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NUTRITIONAL RESEARCH IN ONCOLOGY: FROM PROSPECTIVE OBSERVATIONAL STUDIES TO DIET TRIALS FOR POPULATION HEALTH

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Cancer is the second leading cause of death in Europe (Eurosta news 2015). For a total population of 504.6 million inhabitants in 2012, the estimated cancer burden was approximately 1.43 million new cancer cases in men and 1.21 million new cancer cases in women (Ferlay et al., 2013).

It has been estimated that up to half of the cancer burden is preventable (Parkin DM et al., 2011; Danaei G., et al. 2005). Successful primary prevention requires a combination of individual preventive action (by avoiding or reducing exposures) and group action (when exposure is eliminated or reduced by measures effective at the population level). Furthermore, identifying modifiable risk factors associated with cancer progression and recurrence is necessary to extend the life span of cancer survivors.

Cancer is a complex multistage disease associated with accumulation of multiple DNA mutations that cause deregulation in cell proliferation and differentiation, loss of normal tissue organization, and eventually tissue invasion and progression to distant sites (Longo VD. et al., 2010). Obesity, a known risk factor for several cancers, can mediate many of these cellular processes. Metabolic, hormonal and growth factor alterations associated with increased food consumption, decreased physical activity, and excessive adiposity, affect the

regulation and expression of genes involved in DNA repair, cell proliferation and differentiation or apoptosis, allowing cells to accumulate damage and mutations, survive, proliferate and under permissive conditions, undergo malignant transformation (Longo VD. et al., 2010). In humans, sedentary lifestyle and/or calorie-dense diet (rich in refined products and sugary drinks) have greatly contributed to the growing prevalence of obesity and metabolic syndrome (MetS), which, together with tobacco, are the major preventable causes of cancer (Longo VD. et al., 2010). Excessive adiposity as a result of chronic energy imbalance is associated with increased oxidative stress, insulin resistance, inflammation and changes in hormone and growth factor concentrations that play a key role in the pathogenesis of cancer (Longo VD. et al., 2010). Recent data suggest also that obesity, and other markers of insulin resistance such as high blood glucose, and the metabolic syndrome, may effect cancer prognosis too.

The prevalence of MetS in adult population ranges between 20 and 40% in different western countries. MetS is defined as a clustering of cardiovascular disease (CVD) risk factors of metabolic origin. The most frequently used criteria are those of the National Cholesterol Education *Program* Adult Treatment Panel III (Jama 2011), which defines MetS as the presence of three or more of the following conditions: Waist circumference ≥ 88 cm in women or 102 cm in men, Glucose ≥ 5.6 (mmol/l), Triglycerides ≥ 1.7 mmol/l, HDL-Cholesterol < 1.0 (men) or < 1.3 mmol/l (women), blood pressure $\geq 130/85$ mmHg. Classical studies showed that the MetS is accompanied by a two-fold increase in the risk of CVD and a five fold increase in the risk of type 2 diabetes mellitus. More recently, several studies showed that MetS is also associated with increased risk of cancer, neurodegenerative diseases, non-alcoholic

fatty liver disease and cirrhosis, chronic kidney disease, prostatic hyperplasia, and other chronic conditions. MetS related cancers include colorectal, liver, gallbladder, pancreas, breast, cervix, endometrium, ovary, kidney, esophagus (adenocarcinomas), and probably prostate and lung cancer, representing two thirds of total cancer incidence. The mechanism is likely to involve hyperglycemia, hyperinsulinemia, and its effect on the synthesis and bioavailability of sex hormones, growth factors, and pro-inflammatory cytokines, increased leptin and decreased adiponectin levels also disrupt homeostatic signalling pathways involved in cell proliferation, cell-cycle regulation, and angiogenesis.

There is increasing observational and experimental evidence that improving diet and lifestyle may modify the risk of develop the MetS and the other chronic diseases associated with cancer. Classical studies showed that MedDiet (i.e. a diet that was largely based on unrefined cereal products (mainly bread and pasta), pulses, vegetables, olive oil, nuts, fruit, moderate wine, occasionally fish and cheese, and rarely other animal products) is associated with lower risk of CVD and diabetes. Subsequently it became clear that subjects with the highest adherence to a traditional MedDiet have lower cumulative incidence of MetS, and of several chronic diseases than those with the lowest adherence. Randomized intervention trials showed that MetS can be reversed with MedDiet, with up to 69% reduction of MetS prevalence after 2 years of diet. Several other trials supported favourable effects of MedDiet on body weight, abdominal adiposity, plasma lipid profile, and endothelial function. Lower adherence to MedDiet is also associated with the development of cognitive impairment and of Parkinson and Alzheimer disease. Several observational studies on dietary patterns showed that MedDiet

is significantly associated with lower risk of breast cancer, colon cancer, melanoma, coronary heart disease), stroke, diabetes, Alzheimer disease

Consistently, the systematic literature review by the World Cancer Research Fund (WCRF) suggests that a diet low in red and processed meats and higher in vegetables, fruits and whole grains is associated with a lower risk of many types of cancer (World Cancer Research Fund, American Institute for Cancer Research, 2007).

Our dietary randomized controlled trials in postmenopausal women (the DIANA - Diet and Androgens-trial) showed that a comprehensive dietary modification, based on macrobiotic principles and MedDiet, elicited a very high compliance and dramatically improved, over a few months, the hormonal and metabolic pattern associated with MetS and breast cancer risk, decreasing body weight (4.1 Kg), waist circumference (4 cm), glycaemia (-6%), triglycerides (-15%), total cholesterol (-14%) testosterone (-18%), free estradiol (-23%), and insulin (-10%), and increasing sex hormone-binding globulin (SHBG, +25%) and insulin-like growth factor-binding protein (IGFBP-I, +12% and IGFBP-2, +25%), thus decreasing the bioavailability of sex hormones and IGF-I. Such favourable effects may have been largely due to the moderate calorie restriction that we obtained reducing highly processed calorie-dense food and refined carbohydrates and increasing the consumption of highly satiating unrefined cereals, legumes and vegetables (Berrino F. et al., 2001; Berrino F. et al., 2006; Kaaks R. et al. 2003; Berrino F. et al., 2005).

We are now promoting at the Fondazione IRCCS Istituto Nazionale dei Tumori di Milano research programs structured in two main investigative approaches: 1.

prospective cohort studies, to define individual risks related to diet; 2. intervention studies, to test strategies for prevention and recurrence of cancer and other chronic-degenerative diseases.

