which lead to 250,000 more deaths each year due to malaria and diarrhoea, heat stress, and malnutrition, especially among children, women, and more vulnerable segments of the population.

- ***dietary imbalances*** (production and consumption): according to the IPPC 2019 Report, climate change negatively affects agricultural productivity by threatening food security in arid areas of the planet, particularly in Africa, and in the mountainous regions of Asia and South America.

C. Diseases caused by pollution from toxic or irritant gases, with acute or flare-ups of cardio-respiratory syndromes. In turn, pollution must also be taken into account in various outdoor and open air environments (car exhaust pollutants, noxious gases (NOx, SOx), toxic gases (DEP diesel exhaust particulate matter, carbon monoxide, CO). As well as indoor environments, where gases such as unburnt methane, canister propellants, corrosive liquids with acidic or basic pH values, phospholipids, make-up ingredients, flame retardants, and bisphenol A are capable of provoking serious respiratory diseases, such as allergic alveolitis or pulmonary fibrosis.

Global warming and climate change are closely related to and are already anticipating the signs of how human being have altered the natural processes. All the substances listed above are also capable of polluting the interiors of homes, offices, public facilities, and even our cars, where the external pollutants are combined and concentrated with internal ones to form a deadly mix.

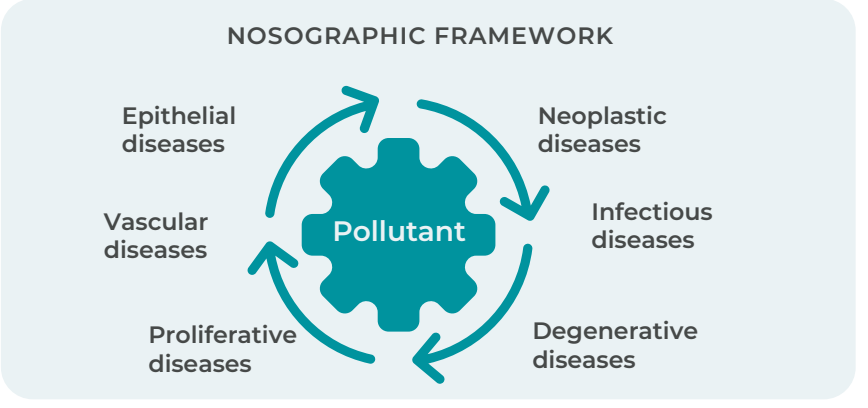


TABLE 1 Schematic example of the main Nosographic Classes upon which pollution acts as an adjuvant or aggravating factor.

The release of heavy metals due to the latest mechanical innovations means that heavy metals will soon become the most hazardous pollutants in the near future.

In the classic nosographic framework, which is summarised in table 1, pollutants act as triggers for the pathogenesis of inflammatory, infectious, and degenerative diseases, not only affecting systems like the cardio-respiratory system, but also apparatuses like the urogenital, gastro-enteric, haemopoietic, and endocrine systems on individual subjects, and can even affect multiple population layers depending on the type of pollutant (toxic or irritant). In the case of genetic, acquired, or acute diseases, the pollutant acts as an enhancer. Nowadays, therefore, we increasingly find ourselves dealing with community diseases. Consequently, prevention is only possible if communities, and not individuals, lead pollutant-free lifestyles, when we abolish fossil fuels as an energy source.

Vaccinations

It is estimated that vaccines save **4.4 million lives** each year.

Yet, according to Unicef's annual report, between 2019 and 2021, as many as 67 million children did not receive their vaccinations, with vaccination coverage levels declining in 112 countries due to several factors, including the impact of the pandemic, increasing access to misleading information, and declining trust in health authorities.

Misinformation in healthcare poses a risk to both individuals and society as a whole, and it is therefore extremely important to heed the advice of authoritative sources. **Fondazione IncontraDonna** collaborates with the Ministry of Health to promote communication and information campaigns, and the **Vaccination Calendar** Disc produced by Fondazione IncontraDonna is an excellent example of this synergy.

The **Vaccination Calendar Disc** is a convenient reference tool **in support of the #LaVaccinationNonHaEtà awareness campaign** that will be distributed with **Frecciarosa 2023**, and during all community outreach activities promoted by Fondazione IncontraDonna. The Vaccination Disc will contain all vaccinations envisaged by the 2023-2025 National Vaccine Prevention Plan (NVPP), the goal of which is to standardise the vaccination strategies in place throughout the country, in order to ensure that everyone is able to be fully vaccinated, regardless of their place of residence, income, or social/cultural level. The new National Vaccine Calendar (which was approved as a separate document from the Plan in order to allow it to be rapidly updated), indicates the recommended vaccinations currently offered free of charge by age and for people belonging to specific risk categories.

All the vaccinations recommended based on age, health conditions, and specific types of behaviour or conditions are to be understood as currently offered free of charge.

The vaccinations recommended for individuals at risk of occupational exposure are to be understood as currently offered at the employer's expense, or as envisaged under the current regulations. With the exception of those included in the vaccination calendar, vaccinations for travellers are the responsibility of the individual concerned.

Visit the Ministry of Health website at www.salute.gov.it

FOCUS

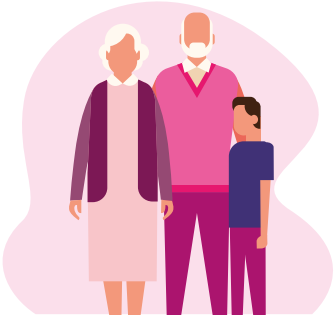
RISK CATEGORIES BY AGE AND DISEASE

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 an 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.



While some of the most common infections (e.g. influenza, pneumococcal disease, and shingles) are can be effectively prevented using vaccines, knowledge of their benefits and the use of these preventive strategies still remains excessively low among the population (especially those at risk).

People ≥ 60 years of age

- **Annual influenza vaccination:** currently offered free of charge starting at age 60, according to the indications contained in the Ministry of Health Memorandum.
- **Pneumococcal vaccination:** vaccination offered to those over 65 years of age, as a priority. The offer may also be supplemented with a sequential schedule (PCV+PPSV), depending on the type of PCV vaccine used. It can be administered at the same time as the influenza vaccine (which is an excellent opportunity in this case), or else can also be administered independently, and **at any time of year**.
- **Herpes Zoster vaccination:** 1 or 2 doses depending on the vaccine used, to be offered annually to those over 65 years of age and at-risk individuals over 18 years of age. This vaccination can very effectively reduce the risk of developing herpes zoster (commonly known as Shingles) and post-herpetic neuralgia (one of the most frequent and debilitating complications of the disease).

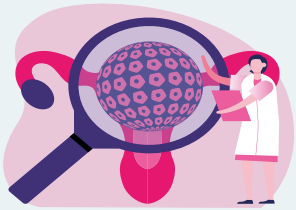
People at risk of disease

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), who are more vulnerable and fragile and, therefore, fall into groups of individuals for whom specific vaccinations are indicated, regardless of their age.

For more information, please refer to the indications provided on the "people at risk of disease" page of the Ministry of Health's website.

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, Fondazione IncontraDonna, Fondazione Umberto Veronesi, Consiglio Nazionale dei Giovani, Cittadinanzattiva, FAVO, ThinkYoung, LILT, ACTO Italia, Società Italiana di Igiene, Europa Donna, Fondazione PRO, FOCE, Insieme contro il cancro, AIOM, SIP, FIMP, Loto Onlus and aBRCAdabra have drafted and signed a Manifesto for the elimination of cancers caused by human papillomavirus.

In fact, while our country ranks highly with regard to the provision of services related to the primary and secondary prevention and treatment of cancer, our vaccination coverage and adherence to screening programmes are still far from the targets set by the WHO and the Europe's Beating Cancer Plan.

In addition, the COVID-19 pandemic further weakened oncological care by causing not only the numbers of planned diagnostic screenings and the number of oncological examinations to plummet, but also the numbers of HPV vaccinations, for which, once again, insufficient coverage rates and large regional disparities have been noted, as highlighted by the latest data from the Ministry of Health.

Manifesto objectives

1. **Adoption of health policy documents** at the national level agreed upon with the regions to strengthen and make vaccination prevention and screening services more accessible
2. **Launch of information and engagement campaigns** on HPV cancer prevention
3. **Promotion of primary and secondary prevention programmes** to ensure that everyone has safe access to the opportunities offered by the National Health System
4. **Monitoring of vaccination and screening coverage levels** via digital tools at least every six months
5. **Approval of an Extraordinary Oncology Plan**

Family history

MARIA PIANE AND SIMONA PETRUCCI

Cancers generally aren't hereditary diseases. However, many individuals diagnosed with cancer often report the recurrence of cancer in more than one family member. This recurrence may be in part due to this type of disease's high degree of frequency among the general population, especially the elderly, as well as shared risk factors among members of the same families.

Several factors can cause these mutations: exposure to certain chemical and physical agents, unhealthy lifestyles, and a reduced effectiveness of DNA repair mechanisms, which is inevitably associated with ageing. In certain rare cases, alterations predisposing the individual to the development of an oncological disease may already exist at the time of birth, as they are present in the sperm or the oocyte of a parent. In these cases, the genetic alteration is found in all the cells of the individual's body (germline mutations), and can be passed on to subsequent generations.

With respect to the general population, the presence of germline mutations increases the likelihood that individuals will develop tumours. Cancers resulting from this type of genetic alteration are called hereditary, and are characterised by an early age of onset, the presence of various types of tumours in the same individual and/or family, and recurrence in line with the Mendelian inheritance patterns (usually autosomal dominant AD inheritance, with 50% risk of recurrence in offspring). However, those who inherit these types of mutations do not inherit the cancers themselves, but rather an increased predisposition to develop them.

Then again, the recurrence of cancer within a family is not always a hereditary condition. In fact, cancers are extremely common diseases, and families not only share a genetic make-up, but also often share the same environments and lifestyles. Familial cancers have some, but

not all, of the characteristics of hereditary cancers: the age of onset is later, and recurrence in multiple relatives is not consistent the AD inheritance patterns.

For the purpose of assessing cancer risk, for specific cancers, awareness of family history is of paramount importance in determining whether one is dealing with a "familial" recurrence or a hereditary condition, and should be detailed within the context of a cancer genetics counselling (CGC) session.

A family history spanning at least three consecutive generations (siblings, uncles, grandparents, and cousins), providing information on the type of tumour and the age of onset in the affected relatives, plays a fundamental role in planning health surveillance and assessing whether and which cancer predisposition syndromes should be investigated. The risk of falling ill increases with the number of affected relatives, the degree of kinship, and the age of early onset. Specific software applications are available, which, taking into account all the risk factors for the specific type of cancer, can help the CGC specialist estimate both the risk of developing the disease and the risk of being a carrier of a pathogenic variant in a gene associated with hereditary forms of cancer (e.g. IBIS, Boadicea, BRCApro, for breast cancer; PREMM5, MMRpro, MMRpredict, for colon cancer; MELpredict, MELApro, for melanomas), as well as to plan appropriate prevention pathways and possible genetic investigations.

In particular, for individuals with family histories of certain cancers, it is important to plan specific surveillance for at-risk organs, with checks (examinations and instrumental investigations) being carried out earlier and more frequently with respect to the general population.

When genetic investigations make it possible to identify the altered gene responsible for a family's increased risk of developing certain cancers (hereditary forms), surveillance in carriers of the causative variant should also be extended to cover the other organs targeted by that specific condition.

In Europe, primary prevention (i.e. the combination of strategies to be

implemented in order to reduce the risk of developing cancer) is based on the adoption of a healthy lifestyle (such as avoiding exposure to predisposing physical and chemical agents, not smoking or consuming alcohol, avoiding a sedentary lifestyle, being overweight, poor dietary habits), and preventive surgery for carriers of PVs in specific associated genes, and those at high risk of developing certain cancers (see the table). For example, bilateral mastectomy, salpingo oophorectomy (removal of the fallopian tubes and ovaries), hystero adnexectomy (removal of the uterus, fallopian tubes and ovaries), gastrectomy and thyroidectomy are primary prevention strategies to significantly reduce the risk of breast, fallopian tube and ovarian, endometrial, stomach, and thyroid cancer, respectively, in individuals with PVs predisposing them to these diseases (see the table). Dedicated counselling and psychological support should always be available.

Chemoprevention has recently been introduced in Italy as a primary prevention strategy, and is currently limited to the administration of tamoxifen and raloxifene in healthy women at high risk of developing breast cancer. Discussions are still ongoing with regard to the benefits of other possible pharmacological risk reduction strategies, such as the use of acetyl salicylic acid for the prevention of colorectal cancer.

In short, risk assessment for familial/hereditary cancer cases is carried out by offering healthy individuals a multidisciplinary (interaction between multiple specialists) and multi-step approach.

These steps provide for the proper assessment of hereditary risk and, if recommended, genetic testing, and the establishment of a personalised risk prevention programme.

