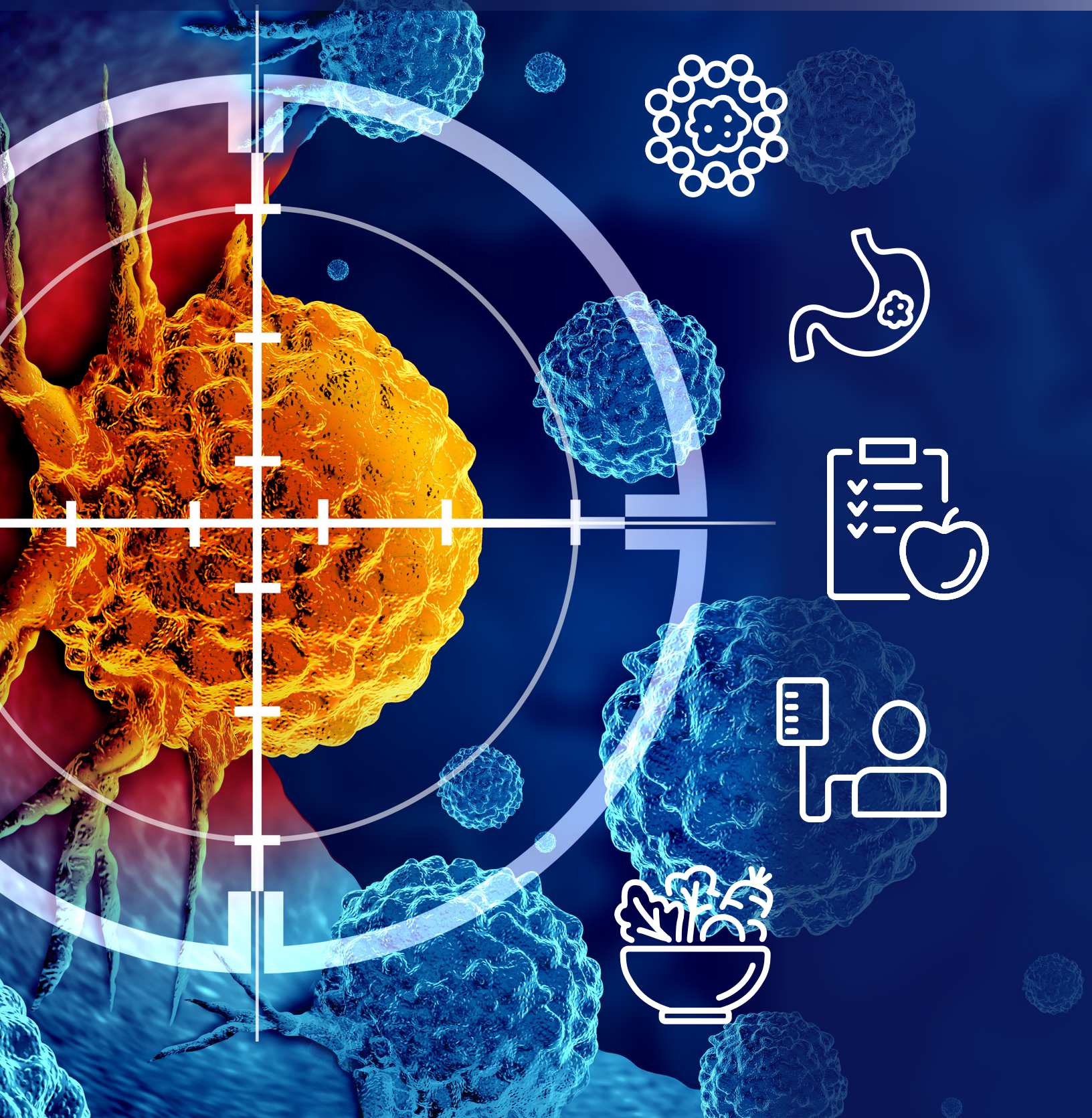
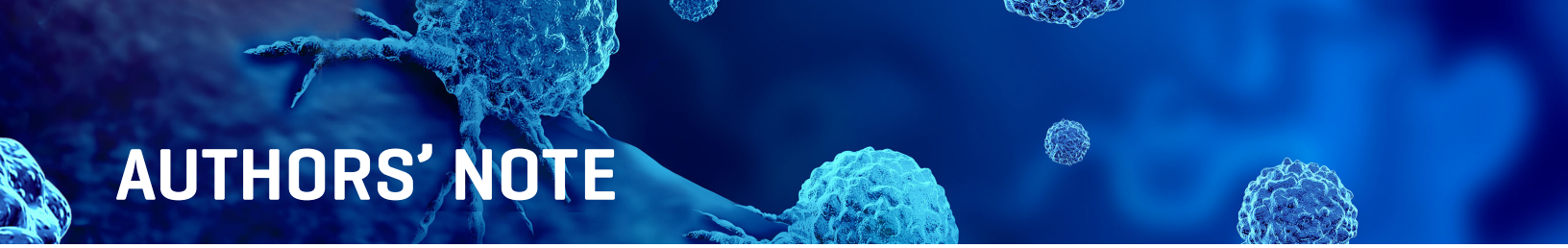
MEDICAL NUTRITION THERAPY IN INDIVIDUALS WITH CANCER

FROM EVIDENCE TO CLINICAL PRACTICE





AUTHORS' NOTE

As a surgeon with extensive experience in clinical nutrition and patient care, I have always been deeply concerned about individuals battling cancer. This concern stems not only from the profound impact of the disease on their nutritional well-being but also from the stigma and misconceptions that persistently surround it. Furthermore, despite the significant advancements in oncologic treatments, which have extended life expectancy for many, we must remember that quantity of life does not always equate to quality of life. Nutrition, being fundamental to sustaining life, also serves as a source of pleasure and comfort. Unfortunately, numerous cancer patients are deprived of this pleasure, and even worse, many struggle to meet their nutritional needs owing to various factors, often stemming from a loss of appetite.

As healthcare professionals, it is our duty to ensure that these individuals receive adequate nourishment to face the challenges of their treatment. However, what we frequently observe is a lack of awareness concerning the crucial aspect of nutritional care for cancer patients, resulting in a widespread derangement of their nutritional status, which significantly hinders their journey through cancer treatment.

Providing these individuals with timely and adequate nutrition is of paramount importance in guiding them through their cancer journey. However, regrettably, the landscape of clinical nutrition and cancer is clouded by a multitude of questionable findings in the literature, including those found in systematic reviews. This is unsurprising given the inherent diversity in cancer types and the presence of multiple comorbidities, particularly among older patients, making it challenging to assess all outcomes under a uniform framework.

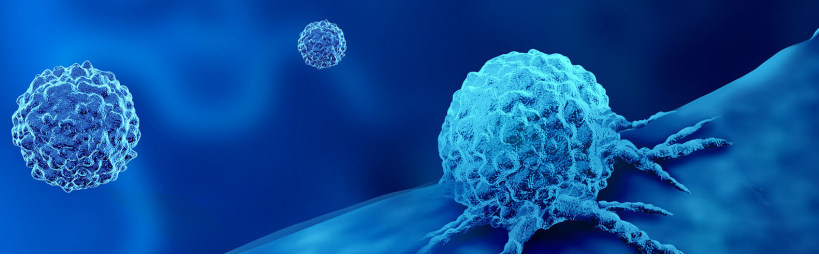
Despite this complex clinical reality, it is undeniable that an individual's nutritional status plays a pivotal role in their prognosis. Astonishingly, malnutrition, rather than cancer itself, accounts for at least 20% of deaths in this context. Furthermore, malnutrition profoundly influences a patient's ability to tolerate treatments and directly impacts their overall quality of life. This reality is underscored by the simple fact that human life cannot be sustained without adequate nourishment.

Recognizing this critical issue and the importance of tailoring care to each patient's unique needs, my coauthor and I embraced the challenge of creating this manual. It is intended not only for the patients themselves and their dedicated caregivers but also for the healthcare professionals responsible for their well-being, including oncologists, nutritionists, and members of the interdisciplinary nutrition therapy team (whom we refer to as "nutrition experts"). Our primary goal is to raise awareness and provide valuable insights to help identify and address nutritional deficiencies early on, thereby enhancing the quality of life for these patients. This manual serves as a resource, offering "food for thought" in the hope of fostering a deeper understanding of the vital role that nutrition plays in the cancer journey. We truly hope it will be of help!

M. Isabel T. D. Correia

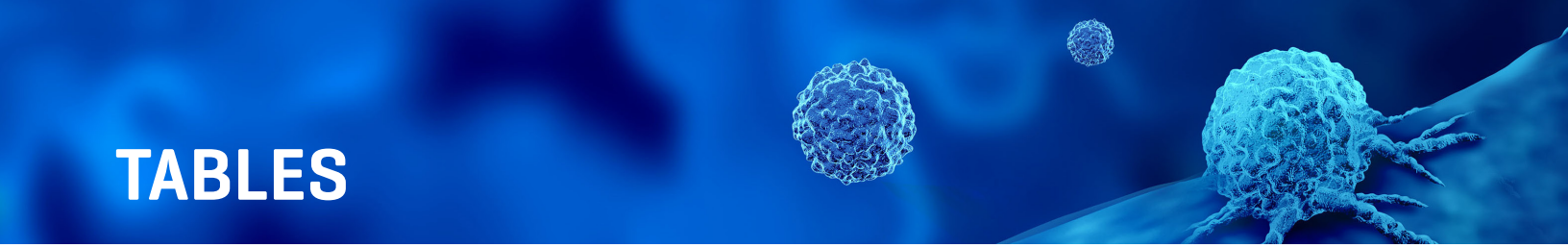
Gabriel Gomez

This manual is dedicated to Rafael Enrique Gomez, a brother who leaves many teachings.



INDEX

INDEX



TABLES

FIGURES

INTRODUCTION

1.1 — General aspects

Cancer is a worldwide epidemic and is the second leading cause of death in Latin America.[1] Cancer treatments vary, and their combinations are infinite. These include surgery, radiation therapy, and systemic therapy (chemotherapy, hormonal therapy, and biological treatments). There are 2 macro goals of cancer treatment: (i) cure, when achievable, and (ii) prolongation of the patient's life, while maintaining quality of life and physical, psychosocial, and spiritual well-being and providing the palliative care needed for end-of-life stages.