Among the randomized intervention trials the following are ongoing:

The **COS study** (Pasanisi P. et al. 2014) is a randomized controlled trial of diet and physical activity in BRCA mutation carriers. The aim of the study is to test whether moderate caloric and protein restriction (including avoidance of milk protein) together with physical activity, decrease IGF-I, insulin, and insulin resistance in women with a genetic susceptibility to breast cancer. The study is recruiting a cohort of 300 BRCA mutation carriers and 224 women have been already randomized. This trial is now expanding thanks to AIRC funding to randomize 600 mutated women. This large cohort of women with BRCA mutations will allow to test potential modulators of penetrance and prognosis.

The **TEVERE (Diana-4) study** is a blinded randomized controlled trial of diet and metformin for primary prevention of breast cancer. The study is recruiting healthy women aged 45–74 years, with waist circumference >85 cm, and at least one feature of metabolic syndrome. The aim of the study is to test the effect of metformin, an antidiabetic drug, on breast cancer occurrence. The study hypothesis is that study participants treated with metformin (1700 mg/day) will have a lower incidence of breast cancer in comparison with women given placebo on breast cancer prevention during 5-year follow-up. Participants also receive dietary recommendation

to reduce the risk of metabolic syndrome and insulin resistance. At the moment, we have recruited 542 women and 380 are under treatment.

The **MeMeMe study** is a randomized controlled trial of diet and metformin for primary prevention of age-related chronic diseases (ArCD). The plan is to carry out a randomized controlled trial on 2,000 healthy men and women, 55-74 years of age, at high risk of ArCD because of metabolic syndrome. The aim of the study is to evaluate the effect of comprehensive life-style intervention (including moderate physical activity and Mediterranean/macrobiotic diet with moderate caloric restriction), and treatment with metformin for prevention of ArCD. The recruitment is in progress and about 400 persons are already under treatment.

The **DIANA-5 study** (Berrino F. et al., 2016; Berrino F. et al., 2014; Villarini A. et al., 2012) is a multicenter randomized controlled trial of the effectiveness of a diet based on Mediterranean and macrobiotic principles, associated with moderate physical activity, in reducing additional breast cancer events in women with early stage invasive breast cancer at high risk of recurrence because of metabolic or endocrine milieu. The intervention is expected to reduce serum insulin, sex hormones, serum IGF-I, and metabolic syndrome (defined by the presence of at least three among abdominal obesity, hypertension, low plasma HDL-cholesterol, high plasma glucose, and high triglycerides), which were associated with breast prognosis in previous studies.

The study enrolled 2,356 women diagnosed with invasive breast cancer within the previous 5 years who had not

developed distant metastasis, local recurrence or second primary breast cancer. All participants were asked to change their diet according to the WCRF/AICR (2007) guidelines for prevention of cancer and were allocated to one of three different groups. Women with no metabolic/endocrine traits of high recurrence risk (ER- tumor, metabolic syndrome, high serum testosterone or insulin level) were allocated to an observational group (n=681). Women with one or more of the above high risk traits were randomly assigned to a control group (n=833), which received only WCRF/AICR recommendations, and an active intervention group (n=842) requested to participate in kitchen courses and physical exercise sessions. Compliance assessments in control and intervention group include repeated 24-hour food frequency and physical activity diaries, anthropometric measures, impedance evaluation of body fat distribution, one week registration of energy expenditure integrating the measure of movement, and several other physiological signals collected with a SenseWear Armband, plasma glucose, cholesterol, triglycerides, insulin, SHBG, and sex hormones. At baseline and after 12 months, blood samples are collected. The collection of additional blood samples is planned at 36 and 60 months.

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THE CORRECT INFORMATION ON NUTRITIONAL STYLES. TARGETED PREVENTION IN CANCER PATIENTS

Valentina Grado

Healthy eating is, together with adequate physical activity a key element in the prevention of many diseases.

It is, in fact, demonstrated that the lifestyle and food choices act incisively in the ability to prevent the development of diseases, to monitor its evolution or, on the contrary, cause the onset. It is worth mentioning that although the diet is a therapeutic path, the act of eating cannot and must not be disconnected from its human and social context in the research of an exasperated rationalization.

If nutrition is giving the body the quantity of substances which the biological machine needs to work properly, eating, sitting at the table, mean relating with other people, through more communication codes, obtaining from the meal not only food, but also gratification.

Energy malnutrition in excess, which is responsible for the “pandemic” of obesity, is the result of an alteration in the State of nutrition in both quantitative and qualitative terms with a wrong proportion of the nutrients provided with feeding.

To protect your health is very important to control and normalize your weight.

Unfortunately, the epidemic of overweight and obesity is increasing in all age groups.

The entire population, at an early age, must learn the correct rules of proper nutrition that should not be the medicalization of the act of eating but rather a way of life for preserving health. Since ancient times people have always preferred cereals such

as legumes and seeds, as staple foods. In fact these foods offer the perfect combination of good quality food rich in fiber, fat and other nutrients needed to operate the complex biochemical processes that control the balance of the body.

Over the last century, especially in Western countries, the food style underwent substantial changes, diversifying several traditional life styles. Priority was given to animal products that were once available only occasionally.

It also introduced new foods, which can be obtained using modern technologies (sugar and refined flours) or food produced only industrially as hydrogenated fats and margarines. This change has led to a high-calorie, high-protein diet rich in refined carbohydrates but low in vitamins, fiber, micronutrients, antioxidants and other substances essential and useful for the well-being of the organism.

In recent decades, global investigations were made on the evaluation of the relationship between diet, physical activity, body weight and cancer.

In high income countries there was an increase of 37% of cancers and among the established risk factors in addition to smoking and alcohol consumption, there are overweight and obesity. It is believed that primary prevention actions can significantly reduce mortality from cancer. Among the major strategies to achieve this there is the change in eating habits.

It highlights the urgent need to fight the epidemic of overweight and obesity affecting many European populations including the Italian one.

In November 2007 the WCRF (World Cancer Research Fund) and the AICR (American Institute for Cancer Research) presented international guidelines for maintaining health and cancer prevention, in parallel with other chronic diseases.

The document is the result of the review of more than 7000 papers products worldwide on the correlation between diet,

lifestyle and risk of developing chronic diseases like cancer. These two authoritative scientific societies have developed a set of recommendations for cancer prevention.

A list of ten simple rules that forms the basis of a healthy and varied diet. We recommend the consumption of fruits and vegetables, legumes and whole grains, limiting the consumption of salt and red meat, especially cold cuts and sausages. We do not recommend the sugary drinks and high energy density foods, in addition to the abuse of alcoholic beverages and the use of dietary supplements. It is recognized that a diet of this kind can provide the body with vitamins, minerals and other beneficial compounds that defend the body from cancer and other chronic diseases. A diet can not only prevent cancer but also control tumor growth at different stages of the disease.

The cure for cancer now allow most people to live long healthy lives after being diagnosed with cancer. Often these people have an increased risk of developing chronic diseases such as diabetes, osteoporosis or cardiovascular diseases. It is therefore of utmost importance to choose the correct eating habits and a healthy lifestyle to prevent these problems and the risk of recurrence.