Table below: *Major cancer susceptibility syndromes and their causative genes. Some cancer susceptibility genes that increase the risk of cancer under heterozygous conditions (only one copy of the mutated gene) cause rare childhood autosomal recessive disorders if two copies of the mutated gene are inherited. Therefore, the identification of a pathogenic gene variant that predisposes an individual to develop cancer is an indicator that their family members should also be tested, not only to assess their susceptibility to develop cancer, but also to assess the reproductive risk of each individual/couple.*

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
Breast cancer/ Fanconi anaemia susceptibility	RAD51C	AD/AR	breast: 20-40% ovary: 10%-15%	Salpingo-oophorectomy at 45-50 years, recommended
Susceptibility to breast cancer	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%	–
Susceptibility to breast cancer	*BARD1*	AD	breast: 20%-40%	–

Syndrome	Genes	Inheritance	Related cancer (% risk of falling ill)	Surgical primary prevention strategies
Li-Fraumeni syndrome, variant	*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%	–

Sources: *NCCN (National Comprehensive Cancer Network) Guidelines 2023. PMID: 20301710; PMID: 20301434*

Legend: *AD: autosomal dominant; AR autosomal recessive; gen. pop.: general population; NET: neuroendocrine tumour. Cancers for which primary surgical prevention is envisioned are shown in bold.*

Screening

ALESSANDRA BARCA

According to estimates produced by the International Agency for Research on Cancer between 2020 and 2040, the absolute number of new cancer diagnoses will increase, especially for the most frequent types of cancer.

According to data from the Airtum report, **Cancer figures in Italy 2022**, there will be an estimated total of 390,700 new cancer cases (with the exception of skin cancers other than melanoma) in Italy in 2022. Of these, about 40% can be prevented by adopting a healthy lifestyle and being diagnosed at an early stage, or rather before the condition manifests itself clinically.

In order to ensure equal access to early diagnosis, the National Health Service operates **three cancer prevention screening programmes**, two for women (breast and cervical), and the third for both men and women: screening for colorectal cancer, a disease that, in terms of frequency, has become the second most common cancer in women and the third most common in men.

If executed correctly in terms of timing and methods, these programmes can serve as tools for altering the natural course of breast, cervical, and colorectal cancers, by reducing the likelihood of falling ill, with the possibility of early diagnosis allowing for less invasive and more effective interventions.

In fact, as a public health model, screening makes it possible to detect cancers at an early stage, potentially even before they occur or become invasive. This allows for certain lesions to be treated more effectively, and offers patients better chances of recovery.

These public health measures are intended for people who fall into specific age groups and are at generic risk for these diseases.

1. mammogram: this screening is intended for women **50 to 69 years of age**, and consists of performing a **mammogram every 2 years.** In some regions, the programme is being proposed to a broader age group (**45-74 years**), and its effectiveness is being evaluated

2. cervical cancer screening: Pap-test and HPV-DNA test for women 25 to 64 years of age.

3. colorectal cancer screening: used in almost all programmes, this screening consists of the **faecal occult blood test** for people **50 to 69 years of age**.

The screening programmes follow the nationally standardised protocols. They entail an active invitation from the Local Public Health Office, and the performance of the screening test (first level test).

If the screening test shows a normal result, the person is notified by the health facility, usually by letter, to take the screening test again after two years (in the case of breast or colorectal cancer screening), or else after three or five years (in the case of cervical cancer screening).

If, on the other hand, the screening test shows a suspicious or positive result, the person is contacted by the health facility by telephone within a short period of time (4-5 days from the test report, depending on the region) for referral to the second level procedures. An appointment for the necessary in-depth examinations is proposed at a regional facility belonging to one of the regional cancer networks.

Mammogram

A **mammogram** consists of a radiographic image of the breasts. The examination is performed by placing the breasts one at a time on a surface, where they are slightly compressed and X-rayed horizontally and vertically. The examination is usually painless, and does not entail any health risks, as the radiation doses emitted are very low. If the mammogram proves returns a suspicious or positive result, the person is contacted by the health facility for further examination. These can include breast examination, a more detailed tomosynthesis mammogram, breast ultrasound, an MRI with mdc (magnetic resonance imaging with contrast medium), or needle aspiration or biopsy for cytological or histological examination. The examinations proposed will depend on the specific case.

Cervical screening

The tests for cervical cancer screening are the **Pap test and the Human Papilloma Virus test (HPV-DNA test)**. The test utilised up until now has been the Pap test, which is offered every three years to women between 25 to 64 years of age. However, since recent scientific evidence has shown that, **over the age of 30, it is more effective to perform a Human Papilloma Virus test (HPV-DNA test)** every five years, all regions are striving to adopt the HPV-DNA test-based model for the 30-64 age group.

We know that HPV (Human Papillomavirus) is a DNA virus that causes a very frequent infection. Most people come into contact with it at least once in their lives. This infection generally does not cause any alterations, and resolves itself on its own, especially in young girls. In a minority of cases it causes cervical lesions, which can be identified through screening. While most lesions heal spontaneously, some, if left untreated, can slowly develop into forms of cancer.

If a screening or triage test (Pap smear after a positive HPV-DNA test) returns a positive result, the person is called back to undergo a colposcopy (second-level examination) for the possible treatment of the lesions detected.

In order to achieve the goal of eliminating cervical cancer, it is necessary to strengthen the synergy between the primary and secondary prevention measures by improving HPV vaccination coverage in adolescent females and males.

Colorectal screening

There are two tests used to screen for colorectal cancer: the faecal occult blood test (FOBT) and rectosigmoidoscopy (inspection of the lower part of the intestine using an optical fibre). That which is utilised in almost all the programmes is the **faecal occult blood test**, which is recommended for people **50 to 69 years of age**.

The test detects the possible presence of blood in the faeces that is invisible to the naked eye, or else hidden from view. It is performed by collecting a stool sample at home in a special container, which is then analysed at the laboratory. The faecal occult blood test used in the Italian screening programmes does not entail any dietary restrictions prior to being performed. In some regions, the faecal occult blood screening test is also available from the pharmacy network; this is to improve accessibility to the screening pathway, and to increase participation by the target population.

If the screening test is positive, the person is called by their health facility for a pre-endoscopic visit in order to perform a colonoscopy (RSCS), an in-depth diagnostic examination that involves the removal and histological analysis of any polyps detected

The screening pathways are free of charge, and the timing and methods of each phase are monitored through quality indicators, in order to ensure the quality improvement of these public health measures.

It is important not to miss the opportunity to take part in these important prevention pathways. For this reason, some regions have established online portals for booking screenings, in order to overcome the possibility of the invitation letters not reaching their destinations.

Why are there only three screening programmes?

Effective screenings capable of detecting cancer at an early stage, even before symptoms appear, and that offer the possibility of selecting specific cases requiring further investigation from among the population groups examined, aren't available for all types of cancer.

In collaboration with regional government bodies, the Ministry of Health is implementing pilot projects to expand the organised screening programmes to include other diseases of relevance in terms of frequency and mortality, such as **prostate, lung, and stomach cancer, in line with the new European recommendations (the Europe's Beating Cancer Plan).** These programmes are and will be targeted at a people based on their individual risk levels, and not based on their age, as is the case with the screenings described above.

Cervix

ENRICO VIZZA and BENITO CHIOFALO

The secondary prevention of cervical cancer is implemented through regionally organised screening programmes, using traditional Pap tests, Papilloma Virus HPV DNA testing, and colposcopy.

The **Pap test** is one of the most effective and well-established means of secondary prevention for this type of cancer, and involves the collection of cells from the cervix with a spatula via the insertion of a vaginal speculum. The harvested cells are smear-swabbed onto a slide or placed in a test tube containing a liquid solution. Then, after fixation and staining, they are observed by an expert cytologist to see whether there are any cell changes, which indicates the need for further investigation. Pap-tests are usually offered every three years to women 25 to 30-35 years of age. Even women who have followed the primary prevention (vaccination) protocol must undergo secondary prevention checks, as the vaccine does not guarantee total protection.

The **HPV DNA** test is a more sophisticated and expensive test; the sample is obtained through a procedure quite similar to the Pap test. The cervical cells collected in this manner are subjected to viral DNA testing in order to determine whether there is a Human Papillomavirus infection that poses a high risk of cancer. A positive test does not necessarily indicate illness, but is indicative of a greater risk requiring further examination (pap test, colposcopy with possible biopsy) in order to exclude the possibility that the HPV virus has caused any pre-cancerous or cancerous lesions on the cervix or vagina.

In the event of a positive HPV-DNA test, a Pap test is performed; if no atypical cells are detected, the patient will be re-tested one year later to see whether the infection has resolved, or whether the virus has become chronic within the cervical cells.

If the Pap test reveals cell changes, a second-level examination, or **colposcopy**, is performed. Colposcopy is a simple and minimally invasive examination involving the insertion of a vaginal speculum, the exposure of the cervix and vaginal walls, the application of two vital dyes (acetic acid and Lugol's solution), and observation under magnification by a gynaecologist with expertise in lower genital tract pathology. If the colposcopy reveals suspicious lesions, the doctor will decide to perform a biopsy (the collection of tissue upon which to perform a histological examination).

The aim of these tests is to detect precancerous lesions, which if misdiagnosed and/or left untreated can develop into invasive cancer.

Adherence to the regional screening programmes (secondary prevention) is very important. In fact, without these programmes, cervical cancer would be the most frequent form of cancer affecting women in Italy, just as it is in other countries where there are no prevention programmes. Thanks to primary and secondary prevention, cervical cancer is becoming rare among Italian women, and our goal is to eradicate it completely within a few decades. However, this will require all young people to cooperate, and receive their HPV vaccinations.

Colon/rectum

EMILIO DI GIULIO

Colon cancer is a very common form of cancer. In fact, it's the form with the second highest mortality rate in Italy and other Western countries, preceded only by lung cancer in men and breast cancer in women.

Regardless of the causes, most colon cancers arise from **adenomatous polyps**, which are initially benign lesions.

Over time, adenomas can transform into malignant tumours, and the risk of transformation depends on numerous factors, such as size, number, and histological features. In most cases, polyps do not cause symptoms.

However, it is very important to pay attention to certain symptoms and signs, which, although non-specific, may indicate the presence of polyps or colon cancer, such as **blood in the faeces** (visible or occult, i.e. detected by specific tests), **anaemia**, sideropenia (iron deficiency in the blood), and/or changes in bowel movements (constipation or recent onset diarrhoea).

It is estimated that it takes about 10 years for an adenoma to turn into a tumour, so being able to detect the lesion and remove it during this long period, when it is still benign, allows this sequence to be interrupted.

Risk factors

Starting at the **age of 50**, the risk of this type of cancer occurring becomes considerable in both sexes.

The main risk factors for the development of colon cancer are the following:

- **Age:** most colon cancers develop in individuals over 50 years of age
- **Family history:** of colon cancer and/or adenomatous polyps
- **Hereditary diseases:** Familial Polyposis (FAP), Hereditary Non-Polyposis Colon Cancer (HNPCC)
- **Personal history:** of previous polyps and/or colon cancer
- **Overweight condition or obesity**
- **Diet high in animal fat** and red meat, and low in fibre
- **Sedentary lifestyle**

Prevention

Like with other cancers, primary prevention consists of changing lifestyle, and paying greater attention to physical activity, diet, and body weight. However, all this is not enough.

One extremely effective health measure for the prevention and early detection of colon cancer is **screening**. The current screening test most widely used worldwide to select patients who should undergo colonoscopy is the **faecal occult blood test**, which is free of charge for patients 50 to 74 years of age, and is offered by local health authorities. This test checks for the presence of any minute traces of blood invisible to the naked eye released in the faeces from a benign or malignant lesion.

However, occult blood could result from any other lesion of the mucosa along the entire gastrointestinal tract, so this test is only used to select subjects to undergo colonoscopy, and **in 75% of the cases that test positive, neither a polyp nor cancer is present**. If the test results are negative, on the other hand, the test has to be repeated every two years regardless. Despite the fact that the colon cancer screening programme has been active in Italy for several years, and is a highly effective health measure, increased awareness and communication with citizens are nevertheless needed, since, according to data from the National Screening

Observatory (2019), only around 40-50% of citizens invited to perform the occult blood test actually participate, with much lower rates in certain regions.

Certain categories of people with major risk factors (personal or family history of colon polyps or cancer, genetic syndromes, chronic inflammatory bowel disease) are advised to undergo **colonoscopy** directly, regardless of their age and/or whether or not they have received a positive occult blood test result.

In fact, among the hereditary syndromes, so-called **Lynch syndrome**, which occurs in 2.8% of new colon cancer diagnoses and in 2-5% of patients diagnosed with endometrial cancer, is particularly worthy of mention. This syndrome is characterised by a generally younger onset of the cancer, the presence of multiple cases among family members, even of different generations, and, in some cases, association with cancers affecting other organs. Today, a genetic test is proposed for individuals with colon cancer, in order to subject their family members to further investigations if they test positive.

An increased risk for colon cancer among women with a personal history of breast cancer has been hypothesised in the past, but the evidence for this has not been confirmed. **Therefore, for a subject who is only exposed to a generic risk of colon cancer by age, prevention with faecal occult blood testing starting at the age of 50 is recommended**.

Colonoscopy

Colonoscopy is the most effective diagnostic test for preventing colon cancer.

Colonoscopy consists of inserting a flexible probe (colonoscope) into the anus to obtain a direct view of the colon. While the examination is very thorough, there is always the possibility that a pathology and/or lesion may not be recognised. The examination takes about 15 minutes and causes modest and generally well-tolerated discomfort during the introduction and progression of the instrument, which is why sedation is usually performed.