Patients with cancer are at risk for malnutrition from several causes, which adversely affects treatment outcomes. Medical nutrition treatment (MNT) is an individualized approach to improving a patient's nutritional status by managing symptoms and signs associated with cancer or its treatment, and correcting or addressing nutritional deficiencies. This manual aims to raise awareness of MNT in cancer and to empower both patients and clinicians to pursue a holistic approach to cancer treatment that emphasizes nutrition. The manual is intended for 4 audiences:

- Patients, their families, and their caregivers
- Oncologists and other treating physicians who are not nutrition experts ("non–nutrition-expert clinicians")
- Other health care professionals and administrators
- Members of the interdisciplinary nutrition therapy team ("nutrition experts")

In reference to the goals set by the World Health Organization (WHO) for sustainable development, in 2017 the World Health Assembly passed a resolution urging governments to take an integrated approach to measures aimed at achieving the proposed health goals.[2] Among these targets, zero hunger is the second goal, and although many cancer patients do not experience hunger, the principle supporting the WHO proposal is based on the importance of nutrition. In this manual, we will discuss proposals related to the treatment of already-diagnosed cancer patients. We will not cover those aspects related to the prevention of cancer. Implementing the measures proposed by the global health regulators will require political commitment and centralized cancer management processes, in particular, improved registries and follow-up care. Likewise, optimal investments should be made in treatments that will impact the health of the population while being cost-effective. Implementation will also require the creation of policies, standards, and instruments to guide the overall health system in planning and executing treatment programs; to improve access to early quality diagnosis and treatment; and to educate the healthcare professionals about these policies. In this way, we should be able to adopt best practices to care for the population affected by cancer.

1.2 — Cancer is a worldwide epidemic

Cancer is the world's leading cause of death, and its incidence is expected to increase significantly in the coming years globally. In 2018, 18 million people were diagnosed with cancer. In 2020, nearly 10 million deaths were attributed to this cause, corresponding to 1 of 6 deaths worldwide.[3] Furthermore, cancer is being diagnosed in people at younger ages, and its disease course is more aggressive.

The WHO reports that the most common cancers are those of the breast, lung, colon and rectum, and prostate.[3] Cancers with the greatest mortality are lung, colorectal, hepatic, gastric, and breast, in that order. Many cases are curable if detected early and treated effectively.

1.3 — Cancer is the second leading cause of death in Latin America

In Latin America, cancer is the second leading cause of death, preceded solely by cardiovascular disease[1]. By country, it is important to highlight that in Chile and Peru, cancer has been the leading cause of death since 2017, and in Mexico, it is now the third leading cause of death. By site, the most common cancer is female breast, followed by prostate, and thirdly, colorectal.[3] By cause of death, the first is lung, followed by colorectal, and then prostate.[3]

The survival of people with the most common cancers in Latin America is significantly lower than that reported for the United States and Great Britain, except for Costa Rica. Even with the effects of the COVID-19 pandemic, which decreased consultations and treatments in 2020, 1.4 million new cases were diagnosed that year and nearly 660,000 deaths attributed to cancer were reported.[4] The barriers to access to appropriate health care in Latin America are concerning, with nearly 40% of the population failing to receive adequate and timely care. This is in addition to the high morbidity measured by disability-adjusted life years, which consider premature death, and which increased from 8.2% to 10.2% from 2000 to 2019, increasing the overall burden that cancer represents to the population.[4-5]

1.4 — Cancer in Latin America is diagnosed and treated at later stages

There are few statistics on the number of oncology specialists serving the Latin American region except for Brazil. Cancer records in the region cover only 23.3% of the population, with only 2.4% reliability in the records in Central America and 9.2% in those in South America compared with 98% in the USA.[4]

In addition, there are an estimated 3.5 million patients in palliative care in the eight countries where this specialty is recognized, while only 4% of medical schools have this area of knowledge included in their curriculum, which suggests another gap in the care of patients with cancer.[6]

For the reasons stated, cancer is not diagnosed early in the region, and treatment is also not initiated in a timely manner. Data from 1996 to 2017 suggest that in the region, 64% of women with breast cancer were already in stage IIB-IV at the time of diagnosis.[7] In Brazil, where cancer treatment is better than in the remaining countries of the region, only 33% of women with breast cancer are diagnosed through screening compared with 52% in Germany and 62% in the United States.[8] The diagnosis of other cancers common in the region, such as colorectal cancer, is poor in Latin America, except in Chile.[3]

1.5 — Health expenditures in cancer management

Regarding health expenditures by country, **Table 1** from the WHO reports statistics between 2015 and 2016.[7] The table shows the total health expenditure of each government, including the amount that the patient must pay and the population's health coverage. Limited budgets lead to a need to rationalize costs and health resources. Very little is spent on patient overall care, which suggests that even less money is directed to cancer care.

Table 1: Health Care Expenditure and Universal Health Care Coverage

Country	Public health spending on total public expenditure, 2016	OOP spending on current health expenditure, 2016	Health essential services coverage, 2015
Argentina	14%	16%	76%
Bolivia	11%	28%	60%
Brazil	10%	44%	77%
Chile	20%	35%	70%
Colombia	13%	20%	76%
Costa Rica	29%	22%	75%
Ecuador	11%	40%	75%
Mexico	10%	40%	76%
Panama	21%	27%	75%
Paraguay	16%	38%	69%
Peru	16%	28%	78%
Uruguay	19%	17%	79%

Abbreviations: OOP, out of pocket; WHO, World Health Organization.
Source: WHO global health expenditure database.[7]

1.6 — Global population aging and cancer

According to the WHO, the aging of the world's population has led to new paradigms in health care.[9] Most people with cancer are older adults. Thus, the proposed principles for the care of the aging population are the current guidelines for directing the interventions and therapies administered during the management of diseases, including cancer. Therefore, it is worth reviewing the principles on which the WHO proposal is based so that these can be specifically applied to the management of people with cancer. The first and most important principle is that clinical management, treatments, and interventions should be focused on the individual person with the disease, and treatments should take into account the person's needs and life preferences. The second principle is the goal of adding life to years versus adding years to life.

Healthy aging, which is not the same as the absence of disease, focuses on developing and maintaining the functional capacity that enables well-being. Applying this concept to the cancer patient changes the paradigm of health interventions dramatically. At health institutions, diagnostic processes and treatments should focus on providing all possible measures for patients to enjoy a dignified, independent life. In the case of the patient, health interventions

should focus on pain control and every effort to offer a better quality of life where possible. Interventions should not be limited to prolonging life or eradicating tumors at all costs but to making treatments more effective. The focus is on maintaining the patient's ability to lead a dignified, functional, independent, quality life.

1.7 — Cancer and nutritional status

Cancer is a heterogeneous group of diseases that usually compromises and impairs a person's health status.[10] In addition, the treatments offered have secondary effects on those targeted to eradicate or control tumors, and these secondary effects can significantly impact the individual's health status, temporarily or permanently. This impairment of their health condition leaves the cancer patient, who is often dependent on the treatment, with a compromised quality of life and hinders their return to the community. Recovery times are prolonged and may take years.

1.8 — Medical nutrition treatment (MNT) and cancer

Patients with cancer are at risk of malnutrition, and consequently, the prevalence of malnutrition reported worldwide is between 20% and 70%. Ten percent to 20% of cancer patients are considered to have died of malnutrition and not of underlying disease.[11] Metabolic changes in the cancer patient caused by the tumor or by treatment alter the body's ability to properly use the nutrients in the diet. These changes include inflammation, excess catabolism, inefficient metabolic cycling, and anabolic resistance. Note that nutritional deficiencies are preventable or reversible most of the time.

Malnutrition, especially with muscle loss, negatively impacts the treatment and the progress of patients[11] and leads to poorer quality of life.[12] However, tumor origin, stage, and the presence of symptoms and signs associated with the type of treatment also influence the nutritional status of the patient. **Table 2** shows how the prevalence of malnutrition risk is closely related to the anatomical site in which the cancer originates.[13]

Table 2: Prevalence of Malnutrition Risk According to the Type of Tumor

Risk of malnutrition by MST according to the type of tumor		
Tumor	**Low risk**	**High risk**
Upper GI	42	58
Lower GI	58	42
Thoracic	58	42
Head and neck	66	34
Gynecologic	73	27
Genitourinary	78	22
Others	77	22
Breast	90	10

Abbreviations: GI, gastrointestinal: MST, malnutrition screening tool.
Modified from Kadakia KC, Symanowski JT, Aktas A, et al.[13]

Malnutrition associated with cancer is caused by multiple factors that need to be identified, especially those related to low intake, as they are the axes in the intervention strategy. The most common symptoms and signs associated with low intake include anorexia, taste, and smell disturbances, oral or generalized mucositis, dysphagia, stomatitis, nausea, vomiting, diarrhea, constipation, exaggerated weight gain due to edema, malabsorption, pain, depression, and anxiety.[11]

The nutritional approach, whenever possible, should be to offer a diet tailored to the individual needs of the patient. If not feasible, the use of products that help to improve intake, with nutrition supplements, enteral (through a tube/catheter) or parenteral (infused in a vein) nutrition, should be considered.[14]

In summary, MNT in patients with cancer aims to maintain or improve the nutritional status of the individual by managing the symptoms and signs associated with cancer and its treatment, correcting existing nutritional deficiencies or the high risk of suffering them, and slowing nutritional deterioration. Other goals such as increasing treatment tolerance and avoiding preventable complications should also be considered.

In the following sections of this manual, more specific information on assessment of nutritional status and nutrition in cancer is presented for patients (Section 2), non–nutrition-expert clinicians (Section 3), and other health care professionals and administrators (Section 4). The final section (Section 5), which is directed to nutrition experts, covers MNT in more detail.

NUTRITION IN CANCER:
INFORMATION FOR PATIENTS, FAMILIES, AND CAREGIVERS

2.1 — Patient empowerment

The concept of patient empowerment is more relevant than ever, particularly since the WHO recognized patient empowerment as a necessary action to improve patient care. The concept, which was led by a Brazilian educator, Paulo Freire, is based on education as the backbone for building critical awareness and facilitates integration of the different members of health care teams. Empowerment means educating! Education is equal to freedom! Empowering the patient, family members, and caregivers offers them the opportunity to be an integral part of the care and treatment process. Empowerment gives patients the chance to learn about the reality of their disease and treatments, as well as share responsibilities. In this regard, when patients are involved in treatment and care decisions, they are more adherent to treatments and achieve better outcomes.[15]

Research has shown that in diabetes care, adherence to treatment is improved when patients are empowered and when a holistic approach to care is taken.[16] However, this is not easy to achieve when the physician is still expected to decide and the patient to follow. Empowerment is an ongoing process!