In recent years it has been confirmed that the control of body weight plays a crucial role for people who have had a history of cancer. It seems that keep weight normal is able to stabilize the body's metabolic trim and it discourages the tumor growth. At the same time, a situation of overweight or obesity causes a series of stress to the organism, which in some cases could lead to cancer. A Correct food style associated with a regular physical activity, is important for those who have had a tumor because in addition to helping to maintain a normal body weight, it helps to give strength to the body and to the immune system.

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THE MEDITERRANEAN DIET:

THE NEW DISCOVERY OF OUR TRADITION

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The mediterranean diet is a nutritional model inspired by popular eating patterns in some countries of the mediterranean region, southern Italy and Greece, around the 1960's. It is based on foods traditionally eaten in these countries. The concept of the mediterranean diet was introduced and initially studied by the US physiologist Ancel Keys, who has demonstrated the beneficial effects on longevity and health in the Seven Country Study with the formulation of the first mediterranean diet pyramid and the mediterranean diet score serving , to evaluate the adhesion to the mediterranean diet (Martinez-Gonzalez et al., 2004). Infact in these regions, in the early sixties, life expectancy was among the highest in the world; the incidence of diseases such as ischemic heart disease, some cancers and other chronic diseases related to diet was the lowest in the world; This occurred despite high smoking habits, socioeconomic low level and the shortage of health care. The different dietary patterns identified by Keys showed a high consumption of saturated fats in the populations of North America and Northern Europe and a much lower consumption in southern Europe, especially in Mediterranean areas and Japan. It was shown that consumption of saturated fat was strongly correlated with coronary heart disease. High intake in monounsaturated fat reflected an abundant use of olive oil affecting inversely mortality for heart or metabolic diseases. (Circulation, 1970).

Many people live on the mediterranean coast with great ethnic, cultural, religious, economic and political differences which have affected the quality of nutrition. The identification of common dietary components has been a challenge for researchers. Given the wide variety of gastronomic habits of the mediterranean countries and their variations in the course of history, it was considered necessary to reserve the term of the mediterranean diet to eating habits of Crete and southern Italy . Subsequently, the dietary pattern was extended to include the diets consumed in mediterranean countries olive producers.

The historical and anthropological implications of the Mediterranean diet have led UNESCO to its inclusion in 2010 in the list of intangible cultural heritage of humanity of Italy, Morocco, Spain and Greece; from 2013 this recognition was extended to Cyprus, Croatia and Portugal. Currently the definition of Mediterranean diet has extended to many variations of the original, especially in the field of culinary practice in many countries that claim the quality of their cuisine, so as to include widely heterogeneous dietary styles, for which there are not many scientific evidence (unesco.org). The characteristics of the mediterranean diet are: abundant food fresh vegetable, natural, seasonal, locally sourced; for example: fresh fruit consumed daily, sweets containing refined sugars or honey a few times a week; olive oil as the principal source of fat; dairy products consumed daily in small to moderate amounts; fish and poultry consumed in modest to moderate amounts; red meat in modest amounts; wine consumed in modest to moderate amounts, generally during the meal (C. Pitsavos et al., 2005). This diet has a low content of saturated fat (less than 7-8%), and a total fat content from 25 to less than 35% according to regions. It's associated with

regular physical activity work, for example in the fields or at home. The calories amount does not exceed 2500 kcal for men and 2000 kcal for women.

Regarding cancer incidence, has been observed to be lower in Mediterranean countries compared to that in Northern countries, such as the UK, and the USA. The adherence to a Mediterranean dietary pattern correlates with reduced risk of several cancer types and cancer mortality. Specific aspects of the Mediterranean diet, such as high consumption of fruit and vegetables, whole grains, and low processed meat intake, are inversely associated with risk of tumor pathogenesis at different cancer sites. High adherence to a Mediterranean diet is associated with reduced risk of overall cancer mortality as well as a reduced risk of incidence of several cancer types. The number of cancer survivors in the USA and Europe is rapidly growing (DeSantis CE et al.,2014; Rowland JH et al.,2013). A few prospective cohort studies investigated the association between composition of the diet and cancer survival, reporting inconsistent results (Rock CL et al.,2012). Tumor progression and recurrence as well as survival of cancer patients were shown to be affected by aspects of nutrition such as macronutrient composition or supplementation with specific nutrients, and some of these research studies have been transferred into recommendations and guidelines for cancer survivors (DeSantis CE et al.,2014; Rock CL et al.,2012). Moreover, there are some studies dealing with the effects of food groups in cancer patients. A diet emphasizing fruits and vegetables, whole grains, and fish, but low amounts of red or processed meat and sugars, was associated with decreased mortality rates in cancer survivors (Kroenke CH et al.,2005; Meyerhardt JA et al.,2007).

Regarding the relationship between components of Mediterranean diet and cancer: a protective effect of fruits

and vegetables on cancer initiation and progression might be explained by their high content of flavonoids exerting favorable biological effects such as anti-oxidant, anti-inflammatory, anti-mutagenic, or anti-proliferative properties (Arts IC et al.,2005); higher consumption of fish is recommended especially due to its content of n-3 fatty acids. Thanks to their anti-inflammatory effects, n-3 may suppress carcinogenesis and act in a protective manner against tumor initiation and progression; increased uptake of dietary fiber is regarded to be protective especially against the development of colorectal cancer through in transit time thereby diminishing the impact of potential carcinogenic substances on the colonic epithelium. Metabolization of fiber to short-chain fatty acids by intestinal bacteria may prevent dedifferentiation of colonic cells and support defense mechanisms against initiated cells by apoptosis (Williams MT et al.,2005); Systematic analyses of epidemiological studies on the effects of olive oil on cancer development indicated decreased relative risks or odds ratios for breast cancer, cancers of the digestive system, or neoplasms of the respiratory tract (Pereira MA et al.,2002). Extra-virgin olive oil is rich in both monounsaturated fatty acids and in polyphenolic compounds such as tyrosol, hydroxytyrosol, and oleuropein. It has been speculated that the phenolic content of extra virgin and virgin olive oil is able to specifically affect cancer-regulated oncogenes (Sotiroudis TGet al.,2009; Schwingshackl L et al.,2015). Furthermore, they may exert strong chemo-preventive effects via a variety of distinct mechanisms, including both direct anti-oxidant effects and actions on cancer cell signaling and cell cycle progression (Corona G et al.,2009); moderate consumption of alcohol in a MD is usually characterized by a threshold of <30 g ethanol/day for men and less than 20 g/day for women with a focus on red wine containing secondary plant

substances such as polyphenols. These light amounts of alcohol were found to be associated with a reduced risk of cardiovascular disease in a number of observational studies (Jin M et al.,2013); red and processed meat are regarded to be unfavorable compounds which should be consumed in low amounts. There is considerable evidence derived from meta-analyses linking high consumption of meat and/or processed meat with an increased risk of cancer mortality (Xu X et al.,2013); different and sometimes contradictory results are reported with respect to consumption of milk and dairy products and the risk of cancer.