During the examination it may be necessary to take **biopsies** of the mucosa, which are entirely painless, as the mucosa is not innervated.

To make the examination more comfortable, sedation is performed with intravenous benzodiazepines, often combined with major analgesics. **Such sedation is referred to as conscious sedation, as the patient relaxes, but does not fall asleep**. Deep sedation, in which the patient sleeps, is performed through the administration of sedative-hypnotic drugs by an anaesthetist, and is reserved for select cases (subjects who did not complete the examination with conscious sedation due to the presence of adhesions or other impediments that cause particular pain, particular clinical conditions, etc.). It is therefore important to clarify any such aspects when booking the appointment, declaring any prior abdominal surgery, including caesarean sections, and disclosing all medications being taken, especially anticoagulants or antiplatelet agents, which must be discontinued according to specific protocols after consulting with one's cardiologist, neurologist, or haematologist.

A **"virtual colonoscopy"** is an radiological examination (a CT scan) that uses specific software to virtually reconstruct the subject's colon, indicating the presence or absence of alterations on both the external wall and the lumen. This examination is not an alternative to traditional colonoscopy (known as "optical" colonoscopy), as it does not allow for histological samples to be taken, nor does it allow polyps to be removed, which, if detected, would require the subsequent performance of an "optical" colonoscopy. It also has difficulty recognising any small or difficult-to-detect lesions. However, for screening purposes, "virtual colonoscopy" can serve as an alternative in certain special cases, such as failure of optical colonoscopy, severe diverticular disease, or the presence of major comorbidities.

Stomach

EMILIO DI GIULIO

Gastric carcinoma is a malignant epithelial cancer of the glandular epithelium, and is the most frequently encountered malignant stomach cancer.

Gastric cancer is encountered frequently in developing countries, most commonly in East Asia, where early diagnosis programmes are in place. In Italy, the yearly incidence is 33 cases per 100,000 in males, and 21 cases per 100,000 in females, with broad regional variability. In fact, the incidence is nearly twice as high in central-northern Italy as it is in the south.

Risk factors: not just Helicobacter infection

Classified by the International Agency for Research on Cancer (IARC) as a type I carcinogen, helicobacter pylori (H.P.) can cause pre-cancerous histological changes within a subgroup of patients. **H.P. infection is widespread, and over one third of the adult population in Italy is infected.** Infection can be ascertained through various types of tests, and can be responsible for various clinical ailments: chronic gastritis, peptic ulcer, gastric adenocarcinoma, and other cancers (MALT lymphoma and neuroendocrine tumours).

Eradication of the infection is an important step towards the prevention of gastric carcinoma. However, since the available therapeutic programmes are not always effective, treatment (usually consisting of a proton pump inhibitor and a combination of 2-3 antibiotics) is not straightforward. Moreover, certain forms of antibiotic resistance suggest different treatment protocols in different geographical areas, depending on the epidemiological contexts.

Although Helicobacter pylori infection plays an important role in the process of carcinogenesis, only a small percentage of positive individuals develop gastric carcinoma, suggesting that other fac-

tors (virulence of the bacterial strain, genetic predisposition of the host, and other environmental factors) also play a major role. The treatment of Helicobacter pylori infection for prophylactic purposes is currently recommended in individuals with prior gastric cancer or with a first-degree family history of gastric cancer (parents or siblings).

The consumption of smoked foods, excessive use of salt, and excessive intake of nitrates (present in high concentrations in preserved foods) increase the risk of stomach cancer.

Cigarette smoking and **obesity** (especially for neoplasms of the gastroesophageal junction/cardia) are additional risk factors.

Although most cases of gastric cancer are sporadic forms, a small percentage (less than 5%) are hereditary variants (FAP, Lynch syndrome, Li-Fraumeni syndrome, Peutz-Jeghers syndrome, or Hereditary Diffuse Gastric Cancer), which are subject to specific prevention protocols.

Precancerous conditions: atrophic gastritis

Atrophic gastritis is a precancerous condition caused by the loss of the glands in the stomach that produce hydrochloric acid and the consequent reduction of physiological acid secretion. It's affects about 7% of the population, and may be secondary to Helicobacter pylori infection or an autoimmune process (autoimmune gastritis).

The clinical presentation of this condition varies widely, and it often goes undiagnosed. Haematochemical examinations showing **iron deficiency/sideropenic anemia or Vitamin B12 deficiency/ pernicious anaemia** can be an important indicator.

In the long term, the deficiency of these micronutrients can lead to the onset of tiredness and tingling in the arms and/or legs. Certain gastrointestinal symptoms may also be present, namely difficult or slow digestion, pain in the pit of the stomach, or, less frequently, a sensation of burning or acidity behind the sternum.

The significance of this diagnosis depends on whether the patient is at increased risk of developing stomach cancer. In addition to the risk of carcinoma, some gastric endocrine cells (enterocromaffin cells) may proliferate, leading to the formation of type I carcinoid tumours. These carcinoids tend to have a benign course, and are treated conservatively (endoscopic resection). For this reason, patients with atrophic gastritis will have to undergo surveillance with gastroscopy and multiple biopsies of the antrum and body/fundus every 3 years.

Unfortunately, the symptoms are non-specific in the early stages, which is why diagnoses are often made at later stages. **The presence of any "red flag" symptoms, such as involuntary weight loss, vomiting, or anaemia, must be investigated.**

Diagnosis

The main type of examination for the diagnosis of stomach cancer is gastroscopy with the collection of multiple biopsies.

The use of high-definition instruments for appropriate magnification and/or staining of the mucosa is important, especially for the diagnosis and surveillance of pre-cancerous lesions in patients with atrophic gastritis. Radiological diagnostic techniques (CT, PET) or echo-endoscopy are only useful for determining the presence of metastases and the staging of the cancer.

In light of the relatively low rate of gastric cancer in Italy, there is currently not enough evidence to carry out a screening campaign. Gastroscopy is recommended for:

- **subjects with "red flag" symptoms**
- **patients with precancerous lesions of the stomach**
- **individuals with a first-degree family history of stomach cancer**

Skin

ELENA CAMPIONE

Skin cancer

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

What is melanoma?

Melanoma is the most aggressive type of skin cancer. It has unpredictable behaviour, and is often resistant to chemotherapy. **Melanoma has multiple causes, including both environmental and genetic factors**.

Cutaneous melanoma is more frequent in developed countries: 200,000 cases were reported worldwide in 2022, and was ranked 10th in highly developed regions. Rates of occurrence continue to rise in most countries, predominantly among fair-skinned populations, particularly in the elderly.

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. The other type is **nodular melanoma**, which can be more insidious, because the cells may have already invaded the depths of the tissue.

Sun exposure and the risk of melanoma

The risk factors for the onset of melanoma and epithelial cancers include **overexposure to the sun's ultraviolet radiation (UVR)**, which can cause severe sunburns; **however, a "little and often" protocol for exposure to sunlight is highly recommended for the natural production of optimal vitamin D levels** (essential for bone health and other factors), as well as melanin, which acts as our bodies' true natural shield against solar radiation.

The scientific research shows a correlation between severe sunburn and an increased risk of melanoma, while safe sun exposure is associated with a reduced risk of melanoma.

What should the general population do to avoid the negative consequences from skin cancer diagnosed at an advanced stage?

Melanoma is a highly aggressive and often fatal malignant cancer, especially when diagnosed at a late stage in its natural progression. In fact, compared to just 15 years ago, we now have a therapeutic toolkit (including immunotherapy and targeted therapy) that's capable of achieving an extraordinary therapeutic response. Unfortunately, in the majority of cases these drugs are not a guaranteed cure for the disease, although they are capable of significantly prolonging the survival of patients with metastatic melanoma. **It is therefore crucial to intervene at an early stage in the melanoma's progression**, when it has not yet reached the blood or lymphatic vessels, where it has potential to metastasise.

Diagnosis

Today, most melanomas are diagnosed at stage 0 (in situ) or 1, thus with an excellent prognosis for the patients. This is possible thanks to the screening and dermatological check that patients undergo every 12-18 months, unless different indications are provided based on individual risk factors (family history of skin cancer, number of moles, light phototype, tendency to develop freckles, etc.).

In the case of patients with particular risk factors for skin cancer, checks are recommended at much shorter intervals, even every 3-6 months.

Skin cancers originating from the malignant transformation of keratinocytes mainly give rise to two types of cancers: **basal cell carcinoma, and squamous cell carcinoma**. In the first case, it is important to detect the cancer at an early stage, not because of the risk of metastasis, which is very low for this type of cancer, but because of the possibility that, by growing and invading the surrounding tissues, this kind of neoplasm could become inoperable and cause serious impairments for the patient (imagine a tumour invading the eye or ear).

In the second case, there is a real risk of metastasis, as well as localised damage, and diagnosis at an early stage, through annual dermatological check-ups, is therefore essential.

Moreover, cutaneous squamous cell carcinoma most commonly recurs (70% to 80% of the time) within two years of diagnosis, and **more than one million cases per year are reported**. Close, ongoing clinical surveillance is therefore recommended based on the risk of localised recurrence and metastasis.

In addition to undergoing specialist check-ups, patients are also encouraged to perform monthly self-examinations and to use appropriate means of photoprotection. Special categories of patients, such as transplant recipients, and patients with chronic lymphocytic leukaemia, HIV infection or other forms of immunosuppression, may require increased surveillance.

Epithelial cancers **(non-melanoma skin cancer)** are chronic diseases in high-risk patients who have had five or more skin cancers, with a negative impact on quality of life and high rates of healthcare utilisation. These high-risk individuals with multiple lesions require close surveillance, as

well as secondary prevention measures, which include local medical therapies, such as photodynamic therapy, imiquimod, and 5-fluorouracil.

In the case of squamous cell carcinoma, diagnosis by dermatologists is often "facilitated" by the presence of precancerous lesions in areas that are chronically photo-exposed for work or recreational reasons, which are known as actinic keratoses. The onset of squamous cell carcinoma can be prevented through the elimination of actinic keratoses by cryotherapy or topical chemo- or immunotherapy. Systemic chemoprevention, with the use of oral nicotinamide, can also be a valuable tool for patients at risk.

For basal cell carcinoma, there are no precancerous lesions, but certain syndromic conditions are favourable to its occurrence, such as **Gorlin syndrome** and **Xeroderma pigmentosum**, which require special clinical attention, with check-ups every 4-6 months, depending on the case, sometimes in combination with systemic therapy acting on the Sonic-Hedgehog signalling pathway, a cell growth factor.

What does a dermatological check-up consist of? What diagnostic-therapeutic pathways are currently available?

A dermatological clinical examination entails macroscopic observation of the entire skin area, with possible **observation under epiluminescence or dermoscopy**, which increases the diagnostic accuracy of both melanocytic and other types of lesions (such as neoplastic and pre-neoplastic lesions consisting of keratinocytes).

If a suspicious skin lesion is observed, depending on the demographic and clinical characteristics of the patient, three different approaches can be taken:

1. **An image of the lesion can be acquired using a non-invasive instrumental method**, such as epiluminescence microscopy or digital dermoscopy, for diagnostic confirmation or for monitoring over time, thus postponing the possibility of excision to a later time. In fact, sequential digital dermoscopy can be used to monitor multiple, flat, non-palpable melanocytic nevi showing atypical features, but without evidence of specific melanoma criteria, with the possibility of re-evaluating and comparing any potential changes over the short term (3-6 months) or long term (> 6 months).

2. **The radical surgical excision of the suspected lesion(s) is prescribed**, with a request for histological examination.

3. **Confocal microscopy/OCT examination** is requested in order to analyse the deeper layers of the skin in a manner that is non-invasive but more sensitive than dermoscopy. These instrumental methods are particularly useful for lesions in particular locations, such as the face or genitals, and for patients on whom the removal of the suspected lesion would be difficult or would entail extensive damage. The results of these analyses determine whether it is necessary to proceed with surgical intervention or clinical-instrumental follow-ups (confocal, OCT, video dermoscopic examination), or if no further medical investigations are required, with the patient being referred for an annual clinical follow-up.

Total Body Photography has been available now for a several years, and has been used to create a complete record of the patient's skin surface in order to evaluate any new lesions, or to identify changes in pre-existing lesions. This multimodal application should be combined with sequential digital dermoscopy and limited to high-risk melanoma patients with numerous melanocytic nevi.

Vitamin D and melanoma

Although it exists in several forms, when people talk about **vitamin D** they're often referring to vitamin D3. And there are also multiple forms of vitamin D3, which vary based on the presence and number of 'hydroxylations' present. In other words, the double hydroxylated form, also known as **calcitriol**, is that which is active on both kidney and bone. **Cholecalciferol**, on the other hand, is the biologically inactive form, which forms in the skin when it is exposed to direct sunlight, after having been processed by the liver and kidneys. The biologically active form of vitamin D binds to a receptor inside the nucleus of the cell. In the case of melanoma, this receptor (called the VDR) is malfunctioning. In fact, studying this receptor has allowed us to understand the important role that vitamin D plays in relation to cancer.

Why is vitamin D important in relation to melanoma?