In the treatment of the cancer patient, empowerment is essential because it helps the patient, their family members, and their caregivers understand the different stages of cancer and recognize challenges, difficulties, and barriers. One of the greatest challenges for the cancer patient is the coexistence of malnutrition,[17] which is highly prevalent and impacts the entire course of treatment, progression, and quality of life.[12]

2.2 — Malnutrition in the cancer patient in Latin America

Cancer patients in Latin America present with high levels of malnutrition, as in the rest of the world, but unfortunately malnutrition is not regularly identified and treated, which directly impacts cancer treatment. Therefore, this section of the manual seeks to educate patients, family members, and caregivers about the association between malnutrition, cancer, and treatment, so that they can seek appropriate nutritional care in a timely manner, which is also a fundamental human right.[18,19]

2.3 — For patients: how cancer and its treatment affect nutrition

Choosing nutritious foods in the diet during cancer treatment will help the patient have more energy, feel better, and stay stronger. Depending on the treatment, the patient may experience different side effects. Some of these may affect the diet, such as:

- Loss of appetite
- Constipation
- Diarrhea
- Dry mouth and thick saliva
- Mouth ulcers and mouth pain
- Dental and gum problems
- Nausea and vomiting
- Trouble swallowing food
- Changes in taste and odor
- Weight changes
- Dehydration
- Feeling very tired
- Anxiety and depression

Malnutrition is both a consequence and a cause of complications during cancer treatment. The harmful effects of malnutrition significantly increase the risk for death. Many of the negative effects of malnutrition are tied to reduced muscle mass, which is directly related to the toxicity of chemotherapy and radiotherapy, as well as complications from surgery. Several authors have reported[10,20,21] how the loss of muscle mass can affect the patient during cancer treatment:

- Makes cancer treatments like chemotherapy that affect the whole body (also called *systemic therapies*) less effective
- Increases the negative effects of cancer treatment
- Reduces the tolerance to surgery, radiotherapy, and chemotherapy, which can lead to pause or even stop treatment
- Shortens life and may even cause death (10% to 20% of cancer deaths are related to malnutrition and not the tumor)
- Shortens the amount of disease-free time
- Interferes with the body's defense mechanisms
- Aggravates the inflammatory process
- Disrupts the body's metabolism
- Prolongs the healing and recovery time
- Increases the risk for new symptoms and makes the disease more severe
- Disrupts the quality of life, psychological well-being (leading to depression), cognitive status, and functioning
- Increases the care costs and use of health care resources

2.3.1 — Is malnutrition preventable and treatable?

Yes, malnutrition is preventable and can be treated when screened and diagnosed early through nutritional screening (identification of risk factors) and diagnosis (assessment of nutritional status).[10,14] Simply put, if the patient has: inadvertently lost weight; lost appetite; nausea, vomiting, diarrhea, or pain; or is no longer mobile, he/she is at risk for malnutrition and should be evaluated by a nutritional therapy specialist.

In Latin America, however, there are not always cross-functional teams at all oncology centers that can perform an early nutritional assessment. If the patient has the indicated risk factors, he/she must be referred in a timely manner to a suitable health professional (doctor or nutrition specialist) who can make a thorough nutritional diagnosis, and plan and carry out the most appropriate nutritional treatment according to the individual needs.

2.3.2 — Do patients with cancer have any dietary or physical restrictions?

No, patients with cancer have no dietary or physical restrictions. However, some patients have previous food intolerances that are exacerbated by the cancer treatment. Patients should discuss any food sensitivities with their doctor or nutritionist for nutritional care planning. The most important thing is to know that there are no miracle or prohibited foods.

Likewise, physical activity is very important to ensure muscle health, mobility, functioning, and quality of life. It is very difficult for most patients to continue with the physical activities they were used to, for different reasons. The doctor may refer the patient to a specialist such as a physical therapist or physical educator, who will plan and incentive physical activity routines that are individually tailored.

2.3.3 — Are there nutritional and physical activity recommendations to help people with cancer?

There is no single answer to this question because several individual factors should be considered when nutritional therapy or physical activity is indicated.

The best nutritional therapy is with *natural*, varied food groups, which should be properly washed when *in natura* and prepared with healthy techniques. The doctor should discuss this point with the professionals on the interdisciplinary team, who will be able to identify whether the patient's meals are sufficient and well-balanced. The nutritional team can recommend ways to meet the patient's nutritional needs while respecting the individuality and food preferences.

2.4 — Nutritional, fluid, and medication recommendations

Good nutrition is key for everyone. This is even more true for people with cancer. How the diet changes to meet the needs will depend on the type of cancer, the treatments, and any symptoms or signs that are influencing the ability to consume an adequate diet. The health care team will determine the nutritional needs and how to achieve them through usual or a modified diet. Maintaining an adequate and sufficient diet during cancer treatment will help the patient to:

- Feel better and stronger
- Keep up the strength and energy
- Maintain a healthy weight and body nutrient reserves
- Tolerate treatments and experience fewer negative effects
- Fight infections
- Heal wounds and recover faster from treatment side effects

There is a common misconception between the suggested diet to prevent cancer and the one that is suggested when the patient has the disease. The first seeks to avoid certain foods that, if consumed frequently, for prolonged periods, and in excess, are associated with the development of some cancers. The second seeks to meet the specific needs of a patient with cancer due to the tumor or the treatments administered, which, commonly, increase the need for certain nutrients and energy. For this reason, the frequent error of imposing dietary restrictions on patients with cancer tends to worsen nutritional status, muscle mass, and function, and thus VITALITY.

Meals of cancer patients, like those of any other individual, should not be monotone, tasteless, or restricted. It is important they have variety, color, good taste, and presentation. Dr. Carla Prado et al, in Canada have published a beautiful cooking book for cancer patients that reflects everything described here.[22]

2.4.1 — Let's talk about some nutrients that are important in the diet of a cancer patient

— **Proteins** are key to the repair of body tissues. The muscle produces several hormones essential for a healthy defense system, and muscle quality also depends on the amount and quality of proteins consumed. If the body does not receive enough protein from the diet, it breaks down the muscle to obtain the protein needed to maintain body functions.

Muscle protein actually represents "protein reserve" (which is not really a reserve because these proteins in the muscle are not in excess, as other nutrients). Pulling protein out of the muscle decreases muscle volume and function. Using muscle protein exhausts the availability of the protein needed for wound healing and recovery from metabolic stress, as well as impacts functionality. Cancer patients often require more protein than people without disease. Protein is used by the body during healing and to produce substances needed during treatment, and the tumor itself consumes protein.[22]

In general, there are two sources of proteins: those of animal origin and those of plant origin. Good sources of animal protein are fish, chicken, lean meat, eggs, and milk (low-fat varieties). Consumption of red or processed meats should be limited, without sacrificing protein consumption. Recommended sources of vegetable protein are walnuts or their butter, seeds, dry beans, peas, lentils, and soybean foods.[22]

— **Fats and oils** are a source of energy for the body. Furthermore, fats contain essential elements that cannot be produced by the body, so they should be included in the diet. Fats are a source of energy when they are metabolized and are also stored in fatty tissue. They are an essential component of cells and the brain. They serve as transport molecules for some vitamins important for body functions.

Some fats are better than others, and therefore the patient should always choose foods high in monounsaturated and polyunsaturated fats and avoid trans fats and saturated fats. Monounsaturated fats are found in vegetable oils such as olive, canola, and peanut oil. Polyunsaturated fats are mainly found in sunflower, corn, and flaxseed oils. Saturated fats are mainly of animal origin, including chicken, whole milk, cheese, and butter (the amount should be tailored). Some vegetable oils, such as coconut or palm oil, can increase cholesterol and cardiovascular disease risk, and should be avoided. This is also true for the trans fats formed by solidifying oils, such as margarine. These fats, although not widely used in food preparation because of their harmful effects, can be found in desserts, snacks, and processed foods.[22]

— **Carbohydrates** are the largest dietary source of energy for the body. Some organs, such as the brain, heart and kidneys, depend on carbohydrates to obtain the energy they need for all their functioning processes. In addition, carbohydrates are essential for physical activities. When not enough carbohydrates are consumed, the body breaks down muscle protein to convert it into energy in a very expensive and inefficient process. Good sources of carbohydrates are whole fruits, vegetables, and whole grains. On the other hand, consuming carbohydrate-rich foods without the intake of other nutrients can create a gap for a healthy, complete diet. Empty calories, which are almost always sugary drinks (simple carbohydrates) that do not contain other important nutrients, should be avoided because they may cause early satiety by increasing the volume of the stomach, and take the place of good sources of nutrients essential for the body.[22]

— **Other nutrients:** Other very important groups of nutrients for the body are fibers, vitamins, minerals, and phytonutrients. Whole grains, seeds, and foods prepared from them provide these nutrients. Barley, quinoa, brown rice, and any other whole grains are recommended. Vitamins and minerals are usually found in fruits, vegetables, and cereals.

Vitamins A, C, and E, selenium, and zinc and other nutrients such as carotenoids and flavonoids are classified as antioxidants, which protect cells from damage caused by altered metabolism in cancer and during treatments. These are naturally found in fruits, vegetables, and other foods. But if taking these in the form of medications (pills or other), the health care team should be informed, because very high doses can interfere with cancer treatments. Phytonutrients are natural substances in plants that provide them with their color; consumption of vegetable foods of different colors is recommended.

— **Fluids:** It is essential to drink a variety of fluids, because dehydration is common in patients with cancer. Water is very important for the transport of energy, for nutrition, and for the cells to be able to function. It is recommended that 220mL of fluids be drunk several times a day (around eight times a day, but this is also on an individual basis) to ensure the body is getting the fluids it needs. It is important to highlight that liquids should be avoided with mealtimes so that they do not interfere with adequate nutrient consumption by increasing the volume of the stomach. Liquid foods should be consumed as soups, jellies, milk, and juices.

When experiencing any of the following (**Table 3**), the patient should consult with the healthcare team.

Table 3: Signs and Symptoms of Dehydration
▪ Thirst that cannot be quenched with ingested fluids
▪ Dizziness and light sensitivity
▪ Confusion and difficulty thinking clearly
▪ Tachycardia (palpitations)
▪ Dry and sunken eyes
▪ Dry mouth
▪ Decreased urinary frequency
▪ Fatigue and weakness
▪ Loss of consciousness

2.4.2 — Medications

Typically, cancer patients use many medications that can interact with food or with each other. It is important to consult with the health care team, especially with a pharmacist, who will evaluate potential interactions and advise on strategies to reduce or eliminate them. It is important to emphasize that even medications considered "natural" carry a risk for adverse events or interactions.

In summary, it is difficult to know how each patient will react to treatment; everyone is different. However, it is helpful to follow some steps to cope with changes in the diet and appetite caused by cancer treatments. It's important to talk with the healthcare team about any concerns the patient or the family might have. Meeting with a dietitian to assess the patient's current diet and nutritional status before beginning treatment is desirable. A plan for addressing potential side effects can help the patient feel more in control and ready to make changes.

2.5 — Tips for choosing, storing, and preparing foods at different times in cancer management

Some tips for patients and caregivers on how to choose, store and prepare foods are registered in **Table 4**.

Table 4: Tips for Preparing the Kitchen/Pantry Before Treatment Is Started
▪ A variety of favorite foods should be kept in the pantry and fridge to avoid going shopping in the initial phases of treatment
▪ Foods that are easy to eat, especially when the patient is not feeling well, should be available
▪ Family or friends may/should help the patient with shopping or cooking, especially when he/she is presenting nausea or vomiting
▪ Meals should be cooked ahead of time and frozen to avoid having to cook through treatment
▪ The patient should talk to the healthcare team about how treatment might affect his/her well-being and get advice on how to cope

It is fundamental to eat well during treatment! The body needs a healthy diet to work better. Some treatments work best when the patient is well-nourished and is getting enough calories, protein, and other nutrients (**Table 5**).