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LIFESTYLE AIMED AT STOMACH AND BOWEL CANCER PREVENTION

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Many studies suggest that lifestyle and dietary factors may modulate cancer risk. These relationships have been widely studied in the gastrointestinal (GI) tract, mostly in gastric and colorectal cancer.

Many molecular mechanisms of diet and lifestyle that promote colorectal and gastric carcinogenesis have been discovered suggesting that it will be possible to reduce the incidence of colorectal and gastric cancer modifying them (Durko L. et al., 2014).

Despite its declining incidence, gastric cancer (GC) is still one of the most common malignancies and remains an important leading cause of cancer-related death. In 2003-2005, gastric cancer among males accounted for 5,2 % of total cancer incidence and among females 4,6%, excluding non-melanoma skin cancers. The number of deaths attributable to gastric cancer accounted for 6,9% of male cancer mortality which made it the 4th most common cause of cancer death. In Italy in 2006, 6244 males and 4376 females died from gastric cancer. If the population had not aged, the decline in crude incidence observed between 1998 and 2005 would have been about 50% greater among males and females. Since the downward trends in incidence and mortality have been under way for decades, they currently involve all age groups of the population. Both

incidence and mortality are higher in central Italy, followed by northern and southern Italy. The incidence decline is more pronounced in central and northern Italy (Epidemiologia e Prevenzione, 2009).

Another important malignancy is colorectal cancer (CRC). This cancer constitutes the second commonest neoplasm in women and the third commonest neoplasm in men. In 2003-2005 colorectal cancer accounted for 13,4% of cancer incidence in the male population, in female 13,8% and of all cancer death 10,8% for male and 12,1 % for female population, excluding non-melanoma skin cancer. Colorectal cancer ranked 3rd as to number of incident cases among males , 2nd for females and it was the 2nd most common cause of death from cancer for both sexes. In Italy, according to 2006 data, colorectal cancer caused 9752 deaths among males and 8315 among females (Epidemiologia e Prevenzione, 2009).

The incidence of colorectal cancer is higher in highly industrialized countries, while in developing countries is not so common. This observation strongly suggests that one of the key mechanisms of carcinogenesis of this neoplasm might be associated with microbial and environmental factors a part from age, male sex, hereditary factors (Durko L. et al., 2014).

The main environmental CRC etiological factors studied are imbalanced diet, excessive meat intake and low amount of fiber sources, alcohol consumption, smoking, obesity, overweight, lack of physical activity, sleep deprivation (Durko L. et al., 2014, Baena R. et al., 2011).

There is a consistent evidence that greater levels of physical activity are associated with an approximately 40% reduction in the risk for colorectal cancer thanks to the reduction of insulin

levels, adipose tissue and chronic inflammation (inducing IL6 production and the decrease of iNOS and TNF α) (Durko L. et al., 2014, Gingras D. et al., 2011).

Insufficient physical activity is, in fact, correlated with many chronic diseases. Moderate and regular activity elevate basal metabolism and improve tissue oxygenation, leading to better metabolic efficiency and capacity, reducing body fat, insulin resistance and adipose tissue volume (Baena R. et al., 2011). The American Institute of Cancer Research recommended a minimum of 60 minutes of moderate or 30 minutes of intense physical activity daily to promote health (Durko L. et al., 2014). Many studies have indicated that obesity, defined as a body mass index greater than 25kg/m², is a risk factor for many neoplasm (Durko L. et al., 2014). Multiple biologic processes participate in obesity-cancer relationship. Adipose tissue is a metabolically active organ that can release a lot of hormones and cytokines promoting chronic inflammation and insulin resistance (Durko L. et al., 2014). The balance and interaction between insulin, insulin-like growth factor, insulin resistance, sexual hormones, pro-inflammatory cytokines and C reactive protein determine the CRC risk (Baena R. et al., 2011). Some studies hypothesized that hyperinsulinemia together with IGF-1 can increase cell proliferation and adipohormones (leptin, adiponectin and resistin) can contribute to promotion of inflammation and carcinogenesis (Durko L. et al., 2014). Some authors have investigated carcinogenesis related to chronic sleep deprivation or disruption of circadian rhythm. Maintaining a regular and adequate daily amount of sleep contributes to CRC prevention, because it has been shown that cell proliferation, differentiation, apoptosis and DNA repair mechanism have different day and night activities (Durko L. et al., 2014).

Epidemiology studies have indicated that the Western diet, rich in meat and fat, is a risk factor for gastric and colorectal, whereas diets rich in fiber protect against these cancers (Abreu MT. et al., 2014). Recent meta-analysis indicated that there is convincing evidence that red (beef, pork, lamb, and goat), processed and salted meat are risk factors for gastric and colorectal cancer (Andersen V. et al., 2013; Lippi G. et al., 2016).

The risk increases linearly with higher and higher intake of red and processed meat (Durko L. et al., 2014). The possible carcinogenic pathways or mechanisms underlying red and processed meat have recently been proposed. One of the possible factors is the increased fat intake together with meat intake that causes an increase of insulin resistance and higher production of secondary bile acids which facilitates carcinogenesis (Baena R. et al., 2011). Secondly, processing red meat, frying or grilling at high temperatures cause the production of N-nitroso compounds (NOc), carcinogenic heterocyclic amine (HCA) and the formation of polycyclic aromatic hydrocarbons (PAH) (Baena R. et al., 2011; Andersen V. et al 2013). NOc, HCA and PAH are genotoxic substances that can act directly on DNA causing point mutations, deletions and insertions. Enzymes implicated in the carcinogenic detoxification process and metabolism have been studied to evaluate genetic susceptibility to carcinogenesis (Baena R. et al., 2011). N-acetyltrasferases (coded for NAT1 and NAT2) are critical in the activation of HCA and PAH, and their polymorphism are considered risk factors for CRC (in particular for NAT2) (Baena R. et al., 2011).

Moreover, red meats have a high content of heme iron which is degraded in the small intestine by the enzyme heme oxygenase 1, releasing free ferrous iron (Durko L. et al., 2014).

Heme iron behaves as nitrosylation agent forming NOc,

increases cell proliferation in gut mucosa through the lipid-peroxidation pathway promotes the production of reactive oxygen species (ROS), especially H_2O_2 which induce genetic mutations and the expression of pro-inflammatory cytokines (Durko L. et al., 2014, Baena R. et al., 2011). The World Cancer Research Fund/American institute for Cancer Research and the World Health Organization/Food and Agriculture Organization also indicated that salt and also salt-preserved food, are probably causes of gastric cancer (Abnet C.C. et al., 2015). Many epidemiological studies, in fact, showed a positive association between salt intake and risk of gastric cancer (Umesaw M. et al., 2016).