Another benefit that vitamin D can have for melanoma patients is the anti-proliferative effect that it has on cancer cells, or rather its ability to slow the cancer's growth, and its immunomodulating activity. On the one hand, vitamin D has been shown to inhibit T-helper 17 lymphocytes: cells which should defend our body, but are dysregulated in the melanoma cancer environment. On the other hand, vitamin D up-regulates the expression of PDL-1, **meaning that it increases its production on both epithelial and immune cells**: this increase in PDL-1 is important, as it is targeted by immunostimulant therapy, favouring its effectiveness. **Recent evidence also seems to suggest that certain alterations in the vitamin D receptor can facilitate the development and progression of melanoma and other cancers**.

Even in targeted therapy, the latest 2020 studies revealed the importance of vitamin D supplementation in reducing both therapy-related adverse effects and in improving quality of life among patients.

A recent study showed that **vitamin D supplementation after melanoma removal has a protective effect against the possibility of recurrence**, or rather the occurrence of a new tumour. Patients diagnosed with melanoma can have a better clinical outcome, with a decrease in healthcare costs related to the treatment of distant and regional metastases.

A recent study found that certain alterations in the vitamin D receptor that can compromise its proper functioning are associated with an increased risk of developing melanoma, thus reaffirming how crucial this hormone can be in ensuring the homeostasis of the entire body.

THE DERMATOLOGIST REPLIES

1. Can sunburns I had as a child be linked to the development of melanoma as an adult?

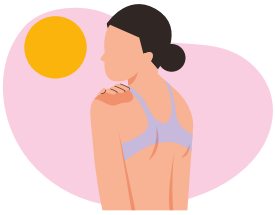
Yes. It has been shown that sunburns suffered as a child lead to an increased likelihood of developing melanoma as an adult.

2. Should vitamin D only be taken by menopausal women?

No. Vitamin D can be taken at any age for conditions such like atopic dermatitis, rickets, and other autoimmune diseases. Severe vitamin D deficiency is associated with an increased risk of infection and cardiovascular disease.

3. Can sun exposure be replaced by taking a vitamin D supplement?

Not really. It's true that UV-A rays increase the concentration of nitric oxide circulating in the blood, which helps control blood pressure and thus reduces the risk of hypertension and cardiovascular diseases. Sun exposure promotes the production of other molecules, besides vitamin D, called mediators, such as dopamine, beta-endorphin, urocanic acid, and glutamate.



For this reason, a vitamin D supplement cannot fully replace sun exposure.

4. What are the ideal vitamin D levels in a blood test?
Between 30 and 60 ng / mL (75-150 nmol / L).

5. If I have a fair complexion, can I still expose myself to the sun to promote vitamin D synthesis?
Yes. With the exception of those with a history of excessive sensitivity to sunlight, everyone in the world, regardless of their skin colour or geographic location, should expose themselves to the sun such as to maintain a serum vitamin D level above 20 ng/mL (preferably at 30-60 ng/mL), while avoiding sunburn. Spending half an hour a day with your face, arms and hands exposed to the sun is enough to achieve good vitamin D synthesis.

6. What's the best type of supplement to take?
Before taking any type of supplement, it is **always a good idea to consult your doctor** and determine whether you have any vitamin and/or trace element deficiencies. There are various vitamin D formulations available on the market, which differ based on the disease to be treated. At the dermatological level, it is recommended to take more structured supplements, which, in addition to vitamin D, also contain copper and zinc.

Breast

ADRIANA BONIFACINO

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

This is the most frequent type of cancer encountered among women of all ages. There are approximately 56,000 new cases of breast cancer per year in Italy. There are currently about 900,000 women in Italy living with this diagnosis. For 6-7% of women, it has already metastasised at the time of diagnosis. 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!

First and foremost, it must be remembered that there are two basic requirements for staying 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. And not only for oncological diseases.

Numerous cancers affecting any organ and apparatus (over 40%) could be avoided! Also by eliminating smoking and drastically reducing alcohol intake. This is true prevention.

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, namely 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.

Breast Cancer Treatment Centres

A patient with a suspected or already confirmed diagnosis of breast cancer must be treated at a public Breast Cancer Treatment Centre that handles at least 135/150 cases of breast cancer per year, as established by Ministerial Decree DM 70 of April 2014. 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. All the breast cancer screening and treatment centres nationwide can be found, complete with geolocation, by downloading the free Pianeta Seno App. Data regarding the Breast Cancer Treatment Centres are provided by Agenas (The National Agency for the Regional Health Services).

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 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.

What are the programmes to be followed if you have a family history, the BRCa 1 -2 genetic mutation, or very dense breasts?

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 public programmes in place dedicated to the highest risk groups, which provide for a different scheduling of the investigations, even at younger ages. For this reason, it may be useful to consult the website for your region, or to contact your doctor for more detailed information. Considering our awareness of the high risk of developing breast cancer, 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.

Information on the instrumental investigations is provided below

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, micro-calcifications, 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 classification: a radiological classification system for lesions, consisting 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.

Information on cell or tissue collection is provided below

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, the recovery rate among women who regularly undergo preventive examinations, with cancer being detected at a very early stage, is 88% (Aiom. Cancer Figures in Italy 2022). *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.

Can breast cancer be hereditary?

About 10% 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. There is no need to fear such counselling visits, as they allow individuals to learn more about their DNA. If positive, this test can allow for appropriate preventive measures to be taken, in order to avoid falling ill at a later time.

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 as-

sessment, 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. Healthy subjects can also be considered as direct candidates for the first test under certain circumstances (e.g. when there is a clear indication for molecular genetic testing, but all the family members who have had cancer are deceased).

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 hereditary cancers or medical genetics.

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

Breast implants and the risk of lymphoma

ARIANNA DI NAPOLI

What are breast implants?

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?

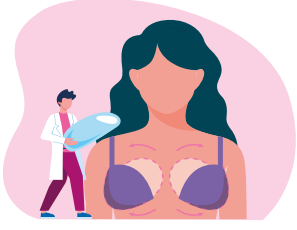
There are various types of implants. In particular, they are available in a rounded shape, with either a smooth or rough surface (macro- or micro-textured), or else in a teardrop shape (anatomical) to mimic the natural shape of the breast, but only with a textured surface. Both are available in a wide 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.

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 US Food and Drug Administration (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 1 April 2021, the FDA reported a total of 1130 BIA-ALCL cases, 59 of which resulted in death, while in Italy, as of 30 November 2022, there were 92 cases reported, with two resulting deaths. Lymphoma develops in equal measure among patients who have received implants for reconstructive purposes (52% of cases) and for cosmetic purposes (48% of cases). 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 was the first country in the world to establish 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. This register will be populated with 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 with Italy for either cosmetic or reconstructive purposes. What should women with textured implants do?

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.

Who should women with breast implants turn to in the event of breast problems detected through palpation, mammography, or ultrasound examination?

If any doubts regarding implants should arise following a breast examination, ultrasound, mammogram, or MRI with contrast medium, it is important to contact an accredited Regional Breast Cancer Treatment Centre, a list of which is available on the free Pianeta Seno App.

Just like before, with breast reconstruction

FRANCESCO STAGNO D'ALCONTRES

After undergoing a mastectomy for breast cancer, breast reconstruction allows women to feel whole again, with renewed self-confidence. This year, the international day dedicated to breast reconstruction awareness **(BRA Day) falls on 18 October**.

Breast reconstruction is a safe operation paid for by the National Health Service, which, depending on the case, may take place either at the same time as or after the patient's mastectomy. Based on the characteristics of the individual (age, body type, etc.) and the disease, the reconstruction may be carried out using the patient's own tissues, such as flaps of skin and muscle taken from the abdomen, or else using devices such as prostheses and expanders.

Every woman is accompanied on her personal reconstruction journey by a qualified Plastic Surgeon, who will be there for her every step of the way. **www.sicpre.it**

Onco-haematology

LUIGI CAVANNA

LEUKAEMIAS

Leukaemias are blood cancers caused by the uncontrolled proliferation of bone marrow cells, with excess production of neoplastic blood cells, which cannot function as normal cells.

Based on the type and clinical characteristics of the cells involved in the process, leukaemias are classified as acute, chronic, myeloid (which also includes monocytic and myelomonocytic forms), and lymphoid, or lymphatic.

Acute leukaemias are rapidly progressing diseases (if left untreated), and are characterised by an accumulation of immature cells in the bone marrow and peripheral blood.

When leukaemia develops, the bone marrow (which acts as a blood cell "factory") is no longer able to produce normal blood cells (erythrocytes, leucocytes, and platelets), resulting in a state of anaemia, which leads to fatigue and asthenia, a state of plateletopenia, which can lead to easy bleeding, such as nosebleeds or gum bleeding, and a shortage of normal leucocytes, which facilitates infections, resulting in fever.

Chronic leukaemias have a slower and more stable progression over time, and are characterised by the gradual accumulation of relatively mature, and partly still functioning, cells within the bone marrow and blood.

Generally speaking, if the **myeloid** cell line is affected, the disease is referred to as either chronic or acute myeloid leukaemia; if the

lymphoid cell line is affected, the disease is referred to as either chronic or acute lymphatic leukaemia.

Acute **lymphoid, or lymphatic, leukaemia** is more common in children and young adults, while myeloid forms are more typically encountered in adults.

Risk factors include numerous chemicals, such as solvents and dyes, and ionising radiation.

A diagnosis of leukaemia can be determined through *haemochromocytometric examination and evaluation of a peripheral blood smear*.

Bone marrow aspiration and immunological characterisation allow the type of leukaemia to be identified and the appropriate type of therapeutic strategy to be determined. It is essential to classify each type of leukaemia through bone marrow cytogenetic investigation and molecular biology, and the use of the new Next Generation Sequencing (NGS) techniques is also important. The therapeutic pathways are constantly improving, and are based on chemotherapy, biological therapies, and bone marrow/stem cell transplantation.

LYMPHOMAS

Lymphomas are diseases that originate in the lymphocytes/lymphatic system, and are divided into two major groups: Hodgkin's lymphoma (HL), and non-Hodgkin's lymphomas (NHL).

Hodgkin's lymphoma (HL)

HL accounts for about 10% of all lymphomas, the majority being cases of the classical type (cHL). The clinical picture is generally characterised by increased volume in one or more lymph nodes at the base of the neck, in the armpits, or in the supraclavicular area: lymph nodes of increased size and consistency, not painful. Often there are no other symptoms, and only 1/3 of patients have

a B symptom (fever, weight loss, night sweats). Diagnosis is made based on an excised biopsy of the affected lymph node, after which an extension (staging) assessment is performed through radiological examinations (CT and PET). Treatment is based on chemotherapy and/or radiotherapy, and the response rates are very good, depending on the stage, even with the possibility of achieving over 90% progression-free survival at 5-7 years.

Non-Hodgkin's lymphoma

Let's now talk about **NHL**; this consists of an extremely heterogeneous group of lymphatic system diseases (according to the WHO classification, NHL includes about 60 different types of lymphoproliferative diseases; the incidence data show that, in 2020, about 13,200 new patients in Italy, about 7,000 men and 6,200 women, were diagnosed with these diseases).

Middle-aged and elderly individuals are most affected, and the most obvious risk factors include exposure to infectious agents, such as Epstein Barr virus (EBV), HIV infection, and for gastric-onset lymphoma, exposure to Helicobacter Pylori. Other factors include exposure to pesticides, benzene derivatives, radiation, and immunosuppressive drugs for prolonged periods of time.

The clinical picture at the time of onset is often characterised by an increase in volume of one or more lymph nodes, which are not painful, in the superficial stations: neck, axillae, supraclavicular, and inguinal. Symptoms may be present, such as fever, which in some conditions may be "undulant", night sweats, which are often very uncomfortable, and weight loss. These are called "B" symptoms.

Diagnosis is based on biopsy and subsequent histological and molecular examination of the affected tissue, and the assessment of the stage of the disease (i.e. the extent to which the disease has spread throughout the body), is also crucial. However, for aggressive cases of NHL, the study of the pathological material examined and the clinical parameters of presentation are more important than the stage itself with regard to prognosis. In fact, the International Prognostic Index (IPI) is used as a clinical and prognostic

trend parameter; fortunately, modern treatments for NHL provide for good survival and cure rates for a significant portion of patients, albeit with important differences based on the various histological types, the IPI, and the comorbidities. The survival rate at five years after diagnosis is 67% in men and 70% in women.

MULTIPLE MYELOMA (MM)

MM consists of the neoplastic proliferation of plasma cells derived from a single clone. Plasma cells are cells that are mainly found in the bone marrow, are derived from B lymphocytes, and are responsible for the production of immunoglobulins, also known as antibodies. The cause of this disease is unknown. It is most frequently encountered in farmers, wood and leather workers, or those exposed to petroleum derivatives. Multiple chromosomal alterations have been encountered in patients with MM. It typically affects older adults, with the average age of diagnosis being 69-70 years, and is rarely encountered in subjects under 40 years of age. Men are affected at a higher rate than women, and black people are affected at a higher rate than white people (approximately twice as many).

- **Clinical picture:** the most frequent onset symptom of MM is bone pain, which is present in over 70% of patients, because the proliferation of the cancerous plasma cells leads to bone erosion due to the activation of bone-destroying cells (osteoclasts) and the suppression of the cells that produce new bone (osteoblasts). Bone damage is usually at the level of the spine and/or the pelvis. If not treated early on, MM can often lead to pathological fractures (i.e. spontaneous fractures occurring with no or little trauma).