Table 5: Orientations for Healthy Nutrition
▪ Patients should not be afraid to try new foods, which may be enjoyable during treatment
▪ Plant-based foods should prevail, and a large amount of meat should be replaced by beans or peas once or twice a week
▪ The intake of more fruits and vegetables, every day, is recommended. Vegetables of different colors and vegetable-based foods contain many natural substances that promote health
▪ A healthy weight and physical activity are indicated. Some minor changes in weight are normal during treatment
▪ Consumption of cured foods (eg, salted, smoked, or pickled foods) is recommended
▪ Intake of red and processed meat should be avoided; however it is important to guarantee the intake of enough protein through other sources

Some people will experience poor appetite and problems chewing, swallowing, or digesting food and will feel very tired during treatment. All of this can affect good nutrition and compliance with the planned treatments. **Table 6** summarizes some important tips for increasing the energy and protein consumption:

Table 6: Nutritional Orientations for Increasing the Energy and Protein Consumption
▪ There should be between more than three to six smaller meals throughout the day
▪ Favorite foods should be encouraged, except when the patient is experiencing nausea or vomiting
▪ Patients should not wait until they are hungry to eat; thus it is recommended to eat regularly throughout the day
▪ The biggest meal should be eaten when the patient is mostly hungry. For example, if it is in the morning that he/she is mostly hungry, breakfast should be the biggest meal
▪ High-caloric and protein foods are recommended at every meal and snack
▪ Light exercise or a walk before eating to build up appetite should be considered
▪ High-caloric and high-protein drinks like milkshakes or dietary supplements, especially between meals instead of with them (consuming foods and drinks together will make the patient feel full faster)
▪ Homemade cereal or protein bars and pudding are good options

2.6 — How to manage some common problems experienced during cancer treatment

People with cancer and during treatments may experience multiple causes that interfere with good nutrition. It is important to always check with the healthcare team to avoid these undesirable effects or to keep them under control. Also, the help of a dietitian for advice on dietary changes that may help is recommended. In the text below, some of these undesirable effects and tips for managing them are depicted:

— **Loss of appetite:** Cancer or cancer treatments can affect the eating habits and willingness to eat. Other causes of loss of appetite include pain, constipation, and nausea. Managing the root cause of appetite loss should help the patient eat better:

- Smaller meals more often instead of eating only three meals a day
- Fluids should be avoided when eating meals
- Meals should represent pleasant moments. A nice table with favorite plates and cutlery, with music, in the company of family and friends is desirable
- Physical activity is important (the health care team's advice should be followed)
- High-calorie, high-protein meals: eggs, nuts, peanut butter, tuna, or chicken is recommended

— **Constipation and bloating:** Constipation refers to having fewer bowel movements with stools that are harder and more difficult to pass, while bloating is the sensation of a full and tight belly, often due to gas:

- The healthcare team should be aware of this in order to prescribe laxatives and/or fiber to help soften the stools
- Going to the toilet at the same time each day, usually after a meal or physical activity, is desirable
- More fluids unless the health care team advises against is recommended
- More fiber-rich foods such as whole grain bread or whole grain cereal; fresh fruits with peels (if edible); raw vegetables, fruit juices, peach, plums, and raisins (this should be individually discussed with health team) are indicated

- Foods that cause constipation, such as apples, bananas, cheese and eggs should be avoided
- Foods and drinks that produce gases such as avocado, beans, peas, squash, broccoli, and whole milk, should be avoided
- Chewing gum and drinking with straws are not recommended
- The use of laxatives may be needed, but patients should not be encouraged to use enemas or suppositories unless prescribed
- Physical activity or any type of movement as walking is desirable

— **Diarrhea:** Cancer treatments and some medications can cause diarrhea - loosen stools. Severe or persistent diarrhea can cause dehydration, weight loss, and weakness; therefore, it demands medical care. The below recommendations may help control diarrhea:

- Plenty of light, noncarbonated, and well tolerated fluids, such as oral rehydration drinks, apple juice, and gelatin
- Foods are to be eaten more frequently during the day
- High-fat foods, such as fried foods or fatty foods should not be eaten
- Foods high in fiber as seeds, whole grains, legumes (beans and peas), dried fruits, fruits, or raw vegetables with peels are not indicated
- Whole milk and other dairy products may not be good, while yogurt and kumis may be fine
- Foods and drinks that cause gas, such as carbonated drinks or vegetables, as well as chewing gum are to be avoided
- Food and drinks high in sodium, such as oral rehydration drinks, crackers, and soups are good
- Potassium-rich foods and liquids, such as fruit juices, potatoes with skin, and bananas help control
- One cup of fluid after each bowel movement is desirable
- Foods that are easy to digest, such as rice, bananas, applesauce, yogurt, mashed potatoes, oatmeal, low-fat cheese, and toast once diarrhea improves may be a good option
- Desserts, sweets, gums, and processed foods are not indicated
- Alcohol consumption or smoke are contra-indicated
- Gum or sweets or desserts containing sugar alcohols, such as sorbitol, mannitol, or xylitol should be avoided
- The healthcare team should be consulted for other options,and if diarrhea worsens

— **Dry mouth and/or thick saliva:** This can be overcome with good hydration which is essential to maintaining moisture in the mouth. Some basic recommendations are:

- Various fluid intake during the day
- Food intake should be in small portions, and chew well
- Liquids with meals and snacks help soften food portions in the mouth and allow to swallow them better
- Dry foods should be eaten with sauces, soups, yogurt, or creams
- Ice chips or sweets and sugar-free gum to boost saliva are recommended. Cinnamon, citrus, and mint flavors can also help
- Cold water drunk in frequent sips to rinse the mouth between meals is also good

- A homemade mouth rinse with one teaspoon of baking soda and one teaspoon of salt in four cups of water helps. Rinse the mouth four to six times each day with this solution
- Artificial saliva sprays sold in pharmacies may also be used
- Petroleum jelly, coconut butter, and balms to keep lips moist can be used
- Alcohol or tobacco are contra-indicated, as well as spicy, highly seasoned, and acidic foods
- Very dry or hard or difficult to digest foods, as well as raw fruits and vegetables are not desired
- Mouthwash containing alcohol is contra-indicated
- If diet intake is insufficiently related to mouth dryness or the patient is on a diet, the healthcare team may consider the use of nutritional supplements and other convenient food sources

— **Mouth ulcers:** The presence of mouth ulcers, or the sensation as if the mucosa of the mouth was injured, frequently occurs during certain kinds of cancer treatments. Thus, several options may help:

- The healthcare team should be consulted on how to manage this problem and what steps to take to improve it
- The mouth should be rinsed frequently with a homemade solution (i.e. One teaspoon of baking soda and one teaspoon of salt in four cups of water). This solution helps prevent infections and helps decrease pain and burning in the mouth. Gargling with this solution to relieve the burning sensation in the throat, but not swallowing the liquid is a good option
- Mild, moist foods such as cream soups, cooked cereal, pasta, yogurt, and pudding are indicated while raw vegetables, fruits, or other hard, dry, or crunchy foods should be avoided because they can hurt the mouth
- Blender puree food is recommended
- Cold or warm rather than hot foods to reduce mouth irritation are a good option
- Fluids should be drunk throughout the day
- Fluids should be drunk with a straw, so they do not touch the damaged mucosa of the mouth
- Foods rich in calories and proteins to accelerate oral healing are indicated
- Alcohol, carbonated beverages, and tobacco should be avoided, as well as very salty, spicy, or sugary foods, and also acidic fruits and juices, such as tomatoes, oranges, grapefruit, limes, and lemons
- Manipulated solutions prescribed by the healthcare team that can be prepared by compounding pharmacies may help these conditions

— **Dental and gum problems:** Many treatments and medicines can cause changes in the teeth and gums. Oral hygiene is critical during cancer treatments to prevent infection and tooth loss, therefore, the below options may be beneficial:

- Consultation with a dentist and dental cleaning before starting anticancer therapy is ideal
- Brushing and flossing teeth regularly is highly recommended while the use of mouthwash will help keep the mouth clean
- The healthcare team should be consulted if white plaques appear on the gums or palate, which may indicate the presence of infection

— **Nausea and vomiting:** These symptoms and signs are very bothersome to the person and may be associated with an unpleasant sensation in the throat or stomach. Therefore some options are recommended such as:

- Avoiding eating the favorite foods when nausea is present because this may change the perception of them (ie, not wanting to consume them, in the future, because of the association with nausea and feeling sick)
- Eating foods that appeal at the time
- Eating more frequently during the day (i.e. snacks may include smoothies, mixed nuts, and fruits)
- Drinking cool, clear drinks during the day, which are better tolerated. Clear liquids are those are fully clear. Some items that may be permitted include water, ice, fruit juices without pulp, sports drinks, gelatin, tea, coffee, clear broths, and clear ice pops
- Consuming oral rehydration beverages and/or gelatin, as well, as sucking on hard candies with pleasant flavors, such as lemon, cinnamon, or mint, to avoid bad tastes in the mouth.
- Eating soft foods
- Eating cold or room-temperature foods to decrease odor and taste; avoiding entering the kitchen when food is being made
- Avoiding greasy, fried, spicy, or very sweet foods
- Trying small, high-calorie meals such as puddings, ice creams, sorbets, yogurts, and milkshakes several times a day
- Using butters, oils, sauces, and milks at mealtimes to increase calories
- Eating acidic or acidified foods, which may be better tolerated unless oral problems co-exist
- A number of medicines that may be helpful should be prescribed by the healthcare team, such Ondansetron etc, as anti-nausea medication at the first sign of nausea may prevent vomiting
- Resting quietly and sitting for at least one hour after each meal, while adding a distraction such as a TV program or the company of others is a good option
- Relaxing, by using strategies as music, massage, deep air inhaling and exhaling etc may help decrease nausea while not yet on medications
- The health care team should help with other valuable tips on how to manage nausea and vomiting, if they don't improve with these measures

— **Problems swallowing:** Some cancers and cancer treatments cause problems swallowing food. Some measures may help with this:

- Small portions of soft food that is high in calories and protein (cream soups, pudding, creamy ice creams, yogurt, and milkshakes)
- Intake of small portions while swallowing them before taking another one
- Straws to consume semi-liquid and liquid meals
- Liquids in thicker forms, such as fruit purees; thickeners may be used in liquids because they are easier to swallow than clear liquids
- Macerated or pureed foods (such as fresh meats, cereals, and fruits) so they are soft and similar to baby food. It may be necessary to add water to certain dry foods
- Cold meals as they may be easier to swallow. If yet, cold foods cause pain, room-temperature food
- Ice pieces and liquids with meals

- Crushed pills (pill crushers are sold in the pharmacy), and mixing them with juices, apple sauce, jelly, or pudding
- The healthcare team (preferably the pharmacist) should be contacted before crushing any pills. Some pills may not work or may even be unsafe when crushed. Other pills have a special coating that allows them to be taken on an empty stomach and prevents them from interacting with food
- Avoiding alcohol, hot, spicy foods, and clear liquids
- Avoiding acidic foods, such as acidic fruits, or carbonated liquids
- Avoiding dry, hard foods, such as cookies, and fried foods
- Sitting up straight when eating, and taking small sips of fluids; remaining upright for a few minutes after meals
- If there is pain in the mouth, the same tips as described for mouth ulcers should be adopted. The health care team should be contacted for a pain-relieving medicine or a medicated mouthwash
- The health care should be informed if there is a feeling of food "stuck" in the throat or if coughing or choking when eating. This requires a referral to a swallowing/language pathologist. They are professionals who will help in the process of swallowing more safely
- Thick products such as purees, porridge, and thick sauces