Whereas processed meat seems to be implicated in carcinogenesis, the protective effect of dietary fiber on risk of gastric and colorectal cancer is well defined (Durko L. et al., 2014; Zhang Z. et al., 2013; Fang X. et al., 2015). Fibers are present in vegetables, fruits and whole grain cereals. Their presence in meals contributes to a shorter gut transit time, delayed absorption of complex sugars, the increase of fecal bolus and bacterial fermentation producing short-chain fatty acids (butyrate, propionate and acetate) (Durko L. et al., 2014). These effects are positive not only in cancer but also in other pathologies like bowel inflammatory diseases or diabetes. The mechanism by which a high intake of dietary fiber may reduce the risk of colon and gastric cancer has been proposed. In acid condition, dietary fiber has been shown to neutralize or reduce the presence of potentially carcinogenic nitrites (Zhang Z. et al., 2013; Den Hoed CM. et al., 2016). The positive effects provided by fruits and vegetables come from the great number of potentially protective substances they contain like anti-inflammatory, short chain fatty acids that interfere with regulators of the cell cycle, anticancer

phytochemicals such as polyphenols, carotenoids, flavonoid, vitamins folic acid (Baena R. et al., 2011).

Dietary fiber is also a rich source of ferulic acid and p-coumaric acid, note to delay the progression of cell cycle and to have anticancer effect (Zhang Z. et al., 2013).

Vitamins contained in rich fiber food, especially B vitamins have received special attention. Natural dietary folic (B9) and B6 intake reduce risk of CRC. A recent meta-analysis also demonstrated the role of vitamin intake in risk of GC. Vitamin A, C and E are associated with a decrease of gastric cancer risk (Durko L. et al., 2014; Den Hoed CM. et al., 2016).

The EPIC study demonstrated an inverse correlation between the levels of intake of fruit and vegetables and the risk of developing diffuse gastric cancer especially in smokers (Gonzalez CA. et al., 2012).

Smoking is also an establish risk factor for colon and gastric cancer. Carcinogens from tobacco, apart from inducing cancer in organs that are directly in contact with cigarette smoke (lung, esophagus), can also reach the colorectal mucosa through the circulatory system and cause genetic damages that lead to cancer development. Tobacco is furthermore consistently associated with an increased risk of colorectal adenoma, precursor lesion for CRC (Gingras D. et al., 2011). Moreover an analysis of European Prospective Investigation into Cancer and Nutrition (EPIC-EURGAST) showed that there was a 45% higher risk of GC in people that usually smoke compared to people that never smoke (Bucland G. et al., 2015). Other prospective cohort studies have suggested an association between alcohol intake and colon adenoma and both colon and rectal cancer. This increased risk is due to the effect of alcohol on folate levels, defective DNA methylation and impairment of the immune system (Gingras D. et al.,

2011). Furthermore, a strong association was demonstrated between alcohol intake and gastric cancer. This association, however, was only found in heavy consumers of alcohol (Den Hoed CM. et al., 2016; Tramacere I. et al., 2012).

Intestinal microbiota can impact in cancer development. Intestinal microbiota regulates multiple physiological functions related to cell proliferation, differentiation and stimulation of immunity (Durko L. et al., 2014). The composition of gastrointestinal microbiome is shaped by a variety of factors including diet, environmental factors and genetic background (Abreu MT. et al., 2014).

Helicobacter pylori (HP) is a gram negative bacterium that selectively colonizes gastric epithelium. Although only a percentage of colonized people develop neoplasia, World Health Organization designate HP as a class I carcinogen because its chronic infection is the strongest identified risk factor for gastric cancer (Abreu MT. et al., 2014). The two HP determinants, that influence cancer risk, are cytotoxin associated gene (*cag*) pathogenicity island (PAI), and the secreted vacuolating cytotoxin A (VacA) toxin. Contact between *cag*⁺ strains and host cells activates multiple signaling pathways that may increase the risk for malignant transformation during prolonged colonization. VacA, instead, causes a wide assortment of alterations in gastric epithelial cells, including vacuolation, altered plasma and mitochondrial membrane permeability, autophagy and apoptotic cell death. Some studies put on light a model, in which early interactions between HP and human tissues alter the structure of the gastric microbiome by promoting gastric atrophy, the principal step in histological progression of intestinal-type gastric cancer. Microbial bloom that develops in response to less-acid condition leads to new microbiome population that might promote carcinogenesis influencing malignant

transformation (Abreu MT. et al., 2014).

Since gastric atrophy is the principal step in gastric cancer development and since the mortality of GC remains high with a less than 35% 5-year survival rate that is largely dependent on stage (Yakirevich E. et al., 2013), selection of high-risk population to undergo diagnostic endoscopy is fundamental for the early detection of GC.

Endoscopy has a primary role for early detection of GC and for surveillance of premalignant gastric conditions, but it is not suitable for screening in medium-risk areas such as Italy due to high cost effectiveness. Therefore, the development of a non-invasive tool is required in order to identify sub-groups of high risk individuals who necessitate strong endoscopic follow-up (De Re V. et al., in press). Recently it has been shown that, combining Pepsinogen I (PGI) and Pepsinogen II (PGII) and Gastrin 17 (G17) serum level in autoimmune chronic atrophic gastritis patients and familiarity, we can identify patients potentially at risk to have Intestinal Metaplasia, and thus patients with a higher risk for GC development. In the presence of corpus atrophy, in fact, PGI serum level and acid production decreases and as a result of decreased acidity, antral G-cells increase the production of G17.

PGI and G17 serum test are relatively inexpensive methods to screen patients at risk for gastric cancer among high risk categories and could provide significant information not only for cancer development but also for prevention by HP eradication, GC surveillance and to better understand the pathogenetic mechanisms leading to diffuse and intestinal GC types (De Re V. et al., in press).

Even intestinal microbiome has a role in CRC. It helps to maintain homeostasis, to immune development, to prevent pathogen colonization, to process drug metabolites and to

release key nutrient. Bacteria alone constitute about 90% of the total cell population in the colon and colonic bacteria have many genes that regulate metabolism. Alteration in the intestinal microbiota may cause chronic colon inflammation, dysplasia and cancer. It is not clear whether there are specific microbes that are directly involved in colorectal carcinogenesis or if the process requires specific interactions between host tissues and microbes, probably a variety of mechanisms are involved (Abreu MT. et al., 2014).

Diet, antibiotics and stress are extrinsic and intrinsic factors that contribute to microbiome dysbiosis.