- **Diagnostic suspicion** can also arise from a simple blood test, called serum protein electrophoresis, which can highlight a monoclonal component, usually in the gamma zone. The addition of immunoelectrophoresis can prove particularly useful in identifying low concentrations of monoclonal (M) component; in addition, 24-hour urine examination is essential for quantifying the presence of light chains. It should also be clarified that asymp-

tomatic individuals who show a small monoclonal component under electrophoresis can be reassured that the clinical picture for myeloma is quite distinct from those who are carriers of an M-component of a non-myelomatous nature, also called M-GUS. While the presence of this M_GUS abnormality should be monitored over time (usually with annual checks), these situations are relatively common, and do not constitute a state of illness.

- **MM diagnosis** is based on blood tests (serum-protein electrophoresis, serum and urine immunoelectrophoresis, IgG, IgA, IgM immunoglobulin assay, blood count, kidney function, and calcium), bone marrow examinations showing increased pathological plasma cells, and radiological examinations to assess bone lesions (nuclear magnetic resonance imaging).

- **MM treatment** is based on an induction phase, followed by consolidation and maintenance. A distinction must be drawn between patients who are candidates for autologous stem cell transplantation, and those who are not. With the currently available treatment options, which are constantly evolving, MM patients have a median overall survival rate of over eight years. The main causes for unfavourable progressions are renal failure, infections, and the onset of leukaemia.

Ovaries

GIUSY SCANDURRA

What is ovarian cancer?

Ovarian cancer, or ovarian carcinoma, is a rare neoplasm that affected approximately 5,300 women in Italy in 2019, and accounts for 3% of all female cancers. There are three types of malignant ovarian cancers: epithelial, germinal, and stromal. Epithelial cancer is the most frequent, and it accounts for 90% of the malignant cancers affecting these organs.

How would I know if I have ovarian cancer?

Due to the late, non-specific symptoms, approximately 75-80% of patients present with advanced disease at the time of diagnosis (FIGO stage III-IV); the initial finding of a neoplasm limited to the adnexa (FIGO stage I) is more rare (10%), and is most often discovered by chance during routine gynaecological check-ups. In the remaining 10% of cases, the diagnosis is made when the disease is still confined to the pelvic region.

These are the most common symptoms:

- sense of bloating and persistent abdominal tension
- vaginal bleeding
- changes in bowel habits, such as the appearance or worsening of constipation
- abdominal pain
- increased abdominal volume
- nausea and vomiting

These symptoms are often underestimated, as they are commonly encountered in other situations of little concern. However, if these symptoms have never been encountered before, and consistently appear every day for more than 10-15 days a month, and for more

than two consecutive months, it is recommended to consult your family doctor or gynaecologist.

Why does ovarian cancer occur?

The causes that lead to the development of ovarian cancer are not yet well known, with the exception of a few conditions.

Obstetrical and gynaecological history

Early menarche and/or late menopause are risk factors. Multiparity (multiple full-term pregnancies), breastfeeding, and long-term use of oral contraceptives reduce the risk of ovarian cancer. In particular, multiparous women who have given birth several times are about 30% less likely to develop it than women who have not given birth. There is also a correlation between endometriosis and ovarian cancer, which is why patients with this condition should have frequent gynaecological check-ups.

Lifestyles

Obesity, smoking, and lack of exercise are additional factors that increase the risk of developing this neoplasm.

At what age is it most frequently encountered?

40-60% of germ cell ovarian cancers are diagnosed in women under 20 years of age, while epithelial tumours tend to affect women of both reproductive and advanced age.

There have been cases of ovarian cancer in my family. Am I at risk as well?

Family history is a major risk factor in 15-25% of ovarian cancers.

One must be very careful if there are multiple cases of ovarian, breast, pancreatic, or prostate cancer, or even uterine or colon cancer, among one's close relatives (i.e. mother, father, sisters, grandmothers, aunts, or cousins).

However, the presence of a familial risk does not necessarily mean that one is certain to fall ill, which is why it is a good idea to consult your family doctor or a geneticist. Alterations in the BRCA1 and

BRCA2 genes can indicate a predisposition for ovarian cancer.

The risk percentage is 39-46% if a BRCA1 gene mutation is present, and 10-27% if a BRCA2 gene mutation is present. Ovarian cancer can also be associated with another genetic syndrome: “Lynch Syndrome”, which is characterised by an increased risk of developing colon, uterine, and ovarian cancer.

Can ovarian cancer be prevented?

While there are currently no scientifically reliable screening programmes for the prevention of ovarian cancer, studies have shown that, in the absence of risk factors, annual visits to the gynaecologist and transvaginal ultrasound check-ups can facilitate early diagnosis.

One study has shown that prolonged use of contraceptives reduces the risk of ovarian cancer incidence in the general population, especially among women with BRCA gene mutations.

? For women at increased familial risk and with established genetic mutations, such as BRCA1/2 gene mutation and Lynch Syndrome, there is only means of prevention.

Surgical removal of the fallopian tubes and ovaries can prevent almost all genetic/inherited ovarian cancers. Prophylactic surgery is now recommended for women with the genetic mutation who have already been pregnant or have reached menopause. It is crucial to discuss the decision and to seek psychological support, especially for women who are still of childbearing age. The age of the individual, the type of mutation, and any plans for pregnancy must therefore be considered when making these decisions. The guidelines recommend the bilateral removal of the uterine adnexa (i.e. the ovaries and fallopian tubes) between 35 and 40 years of age for women with the BRCA1 mutation, and between 40 and 45

years of age for those with the BRCA2 mutation, once they have decided that they no longer want to bear children.

Lifestyle and habits

Based on the current data, it is recommended to lose weight when necessary, to engage in regular physical activity (20 minutes of aerobic activity a day), and to maintain a healthy diet.

How is ovarian cancer diagnosed?

If a pelvic/ovarian mass is encountered, it is necessary to perform a clinical examination of the abdomen, a gynaecological examination, or an abdominal and transvaginal pelvic ultrasound. In some cases, a Ca125 blood test may be recommended by the referring gynaecologist.

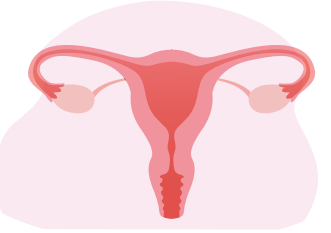
The HE4 protein levels in the blood can also be tested. The combination of HE4 and CA125 can be used to conduct an ovarian cancer risk analysis, using the Risk of Ovarian Malignancy Algorithm (ROMA). The ROMA index estimates the likelihood of ovarian cancer in women with a suspected pelvic mass using the combined measures of CA125 and HE4.

I found out that I have ovarian cancer: who can I go to for treatment?

Advanced stage ovarian cancer is a complex neoplasm that needs to be treated at a highly specialised facility with a proven track record. The management model for ovarian cancer is a multidisciplinary one that revolves around the patient. The patient is at the centre of every medical decision.

Are there any new treatment options available for ovarian cancer?

The first major step in the treatment of ovarian cancer is the adoption of a specialised surgical approach. Nowadays, in order to subject the patient to the most appropriate medical treatment, it is essential to obtain biomolecular information, so that the best treatment options for each specific patient can be adopted. Information regarding the BRCA 1-2 mutations and the characterisation



of the HRD allows for the determination of the patient's sensitivity to the most innovative therapies currently available. Chemotherapy with platinum-based drugs remains the treatment of choice for patients, both for the prevention of relapse in the early stages, and as treatment for advanced stage disease. Molecularly targeted drugs, such as anti-angiogenics and PARP inhibitors, have revolutionised the medical treatment protocols, and have improved the prognoses for patients with advanced or metastatic ovarian cancer. There are numerous ongoing clinical trials aimed at evaluating the efficacy of immunotherapy and other targeted drug treatments. The goal for the future is “personalised care.”

FAKE NEWS

Pap tests are used for the early detection of ovarian cancer
FALSE

It is always necessary to test for the Ca125 and HE4 cancer markers in cases of abdominal pain or swelling, as they serve for early diagnosis
FALSE

Genetic testing for the BRCA1/2 mutations should be performed on all healthy women, even if they have no family history
FALSE

Pancreas

MASSIMO FALCONI AND ALESSIA VALLORANI

What is pancreatic cancer?

The pancreas is a gland located in the abdomen, behind the stomach, and in front of the spine.

It mainly consists of two types of cells: endocrine cells, which secrete hormones like insulin and glucagon, and exocrine cells, which are responsible for producing the pancreatic digestive juices discharged into the intestine through the main pancreatic duct. Anatomically, this gland can be divided into three main regions: the head (through which the biliary tract also runs), the body, and the tail. The head of the pancreas is housed in the duodenum, the first section of the intestine after the stomach. Most pancreatic cancers develop due to a degenerative process that occurs at the level of the exocrine cells in the pancreatic ducts, which are found in greater numbers in the head of the pancreas. This is called ductal adenocarcinoma. This disease is currently considered one of the top 5 deadliest cancers, together with colon, breast, prostate, and lung cancer. In Italy there are an estimated 13,500 new cases per year, with an incidence that shows a north-south gradient, with higher rates in the south. It is also the fourth most frequent cause of death in females, and sixth in males. However, based on the epidemiological assessments, it is expected to become the second deadliest cancer in the western world by 2030.

Risk factors and genetic predisposition

The main acquired risk factor associated with sporadic pancreatic cancer is cigarette smoking, which increases the likelihood of developing the disease by approximately 2 to 3 times. Other predisposing causes include ageing and lifestyle. A diet characterised by excessive consumption of fat and low consumption of fruits and vegetables increases the risk, as does sedentariness, and consequent obesity. Another risk factor, which increases the likelihood of developing this cancer by about 10-fold, is a history of chronic pancreatitis, an

inflammatory condition frequently caused by chronic alcohol abuse, among other things, and may be linked to certain hereditary syndromes common in Italy, such as cystic fibrosis. However, studies of similar cases among close relatives of the same bloodline have shown that about 10% of pancreatic cancer patients have a family history. Some of these familial cases are linked to actual genetic syndromes, including Lynch syndrome related hereditary colorectal cancer, and the presence of mutations in the BRCA1 and BRCA2 genes, which are also linked to the pathogenesis of breast, uterine, and ovarian cancer. These genetic disorders can be diagnosed early thanks to dedicated screening programmes.

Diagnosis and treatment

What are the most common symptoms that lead to a diagnosis of pancreatic cancer?

Unfortunately, due to its minimal or complete lack of symptoms in its early stages, pancreatic cancer is typically only diagnosed once the disease has already reached an advanced stage. The characteristic signs and symptoms are mainly the development of jaundice (yellowish discolouration of the skin and the sclerae of the eyes) due to the localised occlusion of the biliary pathway at the head of the pancreas, the onset of diabetes in the absence of risk factors, worsening symptoms of diabetes previously controlled through treatment, and major weight loss within a few weeks/months. Other symptoms include pain in the upper abdominal region or back, which is characteristic of advanced cancer infiltrating the deep nerve plexuses, and an inability to eat accompanied by vomiting, in cases of cancer affecting the head of the pancreas and occluding the duodenum. If pancreatic cancer is strongly suspected, the main diagnostic tool is computerised tomography (CT), which, thanks to the special radiological characteristics of the disease, typically allows for a diagnosis to be made with absolute certainty.

Treatment

There are currently multiple treatments available for this condition. Given its complexity, it is important to rely on a specialised centre with a multidisciplinary management protocol involving various professional figures, including oncologists, radiologists, gastroenterologists/endoscopists, radiotherapists, and surgeons.

At the early stages, the patient can undergo surgical treatment, either preceded or followed by chemotherapy. At locally advanced stages, on the other hand (i.e. when the cancer has a broader regional extension and involves the neighbouring lymph nodes), chemotherapy is recommended, which, if a satisfactory response is obtained, can be followed by either surgical removal or, if this is not feasible, consolidation radiochemotherapy.

At the metastatic stage, which occurs when the disease is localised in organs other than the pancreas, chemotherapy is recommended. In this latter case, unfortunately, the treatment does not lead to recovery, although recent advances in pharmacology, nutrition, and other supporting fields can still provide ensure good levels of control.

Lung

SILVIA NOVELLO

An analysis of the epidemiological data leaves no doubt as to the aggressiveness of this "big killer": lung cancer kills 34,000 people in Italy each year (and over 1 million worldwide), and the numbers continue to grow. It's the second most frequent form of cancer in men (15%), and the third in women (6%).

Although the percentages may seem to favour women, it should be noted that, in the United States and in many European countries, including Italy, there has been a slight reduction in the incidence (number of new cases) of lung cancer in men in recent years, while incidence among women is increasing, in proportion to the increase in smoking, to the point that it has surpassed breast and cervical cancer in terms of mortality.

Tobacco addiction is the most significant risk factor for lung cancer, considering that a cigarette contains approximately 4,000 chemicals, at least 60 of which are classified as carcinogenic.

Other possible causes include:

- inhalation of second hand smoke by non-smokers;
- exposure to carcinogens, such as asbestos, chromium, arsenic, beryllium, and radon gas;
- environmental pollution
- genetic and family factors.