— **Changes in taste and smell:** Some cancers or cancer treatments can alter the sense of taste and smell. These changes can affect appetite. A metallic taste, very salty, sweet, or bland tastes may occur, in this regard, experimenting with new foods, using marinades or spices, or using different cooking methods may help. Other options are:

- Plastic cutlery, and paper plates or cups
- Sugarless lemon drops, gum, and mints
- Seasoning meals with lemon, citrus fruits, vinegar, and pickles (unless there are mouth ulcers)
- Serving meals cold or at room temperature. This will help reduce odors and flavors by making them easier to tolerate
- Frozen fruits such as melon, grapes, and oranges
- Fresh vegetables, which taste better than cooked, canned, or frozen ones
- Marinated meat to make it softer
- Fresh fruits mixed into smoothies, ice cream or yogurt
- Drinking fluids with a straw
- Foods that do not require cooking
- Avoiding eating in enclosed, hot places
- Mouth rinsing with baking soda, salt, and water before meals may help improve the taste (For this, mix one teaspoon of baking soda and one teaspoon of salt in four cups of water) and spitting out the rinse instead of swallowing
- If red meat tastes odd, other protein sources such as chicken, fish, eggs, or cheese should be chosen
- Keeping the mouth clean and brushing the teeth often will help keep the mouth cool. Also, regularly replacing toothbrushes
- The healthcare team should be contacted for other specific recommendations that may help

— **Weight changes:** Weight changes are common during cancer treatment. Both losing and gaining excess weight are contra-indicated.

To stop weight loss:

- Foods and snacks rich in calories and protein such as nuts, dried fruits, granola, peanut butter, hard-boiled eggs, or cheese
- Smoothies, milkshakes, and nutritional supplements to increase dietary calories and protein
- Favorite foods at any time of the day. Reverse meals (for example, breakfast at lunch or dinner at lunch)
- High-calorie foods such as whipped cream, sour cream, cream cheese, butter, or sauces added to the foods
- Enough fluids and water should be drunk between meals to avoid feeling full to eat at mealtime
- The healthcare team may help with other tips

To stop gaining weight:

- The healthcare team should rule out edema (swelling caused by fluid buildup) as a cause of weight gain
- Eating a healthy, low-calorie diet when edema has been ruled out
- Decreasing salt intake
- Limiting portions of high-calorie foods
- Reading food labels to find out how many calories the food contains
- Being physically active according to individual capabilities
- The healthcare team may help with other options

— **Dehydration:** Dehydration occurs when there is more fluid losses than intake. Some tips may help preventing it:

- Liquids should be drunk several times a day. Sometimes ice chips are easier to consume
- Liquid-rich foods such as fruits, vegetables, soups, jellies, and others
- Cooled drinks on hand so they can be sipped frequently (juices, water, and others)
- Sucking ice chips to soothe the dry mouth if it is a struggle to drink liquids

2.7 — Additional tips for people with a very weakened immune system

Cancer and its treatments can compromise the immune system (the cells that protect the body from diseases and germs). For this reason, the body cannot fight infection as a healthy body does. This also puts the patient at risk for food-acquired diseases. The healthcare team should help on providing some tips that can help when there is this problem:

- Hand washing with warm, soapy water for 20 seconds before and after preparing meals
- Food in the fridge at 4°C or below
- Food served hot above 60°C
- Meats, fish, and chicken are to be thawed in a dish in the microwave to trap all liquid, and not thaw at room temperature
- Thawed foods must be consumed at once and not refrozen
- Leafy vegetables must be rinsed under running water before consuming

- Different cooking utensils should be used to stir and taste food while cooking. These utensils should not be reused; the patient should not use another person's utensils after he/she used it
- Food that looks or smells odd must be discarded and, when in doubt, never tasted. Similarly, food beyond the expiration date is contraindicated
- Clean knives to cut food
- Raw meat in a sealed container away from any food that is ready to be consumed in the refrigerator
- Fridge organization by type of food, and without mixing different types of food
- The fridge should frequently be cleansed with soap and water, with wet, food-safe disinfectant cloths
- Clean, unused dishes must be used for cooked meat
- Foods that are expired, damaged, look odd, or have dented cans should not be bought. If the food should be sealed, it must be sealed before buying it
- Fruits that are overripe or bruised should not be bought
- Prepared and packaged meals, as well as desserts that have been left outside the refrigerator, especially those that have cream, must be avoided. Also, this applies to meals at a self-service counter or food kept for some time in containers
- Vending machine foods containing cream, yogurt, or ice creams are contraindicated as the expiration date cannot be checked
- Cracked or unrefrigerated eggs should not be eaten
- Food must be refrigerated as soon as possible after purchase. Therefore, it should not be left in cars or at room temperature for a long time
- When going to eat at a restaurant, the best times are when the restaurant is not full, and there is fresh and freshly prepared food
- Seasonings or sauces that are stored in bottles and used by multiple people should not be used
- Restaurants with hygiene and freshness of the food concerns, as well as salad bars, meals prepared at counters, and street food, are contraindicated
- Pasteurized juices are preferred over freshly squeezed juices when in restaurants
- Restaurant tables must be clean, free of debris, and with a clean tablecloth that has been recently placed. Thus, tables without a tablecloth are not a good option
- Leftover food taken home should be packed up in front of the customer rather than letting the kitchen staff do it

ASK FOR HELP IN CHOOSING THE FOODS THAT ARE BEST FOR YOU!

2.8 — Physical activity in people with cancer

PHYSICAL ACTIVITY IS VERY IMPORTANT. Physical activity has many benefits for all people, especially those who are sick and have cancer. It helps maintain muscle mass, strength, endurance, and strong bones. It also helps reduce anxiety, depression, fatigue, and edema, as well as improving quality of life, bone health, and sleep. The healthcare team should recommend the best exercise for each patient to stay active!

Exercise before, during, and after cancer treatment has been shown to be safe and useful. It improves quality of life and will give the energy needed to do the things that are important to the patient. Physical activity also decreases the risk of side effects from treatments and complications and helps prevent the development of new cancers in the future.

Here are ways that exercise helps before, during, and after cancer treatments:

- Helps the body and brain work better
- Reduces the feeling of fatigue
- Reduces anxiety and depression
- Helps sleeping better
- Allows the individual to remain active
- Increases muscle strength, improves bone health, and reduces movement limitations
- Keeps the immune system active to maintain defenses
- Increases appetite
- Keeps a healthy weight
- Improves quality of life and health perception
- Reduces the frequency, severity, and duration of harmful effects of treatments

General physical activity recommendations for the person facing cancer include the following:

- Avoiding long periods of inactivity and returning to daily activities as soon as possible after cancer diagnosis
- Participating in regular physical activities
- Starting slowly and building strength and endurance to the extent of individual capabilities
- Doing 150 to 300 minutes of moderate-intensity physical activity and 75 to 150 minutes of vigorous activity per week
- Starting with 10-minute periods of exercise several times a day
- Include endurance exercises at least twice a week (with weights or pushing against a weight)
- Stretch at least twice a week

The goals of physical activity or exercise in the cancer patient can be divided according to the stage of treatment.

a) Before treatments: Maintaining the usual level of activity or increasing it may help the management and recovery from the treatments faster. Studies show that physical activity before surgery can reduce complications after surgery. In addition, physical activity helps manage stress and anxiety, gives more energy, and helps sleep better before the beginning of treatments. Those who have maintained physical activity before treatments recover faster and return to their daily life faster.

b) During treatment: Situations that limit the possibility of usual physical activity may arise. The type of cancer and treatment, and the patient's energy, endurance, and level of physical training before treatment determine how much activity is appropriate during this phase. During treatments, it may be necessary to decrease physical activity, but the goal is to stay at least as active as before the disease.

c) During recovery: Most people start physical activity slowly after the limiting effects of treatments go away. What is medium-intensity activity for a healthy person is a high-intensity exercise for the person who has gone through these treatments. The most important thing is to move as much as possible. In the treatment recovery and disease-free period, most people can increase the duration and intensity of physical activity. Regaining quality of life by following a balanced diet, maintaining a healthy weight, and being physically active will help to manage chronic health conditions and reduce the incidence of other cancers.

The assessment by the health care team when choosing activities, especially for those with heart or lung disease, an ostomy, severe fatigue, equilibrium problems, balance problems, frequent falls, bone diseases, or metastasis, is mandatory. Additionally, medicines may affect physical activity. Thus, it is important to discuss those in use with the physician or pharmacist. Although most people will be able to start and maintain an exercise program, it is ideal to have the assistance of a physical therapist, rehabilitation specialist, or exercise expert. The healthcare team must clear the patients to start any physical activity program, and the attending physical expert specialist must be aware of the cancer diagnosis and any limitations. It is important to choose exercises that are aligned with the treatment and patients' goals, as well as to guarantee the patients' safety.

When starting an exercise program, it is important to consider the following:

- To stay away from uneven floor surfaces that may cause falls
- To find a safe and well-lit place, if exercise is done outdoors
- To avoid crowded sites, for Immunocompromised patients, like public gyms until the immune responses have returned to normal
- To check with the healthcare team first before swimming especially during radiotherapy. If the skin isn't irritated and there are no open wounds, swimming is likely safe. It is important to make sure to bathe with soap and water after swimming to avoid skin irritation
- To bring another person while exercising or inform someone of the patient's whereabouts and how long he/she will be gone while keeping the cell phone close by

It is important to start slowly and to consider the following:

- To be active for a few minutes daily, and slowly increase the frequency and duration of the exercise The muscles will let the patient know when he/she can continue, and when to stop and rest
- To exercise within individual capabilities; thus not to be ambitious about exercise during treatments The patient should listen to the body when it asks for rest. When feeling very tired, it is recommended light exercise for 10 minutes every day and to build from this point
- To avoid exercise if feeling dizzy or unable to stand
- To exercise with rest breaks. For example, walking briskly for a few minutes, slowing down, and then increasing the pace again. Also, splitting the exercise time into fractions during the day will make it easier. The benefits of exercise under these modalities are enormous
- To avoid engaging in strenuous activity without consulting the healthcare team. Walking at a light pace is a good option to start
- To refrain from any activity that places the patient at risk for falls or trauma. If the patient feels dizzy or experiences blurred vision, the healthcare team should be contacted
- If there are problems with the feet and balance, there is a risk of falls, in this regard the healthcare team should offer solutions for each of these problems

Trying more than one type of exercise:

- Exercises should include large groups of muscles such as the legs, abdomen, chest, and back. Strength training, stretching, and aerobic exercise are all important components of a good exercise program
- Exercises to maintain muscle mass and bone health, such as the use of stretch bands and light weights are recommended
- Exercises that increase flexibility and maintain functional joints are a good option
- Pre-exercise warm-up for 2 to 3 minutes are indicated. A good warm-up includes moving shoulders, lifting and joining arms over the head, trying to touch feet, walking, and squatting
- Ending the exercise session with elasticity and stretching movements. Holding the stretch for 10 to 15 seconds and then relaxing. Examples of stretching exercises are stretching arms up, taking deep breaths, and trying to touch toes. This way, all muscle groups are active

Important tips are registered in **Table 7**.