A fiber rich diet results in saccharolytic fermentation of carbohydrates that leads to production of short-chain fatty acids (SCFAs), including acetate, butyrate and propionate. Butyrate has anti-tumorigenic proprieties. Probiotics impact the molecular mechanism of cell growth and differentiation, their presence may also reduce the number of pathological colonic flora, reduce carcinogenic secondary bile acid production and increase production of short-chain fatty acids modulating inflammatory response (Durko L. et al., 2014).

Instead, proteolytic fermentation during consumption of diets rich in meats prompts generation of inflammatory and carcinogenic metabolites (phenols, ammonia, nitrogen rich metabolites) and sulfate producing bacteria that produce hydrogen sulfide. High fat diets also produce bile acids which are converted in secondary carcinogenic bile acids (Abreu MT. et al., 2014).

Since intrinsic and extrinsic factors that can contribute to microbiome dysbiosis and pathologies development are diet, antibiotics and stress it is very important modify lifestyle and diet to reduce mortality and morbidity (Abreu MT. et al., 2014). Screening programs are fundamental for early detection of colorectal cancer and to increase life expectancy. In the last

15 years, several screening programs have been activated in many countries. In areas where screening programs had been set up it was observed an early reduction of CRC mortality. The impact of screening mortality rates is likely to take place mainly through two different mechanisms: the reduction of incidence rates and the improvement of the prognosis of screening-detected cases. Data from Italian national survey on colorectal screening programs showed a better distribution by stage of screen-detected cases versus cases diagnosed outside the screening setting. Therefore, huge changes in mortality, incidence and hospitalizations were observed in those areas where screening programs were introduced (Zorzi M. et al., 2015; Zorzi M. et al., 2015).

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WWWWWWWWWW

Since many years, patients associations urge the recognition of oncologic rehabilitation peculiarities that include various settings: psychological, physical, rehabilitative and nutritional. The concept of rehabilitation as a targeted therapy for the recovery of the injured function is certainly inadequate for cancer patients and today the goal is to arrive at a shared definition of the meaning of oncologic rehabilitation by identifying minimum standards of care on the various rehabilitative aspects.

The rehabilitation aspect should be part of the cancer patient care pathway and should be thought and structured from the moment of diagnosis. In this context, nutritional rehabilitation and relevant information to support the patient to achieve a healthy lifestyle and also for tertiary prevention should be an important aspect of the care pathway in oncology.

Another assumption is that all patients should find in cancer centers, the most appropriate treatment for nutritional support, based on their physical and mental condition and their information needs. Such treatment must be an integral part of a treatment care pathway.

The National Healthcare System - says Carmine Pinto, national president of Aiom (Italian Association of Medical Oncology) - neglects both the phase of post-acute care rehabilitation and the rehabilitation post-total remission, stating in an unacceptable way that oncologic rehabilitation is included in the different types derived from the "International Classification of Functioning, Disability and Health" (ICF) of the World Health Organization.

Even in the definition of the new LEA, oncologic rehabilitation is included within other types of rehabilitation, referring to joints, cardio-circulatory, of the speech, digestive, urinary,

mental and behavioral autonomy diseases. «But the cancer - continues Elisabetta Iannelli, secretary of FAVO - is a different disease from all those listed and determines specific rehabilitation needs, not comparable to the others. It is a particularly penalizing omission for patients, because the results of anti-cancer treatments may cause several difficulties, not only physical but also cognitive, psychological, nutritional, sexual, social and working. The underestimation of these aspects has also led to exclude, at least in the form of consultation, the voice of patients' associations from the *Patto della Salute*».

Various studies and research projects, developed with patients and their representatives, have clearly revealed some needs. One of these needs is the exigency to have a nutritional support since the beginning of the treatment process.

In fact, for cancer patients, a healthy lifestyle and a special diet are important complementary supports to treatments, both from the clinical and the psychological point of view. To actualize this, patients and their families need information scientifically accurate, balanced, understandable and easily accessible. They need also an “emotional” personalized support because information in this fields are never “one size fits all “. In the literature there is evidence that nutritional support is essential for cancer patients.

The publications of the World Cancer Research Fund in 2007 and 2014 and other important papers are milestones in this setting. We want to cite here only a recent article published in *Cancer World* 2014 by Susan Mayor, entitled “Nutritional support for cancer patients” that begins with: *Patients who are receiving adequate nutrition have a better prognosis, respond better to chemotherapy and can tolerate higher doses of anticancer treatments. It is therefore important for oncologists to assess and manage malnutrition.*

According to the National Guidelines for hospital care and catering “The nutritional status contributes to the quality of life of each person and nutrition can be a risk factor for many diseases” [...]. A proper nutrition is an outstanding health factor and nutrition should therefore be absolutely placed in diagnosis and treatment pathways, while an incorrect management of the patient from the nutritional point of view can cause complications and constitute, therefore, “a disease in the disease”.

The nutritional aspect is part of a broader strategic vision of the health pathway within a welfare and clinical activity of quality “.

→ The document refers to the need to proceed with the nutritional assessment as a practice to be made promptly by identified personnel in each health facility.

Therefore, each cancer center should develop a “Pathway for Nutritional Support for Cancer Patients” which should lead to an increase in the number of patients and their families undergoing nutritional evaluation and an increase in the number of patients to whom provide individualized nutritional support. Each cancer patient should have the right to a nutritional counseling in order to provide the guidance on how to maintain the ideal weight, to adjust nutrition according to universally recognized principles as useful in primary and secondary prevention of cancer, as well as adequate information about the type of cancer pathology also in relation to any comorbidities related to medical, surgical or radiation therapies provided.

Another fundamental aspect is that concerning the environmental impact.

The current world nutritional trends, which show a shift towards the consumption of meat and sugar and fat linked to economic development and the increase of *per capita* income,

lead to dramatic expectations not only for the exploitation of resources but also for the incidence of diseases such as type 2 diabetes, cardiovascular diseases and certain tumors. Environmental sustainability and the reduction of health risks would instead be insured by the spread of the Mediterranean diet, vegetarian and with fishes.

Compared to the omnivorous diet, these diets adopted worldwide would reduce the incidence of type 2 diabetes (25%), of tumors (10%), and of deaths from cardiovascular diseases (approximately 20%). In addition, the adoption of these diets or similar alternatives can help to prevent the expected increase in greenhouse gases emissions and the destruction of habitats. With the same caloric intake, beef meat production requires 28 times more land, 11 times more water and 6 times more fertilizer - and frees 5 times more greenhouse gases - than the production of other meats, eggs and dairy products. These foods require from 2 to 6 times the resources necessary to produce wheat, rice or potatoes for an equivalent caloric value, according to an analysis of data related to the United States.