85% of lung cancer patients are, or have been, smokers: never becoming a smoker and quitting the use of cigarettes and other tobacco products remain the most important forms of primary prevention.

The symptoms of lung cancer are usually late and not very specific, with 10-15% of patients appearing completely asymptomatic at the time of diagnosis.

The diagnosis could result from a chest X-ray performed for other reasons.

The symptoms are non-specific, and can be confused with those of other respiratory diseases. The most frequent include: persistent cough, presence of blood in phlegm, shortness of breath (dyspnoea), chest pain, or rapid weight loss with no apparent cause.

The diagnosis of lung cancer is confirmed through examinations such as fibrobronchoscopy or CT-guided biopsy. Although surgery remains the treatment of choice for this disease, it is only possible for a limited number of patients who are diagnosed at an early stage, or rather when the tumour is still relatively small and hasn't infiltrated the surrounding structures or involved any other organs (metastasis). Other treatment options include radiotherapy (alone and/or combined with other types of treatment), chemotherapy, molecular targeted therapies, and immunotherapy.

Some of these treatments rely on additional analyses, often conducted on the same fragment of tissue that allowed for the diagnosis: these are known as "markers", which guide the therapeutic decisions within the context of what is known as precision medicine.

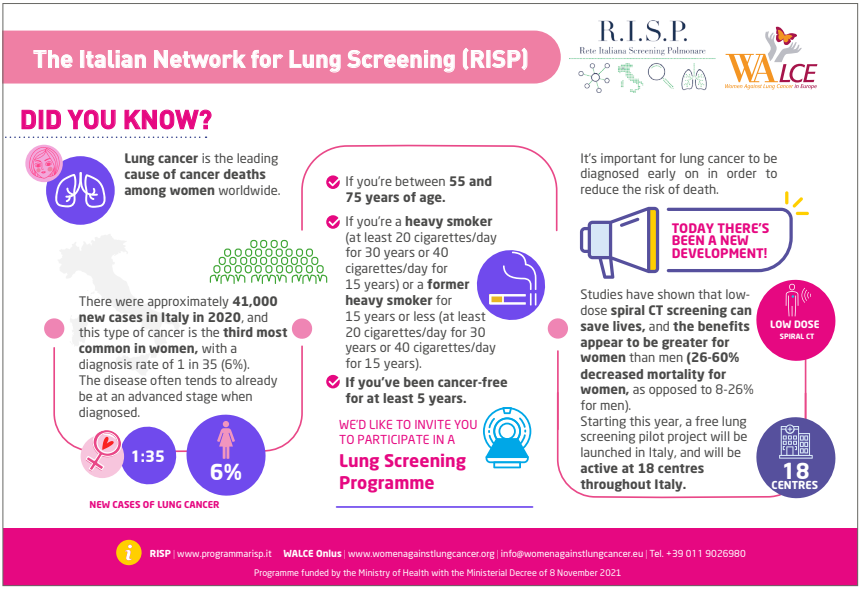
Lung cancer treatment has undergone numerous changes in recent years, offering many patients a longer life expectancy and better quality of life. The optimal treatment options would include assessment by multiple specialists, including a pulmonologist, an oncologist, a radiologist, a anatomic pathologist, a surgeon, and a radiotherapist.

Secondary Prevention and Lung Cancer

There is finally a screening programme for lung cancer. In fact, at least two major studies worldwide have shown a 20% reduction in mortality from this disease through the use of low-dose spiral CT in at-risk subjects. The Italian Network for Lung Screening programme (RISP) consists of 18 centres throughout Italy.

The free programme is open to all Italian citizens (men and women) 55 to 75 years of age who are active heavy smokers (at least 20 cigarettes a day for at least 30 years or 40 cigarettes a day for at least 15 years), or former heavy smokers who have quit for 15 years or less. The RISP programme involves the performance of a low-dose spiral CT scan (without contrast medium) in conjunction with a primary prevention programme (quitting tobacco smoking) in subjects who are active smokers at the time of the examination. The combination of primary and secondary prevention is the most effective way to change this "big killer" into a rare disease.

All the information is available at www.programmarisp.it



Prostate, kidneys, testicles, bladder

MASSIMO ZACCAGNINI

PROSTATE

Prostate cancer is the most frequently diagnosed cancer among men. The familial and "hereditary" issue is becoming increasingly prominent. About 16% of men with prostate cancer were found to have mutations in the genes tested. Testing for BRCa 1 and 2 mutations, with peripheral blood sampling, is recommended accordingly by urologists and oncologists for men with prostate cancer, analysing the family history and even the age of onset in specific individuals.

Is lifestyle an important factor for prostate cancer?

Although no studies showing a statistically significant correlation have been conducted thus far, a healthy lifestyle and diet should never be overlooked when it comes to cancer prevention. Environmental factors are equally important, but even more significant is metabolic syndrome (insulin resistance, obesity, dyslipidaemia, and hypertension), which carries an increased risk of developing prostate cancer.

Which tests should be carried out, and when?

PSA (prostate specific antigen) remains the benchmark test for the early diagnosis of prostate cancer. Our recommendation is for all men to undergo an annual PSA test starting at the age of 50, or at the age of 45 for those with a family history of prostate cancer or of African descent. More recently, the European guidelines issued by the European Society of Urology (EAU) recommend PSA testing

starting at the age of 40 for individuals with the BRCA2 gene mutation.

What examinations are recommended for prostate cancer diagnosis and follow-ups?

The clinical pathway must include examination by a urology specialist, including: personal and family medical history, PSA testing, digital-rectal exam. Further investigations, which the clinician may prescribe based on the specific case and/or suspicion of cancer and/or for patients who have already been diagnosed with prostate cancer, include:

1. **Multiparametric Magnetic Resonance Imaging (MRI mp)** to detect specific areas of suspected cancer within the prostate gland

2. **Sophisticated software** techniques capable of overlaying MRI images with real time ultrasound images (the so-called "fusion" technique) in order to allow for specific, targeted prostate tissue sampling (needle biopsy), preferably using the transperineal approach (area between the testicles and the anus)

3. **PSMA/PET, as so-called NGI (next generation imaging)** exam useful for global staging following a prostate cancer diagnosis or during follow-ups. This type of investigation may soon play a central role in the application of various new treatment protocols.

TESTICLES

Testicular cancer is an uncommon form of cancer, accounting for about 1% of all male cancers, and about 5% of urological cancers. With respect to the various histological types, it is typically considered to be a cancer that affects young people. It predominantly occurs between the ages of 14 and 45, with a peak incidence around the age of 35. Although in the vast majority of cases it is considered a curable cancer, it nevertheless has a highly negative impact on fertility due to its incidence at a young age. Therefore, in case of testicular cancer, it is important to discuss with the specialist how to best preserve fertility.

Are there any risk factors for testicular cancer?

People with testicular dysgenetic syndrome may be predisposed. This syndrome encompasses a set of abnormalities to watch out for, some of which manifest as early as infancy, such as hypospadias (a malformation of the penis in which the external urinary outlet is abnormally positioned), and cryptorchidism (i.e. failure of the testicle to descend into the scrotal sac). With cryptorchidism, the risk of developing testicular cancer increases significantly, even after surgical correction. Reduced spermatogenesis, with reduced fertility, may be a further risk factor.

Are there any symptoms to be watched for with testicular cancer?

The most frequent symptoms are testicular pain and/or swelling of the scrotum, or more simply a newly formed mass noticed by the patient upon self-examination. **There is a need to raise awareness and educate young people so that they have regular check-ups before symptoms appear**, and to set up locations where scrotal ultrasounds can be performed periodically.

Males must also take preventive measures! A suitable venue might already be the family doctor's office, where an objective examination of the genitals can

be requested as part of a routine physical examination. In light of the decline in male fertility observed over the past 30 years, it is recommended for males to take part in prevention programmes by undergoing periodic urological/andrological examinations, not only focusing on reproductive functions, but also with the aim of detecting the onset of testicular cancer at an early stage. The doctor will assess whether it is necessary to have an ultrasound examination performed at a specialised centre.

KIDNEYS

Kidney cancer is estimated to account for 3% of all cancers in both men and women, with an annual incidence of 2%. Several risk factors have been identified, including smoking, obesity, diabetes, and hypertension. It is therefore recommended to avoid smoking, to engage in physical activity, and to maintain a healthy body weight.

Can kidney cancer be hereditary?

About 8% of kidney cancers are associated with familial heredity. It is once again therefore important to know as much as possible about one's origins. Cases of kidney cancer in individuals under the age of 50 are an indication that genetic counselling may be necessary. In these instances, the healthy family members of the individual who has developed kidney cancer at a young age, both male and female, will be referred for surveillance.

What are the symptoms of kidney cancer?

Kidney cancers are insidious, and are therefore a cause for concern, as they tend to develop symptom-free up until their most advanced stages. In most cases, they are encountered by chance during ultrasound imaging and/or CT or MRI scans performed for other reasons. About 50% of these cancers are discovered in this manner. They are referred to as small renal masses (SRMs), and usually have a diameter of less than 4cm.

Cancers not discovered by chance and diagnosed early on, on the other hand, typically involve various symptoms, ranging from lower back and side pain, to blood in the urine (haematuria). It is important not to underestimate these symptoms, and to talk to your doctor about them.

Is it always necessary to remove the kidney if cancer is present?

The surgical protocols have adapted to the "new kidney disease" occasionally encountered without symptoms, resulting in an increase in so-called "nephron sparing" minimally invasive laparoscopic or robotic surgical procedures, which allow for the kidney or a portion thereof to be spared. In certain selected cases, specialised centres also offer active surveillance programmes, with no need for surgical intervention. Whatever the case, these decisions are up to the specialist, who will decide on the type of intervention programme, and the most appropriate technique for each individual case.

BLADDER

Bladder cancer affects both men and women; 75% of this type of cancer occurs in superficial form (meaning that it affects the most superficial layers of the bladder wall) and, in most cases, entails a better prognosis and less aggressive treatment than so-called muscle-invasive bladder cancer.

What role does smoking play in bladder cancer?

Although the urinary bladder is typically ignored by anti-smoking campaigns (which mainly focus on lung cancer), some of the most harmful effects of cigarette smoking are effectively suffered by the bladder itself. It should be noted that the data reported in the EAU (European Association of Urology) guidelines indicate **tobacco smoking as a risk factor in 50% of bladder cancer** cases, and that the low-tar cigarettes of the smoking 2.0 era do not lower this risk.

In this regard, although the risk associated with smoking e-cigarettes has not yet been adequately assessed, known carcinogens are also detectable in the urine of "e-smokers", and so-called e-cigarettes do not eliminate the nicotine addiction associated with smoking.

What are the potential symptoms of bladder cancer, and what exams are recommended?

The main symptom of bladder cancer is haematuria, or rather the presence of blood in the urine. While this symptom can often occur in an intermittent form, and is often misdiagnosed as "cystitis", it should never be underestimated. Promptly contacting your doctor in these cases can make all the difference! Ultrasound imaging of the urinary apparatus is generally the first examination requested to determine the possible presence of cancerous lesions within the bladder.

- **Urethrocystoscopy**, however, remains the primary examination for diagnosis, although it is somewhat invasive. A cystoscope (a rigid or flexible instrument designed to analyse the inside of the bladder with a high degree of precision), is inserted via the urethra.

- **CT (Computerised Tomography)** of the urinary apparatus is the most reliable imaging technique for detecting masses in the bladder, and also provides very useful information regarding the status of the upper urinary apparatus (ureter and kidneys).

- **Urinary cytology (on 3 consecutive urine samples)** is a urine test that allows cancer cells to be detected, especially in cases of high-grade disease, and is very useful at the initial bladder cancer diagnosis stage, and, above all, during the follow-up stages.

NUTRITIONAL GUIDELINES IN ONCOLOGY

GIUSEPPE PLUTINO, ROBERTO COPPARONI, AND NUNZIA LIGUORI

Cancer is the second leading cause of death worldwide. Despite the scientific developments, the number of cancer cases continue to increase, and are expected to double by 2030.

Alterations in nutritional status are highly prevalent in cancer patients, and malnutrition by default, which affects an estimated 33 million people in Europe, is considered a "disease within a disease". Insufficient awareness of nutritional status during cancer treatment has serious consequences, not only on the patient's quality of life, but also on their ability to adhere to the various proposed treatments, resulting in a worse prognosis.

An individual's nutritional status is the result of a complex interaction between their nutritional needs, and their nutrient intake and utilisation, and is a significant indicator of their health status.

Nutritional assessment is an important factor to be taken into account when determining how to approach the cancer patient's treatment, even as early as their first visit.

Early assessment of the patient's nutritional risk, carried out at the time of admission and during subsequent monitoring, makes it possible to counteract the onset of hospital malnutrition and/or to correct situations of pre-existing malnutrition. The results of the nutri-

tional screening should be aimed at seeking appropriate nutritional intervention for evaluation and treatment.

The planning and organisation of the services should provide a "nutritional pathway for the cancer patient", even through protocols of collaboration with freely chosen paediatricians and general practitioners, and through contacts with specialists in the sector, in order to ensure continuity of care.

While awareness of the prevalence and the negative consequences of malnutrition in cancer patients is still quite low among both healthcare professionals and patients themselves, the correct and targeted use of knowledge and techniques relating to adequate clinical nutrition in these patients would have a positive impact on their outcomes and quality of life, as well as on healthcare expenditure.