Table 7: Orientations on How to Practice Physical Activity Safely
▪ Drinking enough fluids based on the recommendations of the healthcare team
▪ Being careful not to pull venous catheters or enteral tubes, if the patient has them
▪ Avoiding infections, it is important to avoid swimming in lakes, swimming pools, or other bodies of standing water without knowing about the water quality
▪ No contact sports with other people or any sport that involves the risk of touching the area where the catheters and tubes, if any, because there is the risk of moving them. The healthcare team is the best to indicate the ideal activities
▪ Avoiding too much weight, in particular if osteoporosis, bone involvement from cancer, arthritis, neurologic damage, poor vision, poor balance, or excess weakness are present as that can cause injuries

How and how much the patient should exercise varies from person to person. There is no one right level of exercise for all cancer patients. The most important goal with physical activity is to keep the muscles strong and active so that the patient can perform all the daily activities he/she wants and needs to do. The more active the patient is, the more physical activity he/she will be able to do, and the better the body will function. Even if the patient discontinues the exercise program, this should only be temporary if possible as it is very important to stay as active as with daily activities. It is critical to keep physical activity simple and fun. Relaxation exercises are ideal for reducing stress and inducing well-being.

Tips to help stay active:

- Practicing short-, medium-, and long-term goals
- Focusing on making it a fun activity
- Trying different things, such as yoga, dance, or tai-chi, to avoid falling into boring routines
- Inviting others, such as friends, family members, and coworkers, to do group activities together
- Keeping a schedule and keeping track of the progress to stay motivated
- Celebrating the progress and owning milestones

Starting an exercise program is difficult for anyone, and it is harder when sick, especially if the patient has not exercised before. Starting slowly with what it can be done right now. If the patient exercised previously, it is important to discuss with the healthcare team during treatment because it may be necessary to decrease the duration and intensity of the activity until he/she feels better.

Adding physical activity to the daily routine is recommended:

- Taking a walk after meals
- Riding a bike
- Doing gardening activities
- Washing the car
- Playing games with children, like frozen or hide and seek
- Taking the dog for a walk (if the dog is easily controlled)
- Dancing to soft music
- Doing any physical activity while watching television
- Walking before lunch
- Parking the car farther away and walking to the final destination
- Using the stairs, not the elevator
- Exiting the bus at an earlier stop and walking to the final destination
- Making space in the agenda for 10-minute walk breaks
- Encouraging others to walk at work after meals
- Counting and recording the number of daily steps
- Keeping physical activity easy and enjoyable!

NUTRITIONAL THERAPY FOR MEDICAL ONCOLOGISTS AND NON-NUTRITION-EXPERT CLINICIANS

3.1 — General aspects

Most short-, medium-, and long-term adverse effects in people with cancer are related to having compromised nutritional status. On the other hand, nutritional status negatively affects the clinical course of the cancer patient and the outcome of therapeutic interventions. Thus, the strategy for implementing care for these patients is designed to see outcomes at the community level, which is where patients arrive after institutionalized treatments and where they remain during outpatient services.

The proposed criteria for care will be those used in the community and, in some way, will serve to assess the overall performance of the health system, for which interdisciplinary care is essential. The involvement of physicians, nutritionists, nurses, pharmaceutical chemists, physical therapists, speech therapists, and others is highly relevant to the care management of people with cancer. Some professionals will be present during all stages, while others will be present only at certain stages of the process from diagnosis to assessment, treatment, and recovery. Essentially, the goal is to reinsert the person in the community functionally, independently, with good quality of life and meeting individual life expectations. Emphasis is placed on the importance of the nutritional care, which has an important role in ensuring nutritional management at every stage of the treatment process (see Section Five: Medical Nutrition Treatment), and which will guarantee the best opportunities during the therapeutic course from the hospital to the community. This practitioner should be aware of the interventions available, until the patient is in the best possible condition. For this reason, introducing nutritional care as part of the structured management of people with cancer will result in better responses to interventions, prevent deteriorations that influence prognosis, alleviate symptoms, and maintain functional status. To further this aim, this section of the manual is designed to educate non-nutrition-expert clinicians in the topics of malnutrition and nutritional therapy in patients with cancer.

The WHO defines intrinsic capacity as the combination of all the physical and mental abilities of an individual, including psychological ones. Functional capacity is the combination of intrinsic capacity relative to the environment in which the person lives. The health professional should be aware of the importance of optimizing the patient's nutritional status and muscle health before, during, and after any conditions associated with a decrease in intrinsic capacity and refer the patient to a nutrition expert or apply interventions to stop or reverse the deterioration. At the level of primary care, the health professional should measure the following parameters that make up an individual's intrinsic capacity:[9]

- Cognition
- Locomotor system
- Nutritional status and muscle health
- Psychological well-being
- Visual and auditory acuity

The nutritional assessment encompasses a thorough examination performed by the nutrition specialist, which will allow evaluating the patient and intervening in a timely and efficient manner. Among the domains that make up the intrinsic capacity of a person, the domain with the greatest capacity to positively or negatively influence the others is the VITALITY DOMAIN,[23] which is composed of nutritional status and muscle health. The vitality domain is the axis for the assessment and intervention by the nutrition professional.

3.2 — The prevalence of malnutrition in Latin America

The prevalence of malnutrition in Latin America, especially in hospitals, is high, reported between 40% and 60% of patients[24] When it comes to cancer patients, the prevalence is high as well, despite the fact that it is often hidden by patients being overweight or obese.

Alvarez and colleagues[25] assessed the nutritional risk during hospital admission of 444 patients diagnosed with cancer in a hospital in Mexico City, using instrument NRS-2002 (Nutrition Risk Screening) and found that 74.5% were at risk of malnutrition; 26% of them had BMI <20 kg/m^2; 50% reported significant recent weight loss and 55% reported decreased food intake in the last two weeks. One-third of the patients were classified at risk of severe malnutrition.

The LASOMO study[26] included 1,891 cancer patients from 52 hospitals distributed in 10 countries, with 81.6% of the population being cared for in outpatient services. Patients' treatments included chemotherapy (55.1%), radiotherapy (17.8%) and surgery 27.1%. 20% of patients had obesity and 8.5% BMI below 18.5 kg/m^2, with 64% of patients reporting unintentional weight loss in the last six months, with an average of 8 kg loss. About 31% of patients experienced weight loss of more than 10% of body usual weight and 64% of patients experienced weight loss of less than 10%, with only 5% experiencing weight gain. Using the Global Subjective Assessment (VGS), 40% were considered nourished, 41.7% had suspected malnutrition or moderate malnutrition, and 17.5% were considered to have severe malnutrition. The percentage of malnutrition was higher in men than in women: 62.8% compared with 53.6%. Malnutrition by type of treatment was 53.3% among those on radiotherapy; 55.9% on surgery and 62.7% on chemotherapy. Among those with digestive tract tumors, 73.3% were malnourished; lung, 62.3%; head and neck, 62.1%; central nervous system, 56.5%; gynecological, 53.5%; renal, 52.1%; soft tissue, 50.4%; and breast, 41.2%. 20% of patients had low blood albumin.

Similarly, studies conducted in Ecuador, Cuba and Brazil found the prevalence of malnutrition to be 45% to 66% in cancer patients.[27-29]

3.3 — Terminology used in cancer-associated malnutrition

One of the most marked problems in defining compromised nutritional status – in cancer-associated malnutrition – is the confusion regarding the terminology used in the literature, which is not homogeneous, as well as in screening tools and in the diagnosis of malnutrition/malnourishment status.[30] The nutritional status of the cancer patient is primarily influenced by loss of appetite/anorexia, nausea/vomiting/diarrhea, obstruction, alterations in metabolic pathways such as insulin resistance and anabolic resistance, as well as inflammatory alterations. In addition, oncology treatments are influencing factors to further deteriorate nutritional status.

With cancer commonly classified as chronic disease, one of the challenges in this classification is that the cancer patient undergoes periods of time more similar to those defined for acute illness or trauma, while there are other periods of time without inflammation and that resemble a fasting situation.

Cancer patients with hypermetabolic and catabolic status with acute complications or clinical conditions as chemotherapy and others, are at higher risk for malnutrition and need specific parameters to be classified for early intervention [**Table 8**]:

Table 8: Parameters to Classify Cancer Patients With Hypermetabolic Hypercatabolic Status

	Cancer patients with hypermetabolic hypercatabolic status	
	Moderate	**Severe**
Energy consumption	<75% of TME > 7 days	<50% of TME >5 days
Weight loss	1-2% 1 week 5% 1 month 7.5% 3 months	2% 1 week 5% 1 month 7.5% 3 months
Loss of fat	Low	Moderate
Muscle mass loss	Low	Moderate
Edema	+	++ - +++
Grip strength	N/A	Decrease

TME, Total Metabolic Expenditure

Cancer patients without controlled disease, in stable periods of time between therapies, recovered from surgeries and other anticancer therapies, are classified as having a moderate inflammatory response [**Table 9**].

Table 9: Parameters to Classify Cancer Patients With Moderate Hypermetabolic Status

	Cancer patients with moderate hypermetabolism status	
	Moderate	**Severe**
Energy consumption	<75% of TME > 1 month	<50% of TME >1 week
Weight loss	1-2% 1 week 5% 1 month 7.5% 3 months 10% 6 months	2% 1 week 5% 1 month 7.5% 3 months
Loss of fat	Low	Severe
Muscle mass loss	Low	Severe
Edema	+	++ - +++
Grip strength	N/A	Decrease

Cancer survivals or cancer patients with a low or not inflammatory response, without treatments are classified as malnourished if they have the parameters described in **Table 10**.