The European code against cancer gives precise indications about the choice of the Mediterranean diet, suggesting a consumption of “many and various grains, legumes, fruits and vegetables”, with a strong limitation of high-caloric foods, preserved meat, red meat and a high-salted foods.

The contentious issues about nutrition are another underestimated aspect. Also for this reason health centers should seriously face the controversial issues, and try to give unambiguous and clear answers to patients and family members, according to the scientific literature and to the results of the researches made by internationally accredited organizations (International Agency for Research on Cancer-IARC, World Cancer Research Fund International-WCRF, American Insti-

tute for Cancer Research-AICR).

Leaving patients with no answer - “you can eat whatever you want ...” - or, even worse, is irresponsible and harmful for citizens health and for the entire community.

According to a shared opinion, a change in the way of thinking and working in modern medicine - in accordance with the need to reform it according to Science, Technology and Humanity – is expected. Volunteers associations and, in particular, patients organizations play an important role in the change of this paradigm of care.

The change of model sees in public health, and specifically in healthcare structures, not “companies” that produce public health by curing diseases, but healthcare and research structures interested in looking for the causes of the disease, taking care of people and in particular of their physical and mental wellbeing.

The renewed public health complements and enhances a concept of community aiming to reduce the weight of the elements that generate diseases (pathogenic) in favor of the resources, even spontaneous, that generate public health and is designed as a fair and inclusive community, economically solid, politically involved, environmentally sustainable, with high performance, healthy and resilient.

The change in the role of patients from users to partners is realized together with the change of perspective. Through the patients organizations focusing on proactive and collaborative voluntary, patients feel the responsibility to take part in the management aspects of public health and, thanks to the systematic use of patients feedbacks, they are able to propose new organization models. These model should be structurally “light” and innovative, less bureaucratic, very pragmatic, based on the use of all the operators skills and on the “learning by doing”.

In this perspective, it is essential to promote the culture of rehabilitation, as the right to the best quality of life, at any stage of the disease, from diagnosis to palliative care. Patients and citizens have the right, but also we would say the duty, to know that today there are treatment modalities that can help you achieve and maintain the most possible independence, alleviating the discomforts that the disease, its complications, the therapies and their side effects can cause. Promoting this culture has a strong bioethics value, related to the principles of “charity” and “self-determination”, but it also has the meaning of “equable distribution of resources”.

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**“IL PROGRAMMA FED”
FORMAZIONE, EDUCAZIONE, DIETA
DELLA REGIONE SICILIANA
PER LA PREVENZIONE DELLE MCNT
E LA PROMOZIONE DI SANI STILI DI VITA**

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Agire con l'intento di “Promuovere salute” garantendo l'efficacia degli interventi è compito ambizioso e complesso che richiede un processo di reale *empowerment* sia a livello di istituzioni e di professionalità interessate che di popolazione. Difficilmente le persone modificheranno il proprio stile di vita se non sanno perché e cosa cambiare, se ne hanno un'idea sbagliata o se non trovano le condizioni favorevoli nel contesto. Sostenere la motivazione al cambiamento significa costruire un nuovo modello di intervento, collegato ad una nuova cultura responsabilizzante, in una visione congiunta tra soggetti diversi per un impegno coordinato e sinergico. Ciò presuppone una serie di interventi multicomponenti, rimodulati in funzione dell'impatto rilevato, e con precise caratteristiche: consigli mirati, supportati scientificamente, che mettano in evidenza i benefici, attività educative per accrescere conoscenze e abilità specifiche, puntuale attenzione alle disuguaglianze e ai diversi destinatari, coinvolgimento delle famiglie e del personale di cura, supporto adeguato come parte di un'azione a medio/lungo termine. Orientare e gestire il cambiamento, per chi opera nella Tutela della Salute, significa possedere capacità di lettura e analisi del contesto, aggiornare costantemente le conoscenze scientifiche e riformulare le proprie competenze, ridefinire i modelli organizzativi, ricercare strumenti e metodi di provata efficacia e sperimentare soluzioni innovative.

Viene di seguito presentato il Programma FED – *Formazione, Educazione, Dieta* - (D.A. Salute 30 dicembre 2013), un modello di intervento integrato di Promozione della Salute attivato su scala regionale.

Partendo dall'efficacia di un sano e consapevole rapporto col cibo e dal valore della dieta tradizionale siciliana per la prevenzione dell'obesità e delle più rilevanti patologie cronico-degenerative, l'Assessorato Regionale della Salute ha posto concrete basi per attuare una strategia di sistema. Il FED si inserisce in un piano che traduce le evidenze desunte dalla ricerca scientifica in attività di prevenzione primaria e di *empowerment* per la Salute. Il Programma si snoda attraverso azioni formative su più livelli e interventi capillari sul territorio, coordinati e monitorati unitariamente dall'istituzione regionale, finalizzati all'adozione e al mantenimento di uno stile di vita sano nella popolazione. La sua realizzazione trae forza dall'attivazione di una rete di rapporti, di interazioni e di sinergie tra i Servizi che istituzionalmente si occupano di sicurezza e di educazione alimentare, di prevenzione e di promozione della salute (SIAN e UOEPSA aziendali) e le professionalità di altre strutture pubbliche o private coinvolte nella promozione di sani stili di vita (scuole di Medicina, assessorati, enti locali, provveditorato agli studi e istituti scolastici di ogni ordine e grado, associazioni di categoria, consorzi di tutela, distretti produttivi e tecnologici, società scientifiche e fondazioni dell'area della nutrizione clinica e dell'educazione alimentare).

Per la definizione del progetto formativo **è stato istituito un Tavolo tecnico regionale che è partito da** un'analisi del contesto regionale: i dati clinico-epidemiologici evidenziano il pesante carico delle malattie cronico-degenerative e un trend in aumento di sovrappeso/obesità, specie tra le fasce più giovani della popolazione siciliana. Numerose evidenze scientifiche attestano che tali problematiche di salute beneficiano di una modifica degli stili di vita e delle abitudini alimentari negative

o scorrette, attuabili con interventi appropriati di prevenzione primaria e di promozione della salute e con il sostegno di un lavoro di rete. In realtà, numerose sono state le iniziative di educazione alimentare condotte negli anni passati in vari contesti e per diversi target. Spesso, però, si è trattato di interventi formativi disomogenei o frammentari, talvolta dissonanti o ridondanti, se non addirittura fuorvianti in merito ai contenuti. Nella maggior parte dei casi è mancato un impianto di valutazione che consentisse di valutarne l'efficacia e le effettive ricadute.