The nutritional management of cancer patients in Italy currently varies greatly from region to region, and nutritional care and support is not always necessary.

For this reason, the Ministry of Health **has issued a document addressing the aspects of nutritional screening and assessment** (which must become part of multi-dimensional cancer patient assessment, throughout the entire course of their active and palliative care pathways), as well as **the ongoing nutritional care of cancer patients** (which must begin at the time of diagnosis, and continue thereafter, within the context of the cancer patients' specific metabolic/nutritional pathways).

Inheritance

MARIA PIANE AND SIMONA PETRUCCI

At least 10% of the world's diagnosed cancers are hereditary. A cancer is considered "hereditary" when its occurrence is strongly influenced by the presence of a harmful genetic alteration (pathogenic variant – PV) within the DNA, which already exists at the time of conception, and is thus present in all the cells of the individual.

Every individual has two copies of each gene, one inherited from their mother, and one from their father. With very rare exceptions, an individual is predisposed to develop cancer when one of the two copies of that gene is altered (heterozygous PV). Carriers of these PVs have a higher risk of cancer than the general population, and have a 50% chance of passing the altered gene on to their children, who will inherit the same increased risk of developing cancer.

Although rare, **hereditary cancers have a significant clinical and social impact**, as they often occur early, affect multiple sites (multiple cancers over the course of the same individual's lifetime), or affect multiple family members.

For families with a high incidence of specific cancers, cancer genetic counselling (CGC) is recommended, both for those with diagnosed/probable cases (usually those suffering from or with a history of cancer), as well as their healthy family members.

During the CGC, the geneticist assesses the likelihood that the consultee is a carrier of a PV, and, based on their findings, proposes the molecular analysis of specific genes from a blood DNA sample. The development of new technologies (Next Generation Sequencing – NGS) has made it possible to identify new genes responsible for hereditary cancer syndromes, which can now be investigated in clinical practice using multi-gene panels.

There are approximately one hundred genes responsible for hereditary cancer syndromes.

The most frequent are listed in the table on pages 30-31.

For healthy individuals with genetic alterations that predispose them to develop cancer, the surveillance pathways are organ-specific, and must focus on all the organs potentially at risk. The checks should begin early, and should be conducted frequently.

By way of example, *for women at risk of hereditary breast cancer, breast examinations are recommended starting at the age of 25, with annual magnetic resonance imaging (MRI) with contrast medium (ages 25-29), alternating with mammograms starting at the age of 30*.

Not only that, *for those at increased risk of ovarian cancer, annual gynaecological examinations and transvaginal ultrasounds are also recommended*, as are abdominal ultrasounds and other imaging methods for studying the pancreas and/or dermatological examinations for increased risk of melanomas, where appropriate.

For **men at risk of hereditary breast cancer**, surveillance pathways are recommended, mainly based on annual *breast examinations starting at the age of 35, PSA testing and ultrasound checks for prostate cancer starting at the age of 40, mammograms starting at the age of 50*, and, like for women, dermatological examinations and pancreatic check-ups, where appropriate.

For individuals at risk of Lynch syndrome, the surveillance strategies mainly include *annual or biannual colonoscopies starting at the age of 20-25*, and *annual transvaginal ultrasounds starting at the age of 30-35* (accompanied by testing for cancer markers).

For individuals with multiple endocrine neoplasia (MEN) syndromes or their at-risk family members, *biochemical metabolite and hormone testing and checks by instrumental investigations (ultrasound, CT and MRI scans) of the target glands are recommended from childhood onwards.*

To sum up, the proper evaluation of hereditary/familial risk and testing for genetic alterations (genetic testing) are currently the basic elements used to **determine a personalised clinical/instrumental surveillance programme** and, where appropriate, the use of cancer risk reduction measures.

LIQUID BIOPSY AND GENETICS

ANTONIO RUSSO, ALESSANDRO PEREZ AND LORENA INCORVAIA

New frontiers in oncology: Liquid biopsy.

Liquid biopsy is now one of the pillars of so-called Precision Oncology.

In fact, the possibility of obtaining a wealth of information regarding various aspects of neoplastic pathologies, including prognosis, disease progression over time, and sensitivity to new antineoplastic agents, with no need to resort to invasive and sometimes uninformative tissue sampling, constitutes a valuable resource, one which has the potential to revolutionise oncological clinical practice, as already demonstrated by the excellent results obtained with lung neoplasms.

Liquid biopsy therefore offers clear advantages with respect the traditional approach of analysing tumour tissue. It is **minimally invasive**, **low-cost**, has a **very fast turnaround time**, and is almost entirely **complication-free**, because it can be performed with a simple blood sample. In addition, it is characterised by a high level of acceptance by patients, and can be repeated without any problems, with serial sampling being performed to reveal the emer-

gence of resistance to treatment in real time and, if necessary, to correct the treatment approach in use.

The emerging clinical applications for this procedure mainly involve colorectal and breast cancer, and advanced stage melanoma. Therefore, it is likely that plasma analysis for this type of disease will soon be recommended in clinical practice. The analysis of circulating tumour DNA (ctDNA), isolated from peripheral blood and/or other biological fluids, currently represents the main liquid biopsy approach utilised in oncological clinical practice. The chances of success are related to the amount of ctDNA present in circulation, which may affect the reliability of the outcome of the genetic analysis. In fact, the amount of ctDNA often depends on volume, disease localisation, and disease stage, and this can lead to the liquid biopsy sample returning "false negative" results.

In the future, it is possible that other blood-derived components, such as circulating tumour cells, circulating tumour RNA, microRNAs, platelets, and exosomes, as well as other biological fluids, such as urine, saliva, ascitic and pleural fluid, will be used in clinical practice to obtain even more information with respect to that obtained from the analysis of the ctDNA extracted from plasma alone. It is also extremely important that the methods underlying liquid biopsy for the assessment of the "molecular traces" of the tumour be standardised as much as possible: this is why the diagnostic approach using liquid biopsy represents an **ideal scenario for collaboration between the clinic and the laboratory**.

In recent years, with the introduction of massive parallel sequencing into clinical practice, the applications of liquid biopsy have taken on a broader scope. Next Generation Sequencing (NGS) makes it possible to simultaneously identify genetic alterations in multiple genes in a single analysis, allowing for the simultaneous profiling of multiple patients at the same time, thus optimising the costs and times. Liquid biopsy establishes **the importance of a multi-disciplinary approach** in a definitive manner. The task of discussing and selecting the cancer patient's diagnostic/clinical pathway is currently assigned to Molecular Tumour Boards: interdisciplinary groups where multiple

experts collaborate to identify the most appropriate clinical and decision-making processes based on the molecular characteristics of the individual patient.

How important is "genetics" in terms of cancer prevention and treatment?

Most cancers are referred to as "sporadic", meaning that they are caused by alterations generated in one or more cells of the body that are not hereditary, and are therefore not passed on to offspring. A smaller, yet significant, percentage of cancers, which varies depending on the type of cancer in question, arise due to the presence of pathogenic DNA variants since the time of birth, which are usually referred to as "genetic mutations." These mutations can be passed on to offspring, and are therefore defined as "hereditary." It should be noted, however, that **it is not the cancer itself that is transmitted, but rather the genetic alteration**, which predisposes the individual to possibly develop the cancer during the course of his/her lifetime.

It is very important to have information regarding the existence of a genetic mutation predisposing the individual to develop certain cancers, for many reasons; one example is the *BRCA1* and *BRCA2* gene mutations. We now know well that *BRCA* gene mutations are associated with an increased risk of developing certain types of cancer, mainly breast and ovarian cancer, but also pancreatic and prostate cancer, as we have learned more recently. The identification of individuals carrying these pathogenic BRCA gene variants makes it possible to adopt important personal and familial cancer prevention and risk reduction strategies, where appropriate.

Cancer genetic counselling and BRCA testing are recommended based on specific "criteria", which take into account information useful for recognising cancers linked to hereditary predisposition, such as age at the time of diagnosis, type of cancer, number of relatives with cancer in the same family, or the presence of multiple cancers. In the event of a positive BRCA test (identified mutation), **the individual's family members will also have access to cancer genetic counselling and BRCA testing** in order to check whether they also carry the mutation. The finding of a mutation makes it possible to

initiate programmes for the early diagnosis of the cancers associated with these gene alterations, and to propose specific strategies aimed at reducing the risk of the developing those cancers.

Finally, it is important to bear in mind that the discovery of a pathogenic BRCA variant also has significant treatment implications for patients already diagnosed with cancer. This is what is referred to as the "predictive" role of BRCA, or rather the fact that the presence of the mutation can help predict the efficacy of specific cancer treatments, such as new drugs called "PARP inhibitors."

It should be noted that the BRCA test should be performed within the context of a multidisciplinary pathway, in which the experts involved express an opinion on the testing recommendation, the most appropriate type of test to be performed, and the results' implications for the patients and their family members.

In order to meet all these new challenges, in collaboration with other Scientific Societies, like the SIGU, the Siapec/IAP, and the AIFET, and with the support of the Patient Associations, the Italian Association of Medical Oncology (AIOM) has promoted the drafting of the **first National Guidelines on hereditary cancer syndromes**. This document will be an essential tool for establishing a standardised and uniform pathway for individuals throughout the country with hereditary cancer syndromes, covering all aspects from prevention, to early diagnosis, and comprehensive care in the case of a cancer diagnosis.

Personalised medicine

PAOLO MARCHETTI AND ANDREA BOTTICELLI

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. 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.

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.

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. One of the most important of these is Trastuzumab-deruxtecan for patients with HER2-positive breast cancer.

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 pa-

tient, the cancer, the drugs administered, and the microbiota now represents a major opportunity, and is the ultimate expression of Personalised Medicine.

APMP, "Patients' Associations, Together for the right to Personalised Medicine in Oncology"

Working in synergy with eleven other Patients' Associations, the IncontraDonna Foundation is dedicated to ensuring that the right to personalised medicine is recognised by the Institutions.

The triumphs in the fields of scientific research (namely genetics, genomics, and molecular biology) and data science are transforming cancer prevention, diagnosis, and treatment. In recent years, we have witnessed the rise of precision oncology, an approach based on the genetic and molecular characteristics of the cancer itself, which are different for each individual, and are independent of the anatomical location where the disease develops. Precision oncology has also evolved into personalised oncology, an approach that focuses on the individual, not just on his or her cancer. The aim is therefore to combine all the information about the individual suffering from the disease (including genetics, lifestyle, genomics, and the environment in which they live), in order to come up with a treatment pathway that best meets the individual's needs from a treatment and quality of life perspective.

Despite its numerous benefits in terms of clinical effectiveness and system sustainability, personalised medicine has not yet been recognised as a right. There is an evident lack of uniform and equal access to personalised medicine throughout Italy, accompanied by low levels of knowledge and awareness on the part of citizens. The time has come for patients, the scientific community, the institutions, and companies to work together to ensure that everyone is offered personalised treatment options.

In light of these considerations, 12 patient associations active in the field of oncology (*Fondazione IncontraDonna, ACTO Italia - Alleanza contro il tumore ovarico, Europa Donna Italia, Europa Uomo Italia Onlus, F.A.V.O. – Federazione Italiana delle Associazioni di Volontariato in Oncologia, La Lampada di Aladino Onlus, IPOP Onlus – Associazione Insieme per i Pazienti di Oncologia Polmonare, PaLiNUro – Pazienti Liberi dalle Neoplasie UROteliali, Salute Donna Onlus – Salute Uomo, WALCE Onlus – Women Against Lung Cancer in Europe and UniPancreas Associazione Onlus)* have committed to work together to ensure that the right to personalised medicine is recognised by the Institutions.

The ultimate goal is **to allow the broadest possible access to this new approach to cancer treatment**. The Group, which is called **APMP - Patients' Associations, Together for the Right to Personalised Medicine in Oncology**, is supported by Roche.

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 triple-negative breast cancer in both the metastatic and neoadjuvant phases. And it is precisely the neoadjuvant phase (i.e. prior to surgery), that represents the real revolution, because it is during this phase that immunotherapy, in combination with chemotherapy, can lead to the complete regression of the cancer.

Today, we are only witnessing the start of these new opportunities, and new immunotherapy strategies will be developed in the near future, such as **cell therapy, and therapeutic vaccines**.

MICROBIOTA

MARIA RESCIGNO

Microbiota is the name given to the set of bacteria, viruses, fungi and protozoa that inhabit our bodies, which, together with our cells, form a true ecosystem.

The microbiota is distributed throughout virtually every organ and tissue, although it is estimated that over 70% of the total resides within the gut.

Thanks to the new tools now available to researchers (such as gene sequencing and single-cell analysis technologies), we are now able to better understand how this complex set of microorganisms affects the functioning of the human body. The fact that the microbiota plays an important role in our health should come as no surprise: **the human body hosts a greater number of micro-organisms than the cells that comprise it**, and the DNA of these micro-organisms is, on the whole, 100 times greater than our own.