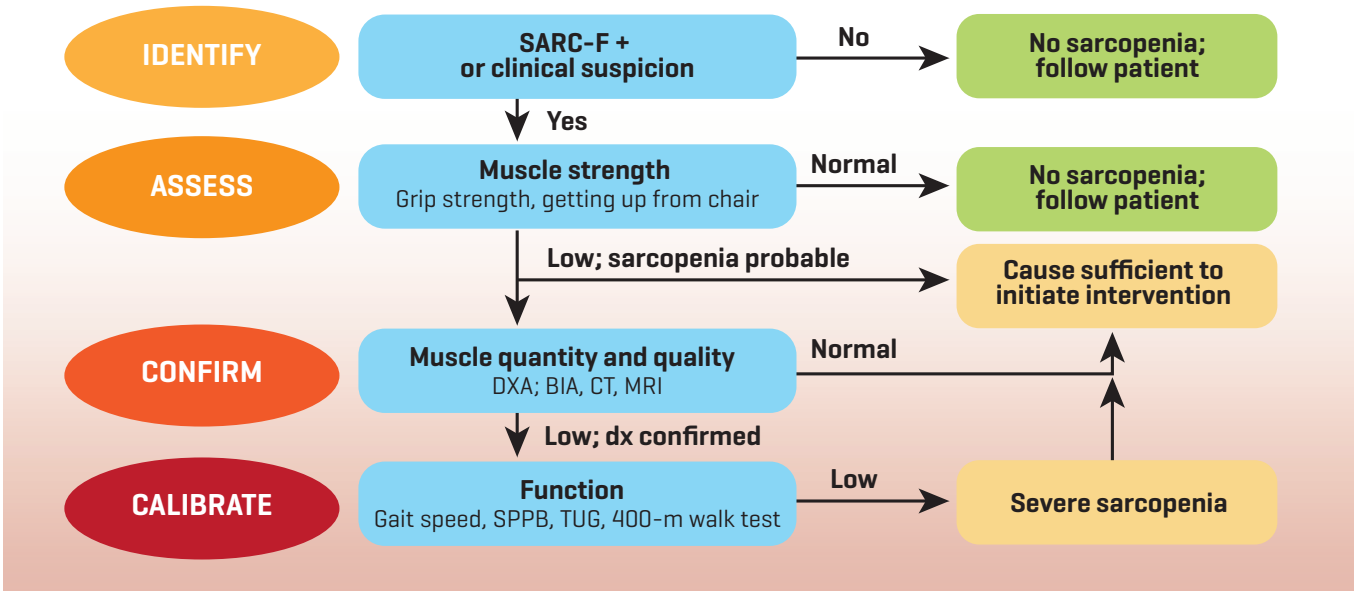
Table 10: Parameters to Classify Cancer Patients Without Hypermetabolism

	Cancer patients without hypermetabolism	
	Moderate	**Severe**
Energy consumption	<75% of TME > 3 months	<50% of TME >1 month
Weight loss	5% 1 week >7.5% 3 months 10% 6 months 20% 1 year	5% 1 week >7.5% 3 months 10% 6 months 20% 1 year
Loss of fat	Low	Severe
Muscle mass loss	Low	Severe
Edema	+	++ - +++
Grip strength	N/A	Decrease

Another great challenge is that the majority of the cancer population is older, and many of these older adults have overweight or obesity, adding to the difficulty in identifying and coping with cancer-associated malnutrition. Thus, the obesity paradox has been described in cancer, in which patients with overweight and moderate obesity have a better prognosis than those with stable or decreased weight. One of the challenges with this approach is that overweight and obesity in patients is defined by body mass index (BMI), which does not allow the assessment of body composition and, thus, this effect can be plausible explanation. Muscle mass is rarely measured, being the largest organ in the body, involved in very important functions such as the secretion of hormones such as insulin and biological processes such as inflammation and hypermetabolism. Thus, the use of "sarcopenia" to define deteriorated nutritional status and muscle loss in these patients is commonly found in the literature. But, by definition, sarcopenia is the loss of muscle mass, strength, and muscle quality, and the term was included in the Disease Classification System, in 2016, with ICD-10 code M62.84.[31] It is divided into primary sarcopenia when associated with aging and secondary when associated with diseases, and thus most cancer patients may coexist with primary and secondary sarcopenia.

A flowchart in the same article by Cruz-Jentoft[31] helps to understand how the diagnosis of sarcopenia and content is made, as shown below [**Figure 1**]:

Figure 1: Sarcopenia Algorithm



Abbreviations: BIA, bioelectrical impedance analysis; CT, computed tomography; dx, diagnosis; DXA, dual-energy x-ray absorptiometry ; MRI, magnetic resonance imaging; SPPB, Short Physical Performance Battery; TUG, Timed-Up-and-Go test.
Source: Cruz-Jentoft AJ, Bahat G, Bauer J, et al.[31]

When there are problems with muscle function, correctly measured, for example by grip strength and chair testing, there are sufficient causes to initiate a structured intervention for recovery. There may be a false sensation of adequate muscle mass being deficient in its quality and unable to recognize if specific studies are not performed, which is the next step in the diagnostic process.

In addition to the loss of muscle mass in cancer-associated malnutrition, other phenomena relating to nutritional deterioration occurs in cancer. Thus, for this reason, since 2011 consensus was made by coining the differentiated terminology for nutritional status associated with cancer from the patient's "cachexia" status.[32] It is defined as a multifactorial syndrome in which there is loss of muscle mass, with and without loss of fat mass, in which an imbalance between protein and energy intake and demand is identified, and that low food intake is often accompanied by metabolic disorders in patients with cancer. Pre-cachexia is defined as an inadvertent weight loss between two and less than 5% of the usual weight in the last six months. Be alert for signs and symptoms that predict worsening of the condition in the immediate future. Cachexia is defined when the individual has inadvertently lost more than 5% of the usual weight in the last six months, has BMI less than 20kg/m^2 and weight loss of 2% in six months, or sarcopenia with 2% weight loss during the same time period. On the other hand, refractory cachexia is marked by all prior alterations, lower functional capacity and less than three months of life [**Table 11**]. Unfortunately, this terminology has not been included in the disease classification system as described above and only the term cachexia appears.

Table 11: Stages and Diagnostic Criteria of Cancer Cachexia	
Stage	**Diagnostic criterion**
Precachexia	▪ Weight loss ≤5% ▪ Lack of appetite, anorexia ▪ Metabolic disorders
Cachexia	▪ Weight loss >5% within 6 months or ▪ Weight loss >2% and BMI <20 kg/m^2 or ▪ Weight loss >2% and low skeletal muscle mass ▪ Reducing the amount of food ▪ Generalized inflammation
Refractory cachexia	▪ Varying degrees of cachexia ▪ Active catabolism ▪ Low efficiency index (WHO 3 or 4)

Source: Adapted from Fearon K, Strasser F, Anker SD, et al.[32]

Cachexia is caused by the interaction between the tumor and the host, causing changes in metabolism patterns, loss of appetite at the level of the central nervous system, alterations in odor and taste, impacting the gastrointestinal autonomic system, inducing fatigue and gradually decreasing the individual's function. Although lack of intake is the major driver for weight loss, metabolic changes and reduced activity contribute to muscle mass loss. The consequences of treatments and diagnostic workup are linked to these factors. It is also important to mention that loss of strength and compromised function are early and pre-weight loss events and may coexist with obesity, obscuring the possibility of early identification.[33] In patients with cachexia, the main disturbances are anorexia, early satiety, nausea, bloating, taste alterations, xerostomia, dysphagia, constipation and hypogonadism.

In an article published in 2020, Ni et al. reviewed the various concepts used regarding the term cachexia and the lack of uniformity in the definition, which does not solve the problems of publications where standards are different and the inability to group the evidence altogether.[34] In addition to the criteria defined by Fearon[32] being included in all approaches and some require the presence of any of the following criteria: measured loss of muscle strength, fatigue, anorexia, low fat mass, early satiety, and BMI. Biochemical studies include elevated C-reactive protein, and elevated IL6, anemia, or serum albumin. It is worth recapturing in the definitions presented so far and the comparison between them, because not all patients present with cachexia nor do they follow a uniform line of evolution when it occurs.

It can be noted that, in these definitions, there are common terms and definitions that overlap one another [**Table 12**]:

Table 12: Overlap of Definitions for Chronic Illness-Related Malnutrition, Cancer Cachexia, and Sarcopenia		
Chronic illness–related malnutrition	**Cancer cachexia**	**Sarcopenia**
Decreased intake or assimilation of nutrients. In cancer, it is associated with inflammation, which increases anorexia and catabolic status, weight loss, alteration of body composition, and impairment of functional capacity	A multifactorial syndrome with loss of muscle mass (with or without loss of fat mass) that cannot be reversed by usual nutritional intervention and leads to progressive functional compromise	Low muscle mass and function resulting in fatigue, decreased strength limiting functional capacity

The important thing is to emphasize that any of the terminology used is to identify the patient at risk, evaluated early to establish the causes of low intake as a main factor for weight loss, as well as the other associated alterations, and ultimately, to be able to intervene before consequences of malnutrition are already present. In this regard, the life expectancy may help in the intervention process to be followed. For example, patients who have an estimated life expectancy between three and six months should go directly to evaluation of intake problems as a next step to improve quality of life, while patients who have a life expectancy longer than six months should undergo screening and nutritional assessment, so that there is early nutritional intervention to prevent deterioration or optimize nutritional status.

The consistent and clear diagnostic flow will allow for early nutritional intervention with the potential to increase life expectancy and decrease complications related to cancer-related malnutrition and the same interventions. In this regard, one of the parameters mentioned in the above definitions is the establishment of the inflammatory grade that differentiates starvation malnutrition. Inflammation in the cancer patient impacts muscle protein lysis due to metabolic changes especially due to systemic inflammation.[32,35] Damaged tissues induce inflammation, cancer cells and immune stromal cells may contribute to the abnormal metabolic state of these patients. This inflammatory state is independently consolidated as a prognostic factor and for this reason should be evaluated or at least be able to identify it as present. There are solid tumors that cause important inflammation such as the pancreas, liver and lung. The Glasgow prognostic scale, based on plasma levels of C-reactive protein and albumin aids in the classification of inflammation.[36] When C-reactive protein is normal, the scale is zero, if C-reactive protein is elevated with normal albumin = 1 and if C-reactive protein is elevated and albumin decreased = 2.

3.4 — Nutritional status, muscle mass and clinical course of the patient

Nutritional status directly impacts the evolution of the cancer patient. Malnourished patients have the increased risk of more complications, especially infectious, longer hospital stay, higher mortality, and poorer quality of life.
The costs associated with caring for these patients are also higher. Regardless of the diagnostic methods used to determine nutritional status and body composition, it is the same when there is no recognized weight loss but with loss of muscle mass, there are more and more reports of studies in which the decrease in muscle mass is associated with a worse overall prognosis. Similarly, patients with muscle loss are more likely to have more frequent and serious side effects to treatments offered such as chemotherapy, radiotherapy, surgery and others [**Table 13**]. In surgical patients, the measured grip strength (measure considered indirect to nutritional status) [**Table 14**] in the preoperative period is associated with poorer surgical outcomes, and especially in worse survival [**Figure 2**].