Attraverso l'analisi delle criticità di contesto, dei target di popolazione, degli stakeholder, di un loro opportuno coinvolgimento e dei possibili punti di forza si è, quindi, passati alla definizione della strategia di progetto e all'individuazione delle modalità operative. I punti più salienti riguardano: l'istituzione di una cabina di regia regionale per la programmazione e il coordinamento con l'identificazione dei vari livelli di responsabilità; la definizione di un modello formativo organico condiviso; l'individuazione di contenuti integrati e aderenti alle più attuali evidenze scientifiche; l'articolazione della formazione su due livelli (un primo intervento centralizzato di "formazione dei formatori" e un secondo di diffusione della formazione nelle Aziende Sanitarie Provinciali); la costruzione e l'attivazione di sinergie di rete sul territorio per promuovere l'adozione di abitudini alimentari corrette e sane, con attenzione ai destinatari finali e all'*empowerment* multilivello; la definizione di *deliverables* (risultati intermedi e finali) valutabili in termini di efficacia, efficienza e sostenibilità rispetto agli obiettivi previsti e ai risultati attesi. Il Programma Formativo Regionale si propone di qualificare figure esperte di Formatori/Educatori che sappiano incidere sul cambiamento culturale, sui comportamenti alimentari e sugli stili di vita della popolazione, agendo specificatamente sui diversi destinatari secondo metodologie appropriate e indirizzi di prevenzione primaria e di promozione della salute

improntati a contenuti e azioni di evidenza scientifica.

Il modello organizzativo prevede una formazione “a cascata” su due livelli, sviluppata attraverso fasi sequenziali: un 1° livello centrale di Formazione dei Formatori FED, a cura del CEFPAS di Caltanissetta, e un 2° livello provinciale di Formazione degli Educatori FED a cura delle nove Aziende Sanitarie Provinciali, seguiti dalla diffusione capillare degli interventi e della comunicazione a livello territoriale. La fase operativa sarà sviluppata secondo tre direttrici d’azione sinergiche: il lavoro di rete per la promozione della salute, lo studio epidemiologico, la tutela e la valorizzazione dei prodotti tipici e delle imprese sul territorio.

Per garantire uniformità di linguaggio, di contenuti programmatici e di intervento, l’esecuzione del Programma FED, coordinata dal Dipartimento Attività Sanitarie ed Osservatorio Epidemiologico dell’Assessorato della Salute, è affidata ad un team di formatori esperti, selezionati sulla base di specifici requisiti di carattere scientifico e professionale tra i Servizi sanitari territoriali e ospedalieri, l’Università, l’Assessorato Risorse agricole e alimentari, la Scuola e le realtà produttive. La metodologia adottata è quella della formazione-intervento, a supporto dei processi di cambiamento e di miglioramento organizzativo secondo il *Project Cycle Management*, con ricorso ad una didattica esperienziale, interattiva, abilitante il lavoro di rete.

I destinatari della formazione, riuniti in aule multiprofessionali, afferiscono da tre macroaree: Sanitaria, Scolastica e Agroalimentare. Nel primo livello l’azione formativa per l’area sanitaria è rivolta alle figure che istituzionalmente si occupano della promozione di corretti stili nutrizionali nelle ASP (SIAN e UOEPSA aziendali) e ai professionisti del SSR che a vario titolo sono coinvolti nella promozione della Dieta Mediterranea per gli aspetti di prevenzione (medici, veterinari, biologi nutrizionisti, dietisti, farmacisti); per l’area scolastica il target è rappresentato dai Referenti di

Educazione alla Salute degli Uffici Scolastici e da insegnanti referenti degli Istituti Professionali di Stato per i Servizi Alberghieri e la Ristorazione, mentre per l'area agroalimentare da rappresentanti dell'Assessorato delle Risorse Agricole e Alimentari e dell'Assessorato Regionale Attività Produttive. Al completamento del programma formativo ai partecipanti viene rilasciato l'attestato regionale *"Formatore FED"* che accredita alla formazione di 2° livello e allo svolgimento del Programma operativo FED riconosciuto e patrocinato dalla Regione Siciliana e dalle ASP.

Nel secondo livello, i formatori FED, acquisiti e condivisi obiettivi e contenuti del progetto FED, riportano il *know how* in ogni singola ASP e, con la supervisione del Tavolo Tecnico Regionale, sviluppano la successiva fase formativa. I destinatari di questa fase sono anch'essi selezionati tra le aree Sanitaria, Agroalimentare, Scolastica, con l'aggiunta dell'area Stakeholders (ristorazione pubblica e collettiva, aziende alimentari, ristoranti e agriturismo, vending, camere di commercio). Ai partecipanti, alla fine del programma formativo, viene rilasciato l'attestato regionale *"Educatore FED"* che accredita allo svolgimento del Programma operativo sul territorio provinciale.

I Formatori e gli Educatori FED, insieme ai docenti del Team regionale, costituiscono la Rete integrata territoriale che opera sotto il coordinamento delle singole ASP, in armonia con gli indirizzi del Tavolo Tecnico, sviluppando la fase operativa del Progetto FED.

I corsi FED di 1° livello si svolgono a Palermo (per il bacino occidentale) e a Caltanissetta (per il bacino orientale) a cura del CEFPAS. Le prime edizioni del programma formativo 2014/2015 hanno abilitato 58 formatori che sono stati inseriti in un albo regionale. I corsi di formazione di 2° livello, inseriti nel Piano aziendale di Educazione e Promozione della salute, sono organizzati con cadenza annuale a cura delle Unità Operative Formazione in collaborazione con i SIAN e le UOEPSA delle

Aziende Sanitarie Provinciali. Tutte le ASP hanno concluso nel 2016 le prime edizioni. Gli Educatori FED abilitati sono inseriti in un albo provinciale. La Rete integrata territoriale curerà quindi la fase operativa, consistente nello sviluppo di un preciso programma operativo provinciale guidato dai servizi competenti delle ASP (SIAN, UOEPSA, Formazione) che prevede, secondo le varie competenze professionali coinvolte: realizzazione di campagne informative; formazione specifica nelle scuole, negli ambienti di vita e di lavoro; attività di promozione e tutela dei prodotti da realizzarsi attraverso la loro identificazione, caratterizzazione, tracciabilità, certificazione e documentazione per raggiungere gli obiettivi di sicurezza alimentare; riconoscimento delle imprese e degli esercizi di pubblica ristorazione in linea col Progetto FED attraverso il marchio *“Vivi sano, mangia siciliano”*.

Il WHO/Europe ha riconosciuto il FED quale Programma in linea con le raccomandazioni dei principali documenti di policy (Action Plan 2012-2016, Health 2020). Il nuovo Piano Regionale della Prevenzione 2014-2018 ha inserito il FED tra i Programmi regionali riferiti al macro obiettivo di riduzione del carico prevenibile ed evitabile di morbosità, mortalità e disabilità delle MCNT, declinando azioni e obiettivi specifici con l'individuazione di indicatori e standard corrispondenti.