In the case of cancer, studies have shown that **the microbiota is capable of influencing the disease's progression**, by interacting with both the cancer cells and the immune cells, as well as the treatments' effectiveness, and that it can do so in two ways: remotely, by releasing molecules (so-called postbiotics) into the gut, which enter the bloodstream; and proximally, by directly colonising **the cancer microenvironment and altering the functioning of the cancer cells**. Depending on the type of cancer and the specific family of bacteria or fungi, the microbiota can have an anti-cancer or pro-cancer effect. Better understanding this interaction can pave the way for new cancer therapies and new prevention strategies.

NEOADJUVANT

GIACOMO BARCHIESI AND GABRIELE PIESCO

In the case of a early-stage breast cancer diagnosis (in the absence of distant metastases), neoadjuvant treatment may be proposed, which consists of a treatment performed prior to surgery.

Various data in the literature demonstrate the effectiveness of neoadjuvant treatment, as well as the relative benefits for patients.

The goals of neoadjuvant therapy for breast cancer are the following:

1. **Reduced rate** of post-operative recurrence.
2. **Increased** patient survival, as per adjuvant post-operative treatments.
3. **Reduction of the tumour mass** with variable results depending on the initial size and type of the breast carcinoma, to the point of the neoplasm's complete elimination, defined as pathological complete response (pCR), which is achieved in 30-50% of cases (depending on the type of cancer).
4. **Increased rate of breast-conserving surgery:** by reducing the initial size of the tumour, neoadjuvant treatment often allows for conservative surgery (quadrantectomy) to be performed rather than radical surgery (mastectomy), thus also reducing the risk of the post-operative complications associated with the latter.
5. **Evaluation of the degree of the cancer's sensitivity** to the proposed treatment: during neoadjuvant treatment, it is possible to definitively determine the cancer's response to the drugs either via a physical examination performed by the doctor, or by performing instrumental examinations (e.g. breast ultrasound).

6. **Customisation of the systemic post-operative treatment** based on the clinical response to the pre-operative therapy in terms of pCR.

There are currently various treatments that can be offered as neo-adjuvants, and they differ depending on the type of breast cancer:

- **Chemotherapy:** this is the most frequently proposed treatment, lasting 5 to 6 months; the therapy involves a combination of several chemotherapeutic agents administered intravenously.

- **Biological therapy:** also called molecular-targeted therapy, mainly directed against the HER2 protein expressed by certain types of breast cancers. This treatment is always combined with chemo-therapy.

- **Immunotherapy:** this type of treatment can now be proposed in cases of locally advanced triple-negative breast cancer. The treat-ment is always combined with chemotherapy in this case as well, and is administered intravenously.

- **Hormone therapy:** in certain cases of hormone-responsive breast cancer (whose cells express receptors for oestrogen and/or pro-gesterone), neoadjuvant hormone treatment may be proposed, administered in tablet form.

It is therefore very important to turn to a qualified Breast Cancer Treatment Centre, where the various figures on the multidisciplinary team (oncologist, breast surgeon, plastic surgeon, radiotherapist, radiologist, and anatomopathologist) will establish the most appropriate diagnostic and therapeutic procedure for each individual patient, thus determining the cases in which neoadjuvant treatment is appropriate.

METASTATIC

GIACOMO BARCHIESI AND GABRIELE PIESCO

A cancer is considered metastatic (stage IV) when cancer cells from the initial organ of onset (breast, lung, ovary, etc.) reach distant organs via lymph and blood vessels.

In most cases, metastatic cancer is **not curable**, but is certainly **treatable**, meaning that it can be controlled with medication, chronicised, and in some cases may even temporarily disappear. Metastatic cancer is not curable because the metastases tend to recur.

Metastatic breast cancer

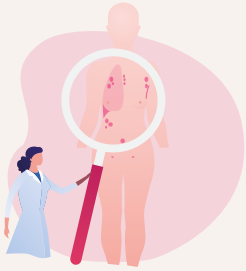
In Italy, there are about 37,000 patients living with metastatic breast cancer. Of these, just 6-7% of the cases were diagnosed at an already advanced stage, or rather with distant metastases.

Thanks to the advances made in diagnostic and treatment methods, the availability of new anti-cancer drugs, and the combination of systemic therapies with local therapies **(e.g. radiotherapy)**, the survival rates and quality of life of patients with metastatic cancer have increased significantly. There are also multiple treatment strategies for metastatic cancer, including chemotherapy, molecularly targeted drugs, hormone therapy, and immunotherapy. The choice of treatment is based on several parameters: type of cancer, characteristics of the patient (age, presence of other diseases, mental/physical situation, etc.), and any previous anti-cancer treatments received.

Metastatic lung cancer

Unfortunately, most lung cancers continue to be diagnosed at an already advanced stage, thus eliminating the possibility of effective surgical treatment. Whereas up until recently chemotherapy was the only treatment strategy in these cases, there are now two major treatment options available that have radically improved the progno-

ses for these patients: **immunotherapy and molecular targeted therapy**.



Both cases offer multiple choices designed to target specific biological features of the cancer. **It is therefore essential to contact a treatment centre that's able to conduct a thorough and comprehensive molecular analysis of the neoplasm**. Some of these treatments have proven to be more effective than chemotherapy, and can be administered without chemotherapy treatment.

Metastatic melanoma

Melanoma is a malignant skin cancer that is not particularly responsive to chemotherapy. The advent of immunotherapy and molecular-targeted therapies has significantly improved the survival rates of patients with metastatic melanoma, with 50% benefiting from long term effects following these treatments.

Metastatic ovarian cancer

Since ovarian cancer is chemotherapy-sensitive, chemotherapy remains a viable treatment strategy in cases with metastases. Moreover, ovarian cancer is also often associated with BRCA1 and BRCA2 gene mutations. This condition has enabled the development of **molecularly targeted drugs** (PARP inhibitors), which have significantly extended the time frames before the disease's recurrence. For patients that do not carry this mutation, on the other hand, biological drugs can be used in combination with chemotherapy.

13 October: National Metastatic Breast Cancer Day

Metastatic Breast Cancer Awareness Day is celebrated in support of all women with metastatic breast cancer.

Doctor-patient-caregiver communication: how to talk about it

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 be 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 generally restores a 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 "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."

TALKING ABOUT CANCER

ROSSANA BERARDI

There is still too much fake news about cancer circulating in the media: about 30% of the news posted on the social networks constitutes fake news, which can have dangerous consequences.

A recent scientific study analysed 200 of the most popular cancer articles on social media, 50 for each of the four most common cancers (breast, colorectal, prostate, and lung). The study, which was published in the Journal of the National Cancer Institute, showed that about one third (30.5%) of these articles contained harmful information that could lead to the postponement or even the avoidance life-saving treatments, with people resorting to dangerous "do-it-yourself" methods based on the use of tools that haven't been scientifically proven. These articles were very popular, to the point that they received an average of 2,300 shares, as opposed to the 1,500 shares received by certified news articles.

Then again, we cannot overlook the fact that nearly 90% of cancer patients use the Internet as a source for information about cancer, and that 49% of millennials do online research the very day that they are diagnosed with cancer.

In order to encourage the dissemination of correct information in the field of oncology, the project **comunicareilcancro** ("talking about cancer" project was born. It includes a website **(www.comunicareilcancro.it)** and dedicated social media profiles). One of the project's goals is to teach communicators (namely doctors, nurses, journalists, representatives of patient

associations and institutions, and communication managers for public and private health and pharmaceutical companies) the rules for talking about health and cancer in a proper and effective manner. In this regard, we have also set up **a dedicated university specialisation course at the Marche Polytechnic University ("Talking about Cancer, Medicine and Health"), the first of its kind in Italy (comunicareilcancro.it).**

The pandemic also unexpectedly brought about a renewed focus on the issues of health, scientific research, innovation, prevention, and healthy medicine. **This renewed awareness, however, must be communicated in a correct and scientifically rigorous manner**. One of the aims of the specialisation course is precisely to teach responsible communication, seeking out safe and certified sources, and using simple language, even despite the complexity of the topics.

Because correct communication is not an option, but a duty, and an indispensable part of the treatment pathways.

Rights of cancer patients

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 **booklet by the Italian Association of Cancer Patients, Relatives and Friends (AIMaC) titled "The rights of cancer patients" (www.aimac.it/diritti-del-malato)**, to which reference can be made for more in-depth information on each specific topic.

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 (national social security institute) 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** by the individual concerned, either directly 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 recom-

mended 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, has the right to be transferred to the place of work closest to his/her home, and may not be transferred without his/her consent. A similar right, to be transferred to the office closest to the assisted person's home, is granted to employees who are assisting an ill family member with a severe handicap.

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. A similar right is granted, to a lesser extent, to workers who are also caregivers of cancer patients. **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).**

Workers who are caring for a loved one suffering from cancer, recognised as disabled or severely handicapped, are entitled to the following leaves of absence:

- **work absences (3 days/month - law 104/92);**
- **twice-yearly paid special leave;**
- **twice-yearly unpaid leave for serious family reasons.**

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 ill individual 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

Sick workers with a recognised civil disability of over 74% are entitled to the benefit of 2 months notional contribution, useful for pension purposes, for each year of service actually rendered in disabled condition.

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.

THE INCONTRADONNA FOUNDATION

Duly registered with the Unified National Third Sector Register, the IncontraDonna Foundation is a non-profit organisation that works to promote a health system that is increasingly based on equity, innovation, and accessibility, in accordance with the needs of the public and of cancer patients (with a specific focus on breast cancer, as it is the most widespread cancer, and continues to show wide margins for improvement at all stages, from prevention to treatment).

Our goals are

- **To raise awareness of the importance of prevention;**
- **To disseminate knowledge of healthy lifestyles** as early as childhood;
- **To actively stimulate dialogue between *Institutions, Scientific Communities, and Associations*** in order to promote a health system that's increasingly based on equity, innovation, and accessibility, and to protect the rights and needs of patients and the public;
- **To improve the public's awareness of the services offered by the National Health System**, to which they can turn with knowledge and confidence;
- **To provide support to patients and "caregivers"** (family members, friends, and colleagues).

Activities

- **Awareness-raising campaigns** on a national and local scale (Frecciarosa is the best known), with free medical examinations and consultations;
- **Patient Advocacy**: participation in technical round tables (we are members of various working groups coordinated by the Ministry of Health, and inter-parliamentary groups dedicated to influencing the legislature in a cohesive manner, even with scientific advice, patient view consultations, and more);
- **Agreements with Agenas** and other leading players in the scientific community for synergistic collaboration on scientific and technological research activities aimed at promoting healthcare

and the dissemination of correct information on breast cancer and other cancer-related issues;

- **Representation of patients' needs to pharmaceutical and diagnostic companies;**
- **Clinical trials and research in the field of oncology;**
- **Free sports and wellness programmes** (e.g. dancing, rowing, nutrition) for both patients and the public;
- **Prevention training and culture** (corporate welfare, patient information and volunteer training, CME training for doctors and nurses).

Our core values are inclusion, equity, and tenacity.

HOW TO SUPPORT THE INCONTRADONNA FOUNDATION

FONDAZIONE Incontra donna
OCCUPIAMOCI DI SALUTE

Become a volunteer at incontradonna.it

Make a donation

To make a donation or payment, please send a bank transfer to:

Recipient: Fondazione IncontraDonna
Reason for payment: membership fee or donation
Bank Account: Unicredit Banca di Roma.
IBAN: IT93D0200805198000400072751

Donate your 5xMille

Your tax return form contains a box dedicated to "non-profit organisations of social utility" (Onlus): simply apply your signature and enter our

tax code 97513990586

Aiom AiomFondazione

Once again this year, the AIOM and the AIOM Foundation are pleased to be part of an important initiative for everyone's benefit. 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 was established in 2005 to bring together doctors, nurses, and patient association representatives within a single organisation. Both are 100% engaged in the fight against a group of over 200 different diseases, called cancers.

These diseases are on the rise in almost every Western country, including our own. In 2022, there was an estimated total of 390,700 new cancer diagnoses in Italy: 205,000 in men, and 185,700 in women. The number of cases increased by 14,100 in just two years. The most commonly diagnosed cancer is breast cancer, with over 55,700 new cases. A total of 2.5 million Italian citizens were living with a cancer diagnosis in 2006, and this number increased to approximately 3.6 million in 2020 (5.7% of the peninsula's entire population).

But while cancer is becoming increasingly widespread, it is also becoming more treatable and curable than in the recent past. These successes have mainly been due to the introduction of new and improved therapies in recent years. But there's also another extremely powerful tool, whose effectiveness is often underestimated: prevention. Primary prevention involves adopting a healthy lifestyle, starting at a young age, and entails not smoking, engaging in regular physical activity, maintaining a healthy and balanced diet, getting vaccinated, limiting alcohol consumption, and maintaining a suitable body weight. In fact, up to 40% of all cancers can be avoided by following these simple rules. Secondary prevention, on the other hand, is aimed at detecting cancer at an early stage, so that it can be effectively treated and cured more frequently. For breast cancer, this consists of free mammogram screenings every 2 years for women 50 to 69 years of age, based on the programmes organised by the various Regions. Some Regions have expanded the age range for mammogram screenings to include women ages 45 to 74.

Unfortunately, there are still a large number of people in Italy who do not take preventive measures. Not enough people are taking part in the screening programmes.

The time has come to boost our cancer prevention efforts! That's why we decided to contribute to the preparation of this Guide.

Saverio Cinieri - AIOM President
Giordano Beretta - AIOM Foundation President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