Table 13: Sarcopenia Increases Toxicity to Systemic Cancer Therapies			
Prado 2007[37]	5-FU	1.7↑ toxicity if >20 mg/kg LBM	Colon
Barret 2014[38]	Fluoropyrimidine ± oxaliplatin, irinotecan	13.5↑ grade 3-4 toxicity at oxaliplatin 3 mg/kg LBM	Colon
Ali 2016[39]	FOLFOX	44% vs 0 without sarcopenia	Colon
Jung 2015[40]	FOLFOX	1.5↑ grade 3-4 toxicity per 1 SD decrease in PI	Colon
Anandavalivedan 2015[41]	Cisplatin + 5-FU	5.5↑ DLT in obese sarcopenic patients	Esophagus-Gastric
Tan 2015[42]	Cisplatin + 5-FU	2.9↑ DLT in sarcopenic patients	Esophagus-Gastric
Prado 2009[43]	Capecitabine	2.5↑ toxicity	Breast
Prado 2011[44]	Epirubicin	Less muscle mass in those who experienced toxicity	Breast
Shachar 2016[45]	Taxane	3.1↑ grade 3-4 toxicity	Breast
Antoun 2010[46]	Sorafenib	6.4↑ toxicity	Renal
Huillard 2013[47]	Sunitinib	4.1↑ toxicity	Renal
Cushen 2015[48]	Sunitinib	1.6↑ DLT	Renal

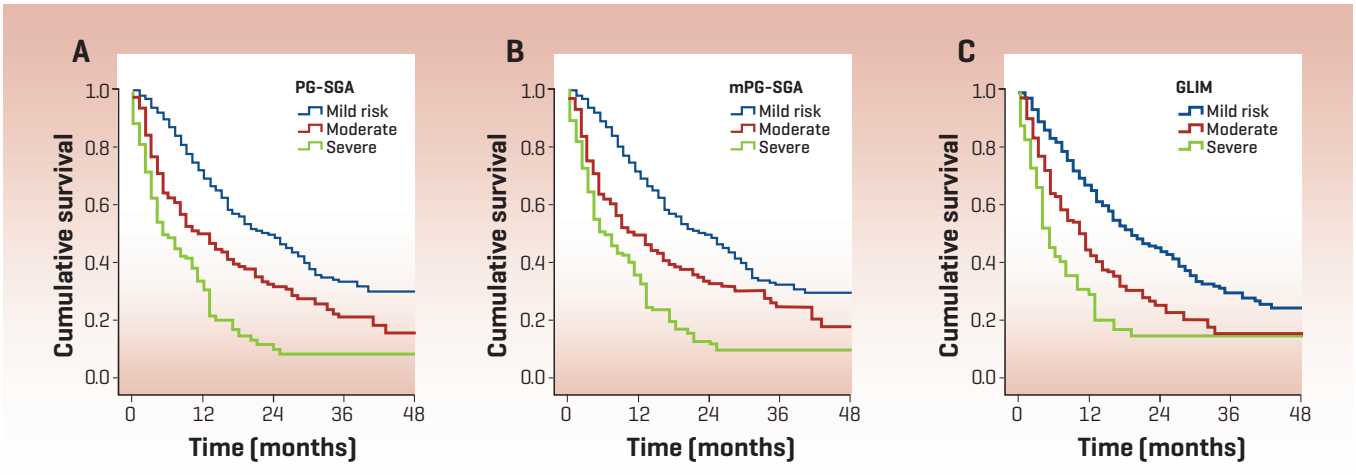
Abbreviations: DLT, dose-limiting toxicity; FOLFOX, folinic acid (leucovorin), fluorouracil, and oxaliplatin; FU, fluorouracil; LBM, lean body mass; PI, psoas index.
Source: Adapted from Bozzetti F.

Table 14: Correlation Between Grip Strength and Various Postoperative Complications After Cancer Esophagectomy

Complications present according to grip strength					
Variable	**Normal (N=91)**	**Intermediate (N=43)**	**Weak (N=41)**	**Total (N=175)**	***P* value (CATT)**
Pneumonia, n (%)	4 (4.4)	4 (9.3)	8 (19.5)	16 (9.1)	**0.006**
Ventilatory support >48 h, n (%)	11 (12.1)	8 (18.6)	11 (26.8)	30 (17.1)	**0.036**
Anastomotic failure, n (%)	2 (2.2)	4 (9.3)	2 (4.9)	8 (4.6)	0.313
Hospital stay, median (IQR)	7.0 (7.0-9.0)	8.0 (7.0-11.0)	9.0 (8.0-14.0)	8.0 (7.0-11.0)	**0.005**[a]
Referral to intermediate care, n (%)	8 (8.8)	10 (23.3)	15 (36.6)	33 (18.9)	**<0.001**
Readmission at 30 d, n (%)	10 (11.0)	5 (11.6)	3 (7.3)	18 (10.3)	0.573
Mortality at 90 d, n (%)	0 (0.0)	2 (4.7)	4 (9.8)	6 (3.4)	**0.004**
Mortality at 1 year, n (%)	6 (7.4)	10 (26.3)	18 (46.2)	34 (21.5)	**<0.001**

Abbreviations: Cochran-Armitage trend test; IQR, interquartile range.
[a] Kruskal-Wallis test.
Adapted from Colcord ME, Benbow JH, Trufan S, et al.[50]

Figure 2: Effects of Nutritional Status on Survival in Patients With Lung Cancer



Kaplan-Meier survival plots using the (A) PG-SGA, (B) mPG-SGA, and (C) GLIM criteria. The plots show the concordance of the 3 measures.
Abbreviations: GLIM, Global Leadership Initiative on Malnutrition; mPG-SGA, modified Patient-Generated Subjective Global Assessment; PG-SGA, Patient-Generated Subjective Global Assessment.
Source: Adapted from Huo Z, Chong F, Yin L, et al.[49]

3.5 – Consultation with oncologist

3.5.1 — Patient with histological diagnosis but no complete diagnosis and staging

During the first meeting, the oncologist sets the stage for diagnostic processes, explains to the patient aspects of the disease, and advises fundamental aspects such as diet and physical activity, so that no further deterioration occurs during this period following the first consultation. In this session, before the definition of the definitive cancer treatment pathway, it is important to perform a nutritional screening in advance; however, we start from the fact that the patient has the initial diagnosis of cancer, which in isolation is consolidated as a risk factor for an impaired nutritional status. Then, if the nutrition professional is available in less than seven days, the patient should be referred for consultation with this expert. If there is no availability, the treating physician should identify risk factors and define a nutritional intervention with conventional and generic oral supplementation, as well as basic exercise recommendations until consultation with the nutrition expert, when the complete nutritional assessment and the indication of nutritional therapy with defined goals will be performed.

Not all patients follow the same path, and many probably already reach the oncologist with the entire diagnostic process made and the tumor already staged. But if there is potential for follow-up and intervention during this preliminary period, prior to a full diagnosis, it should be leveraged to avoid nutritional and functional impairment and, especially, before undertaking selected therapies. From a nutritional point of view, it should be emphasized that any weight loss during these periods should be avoided and, of course, no restrictive diet should be recommended. Likewise, the person should remain active whenever possible, as he/she did before cancer detection.

3.5.2 — Patient with complete diagnosis and staging

The oncologist will assess the patient comprehensively and will propose forms of treatment with either surgery, chemo and/or radiotherapy, and other forms of management. This practitioner should guide the entire treating team according to the goal of the treatment whether it is curative, palliative or general supportive. In this way, the entire team will intervene avoiding unnecessary procedures that cannot achieve healing, or palliation, seeking to increase the life expectancy with good quality or minimal support to improve the comfort and peace of mind of the person.

ESMO recommendations include a way to categorize patients for the purpose of this therapeutic targeting.[51] Patients should be classified into those with curative intent and those in whom management is palliative. Where palliative care is indicated, it should be divided into those with life expectancy of less than six months and those with a few weeks [**Table 15**].

A. In those with survival longer than some months, enteral or parenteral nutritional intervention is indicated, during anticancer treatments and nutritional follow-up should be regular, as well as the others;

B. In palliative care patients who do not receive treatment and for whom life expectancy is a few months, invasive nutritional approaches should be restricted and dietary counseling and oral nutritional supplementation is recommended. Assessment of the intake and symptoms that must be managed should be made, focusing on improvement in quality of life;

C. Patients with a life expectancy of a few weeks should focus all interventions on improving comfort, relieving thirst, stress to food and other debilitating aspects.

Table 15: Nutritional Approach Guide in Cancer Patients According to Their Expected Survival

Life expectancy	Nutritional approach
More than 3-6 months	▪ Screening, assessment, intervention, follow up when required
Less than 3-6 months	▪ Interventions need to be justified and usually go to diet counselling and oral supplementation
Less than 3-6 weeks	▪ Comfort-directed care without adding nutrition stress, avoid dehydration

Modified from Arends et al 2017.[51]

This is a simple and subjective way of categorizing people with cancer, and which can change in the clinical course of the disease, and will really help the entire team of healthcare professionals make the best decisions. This will avoid therapeutic problems and interventions will be done in line with target search. For those with an indication of counseling or nutritional therapy, it is recommended that a written guide with the nutritional recommendations of generic and physical activity be given to the patient throughout the diagnostic and treatment process, which will be the guide to be followed by the experts in nutritional therapy.

The oncologist should consider the principle "**Do not allow nutritional deterioration while characterizing all diagnostic elements of cancer.**" Then, practically and objectively, the patient who arrives at the first consultation with the histological diagnosis of cancer, with a lot of distress, expectations, fear, and questions, should also be oriented on involuntary weight loss, as a common issue, and consolidated as an isolated prognostic factor for complications and mortality.[52-55] Thus, in this first consultation with the Oncology department, where many health professionals will work together, will be of the greatest importance to the patient, the family members, as well as to the treating team.

3.6 — Screening and nutritional assessment

The starting point for identifying nutritional risk is screening. One of the risk factors that is included in the various instruments is involuntary weight loss. The causes of the loss may be multiple and varied such as the presence of anorexia, inflammation, pain and depression, endocrine disease, hypermetabolism, medications, low food consumption, and mechanical or GI malabsorption problems. This inadvertent weight loss is assumed to be a loss of both fat mass and muscle mass.

There are several instruments for screening and nutritional diagnosis. Essentially, choose the one that best fits the local and institutional conditions in which you work, because nutritional therapy cannot be based solely on giving food/nutrients. The current recommendations indicate that even the physician or non-expert healthcare professional can perform nutritional screening, for example using a simple instrument such as the Malnutrition Screening Tool (MST) or the PRONTO tool. The MST[56] has 2 simple concepts: unintentional weight loss and changes in intake. The MST is shown in **Table 16**. In addition, weight loss alone above 10% has been demonstrated as a risk factor for mortality in cancer patients.[57]

Table 16: Malnutrition Screening Tool (MST)

Have you lost weight recently without trying?	
No	0
Unsure	2
If yes, how much weight (in kilograms) have you lost?	
1-5	1
6-10	2
11-15	3
>15	4
Unsure	2
Have you been eating poorly because of a decreased appetite?	
No	0
Yes	1
Total score of 2 or more = patient at risk of malnutrition	

The PRONTO is a newly published instrument by Muscaritoli et al.[58] for cancer patients that takes into account aspects related to nutritional alterations of these patients, and that can be reviewed quickly, thus identifying patients at risk of malnutrition or already malnourished. This tool is designed to be used by non-nutrition expert healthcare professionals, responding to current identified needs on risk and nutritional status, as well as muscle mass. Three essential components were identified to determine the nutritional status of people with cancer and functional status:
1. Body weight; 2. Appetite and food intake and; 3. Strength and mobility as shown in **Table 17** below.

Table 17: The PRONTO Tool

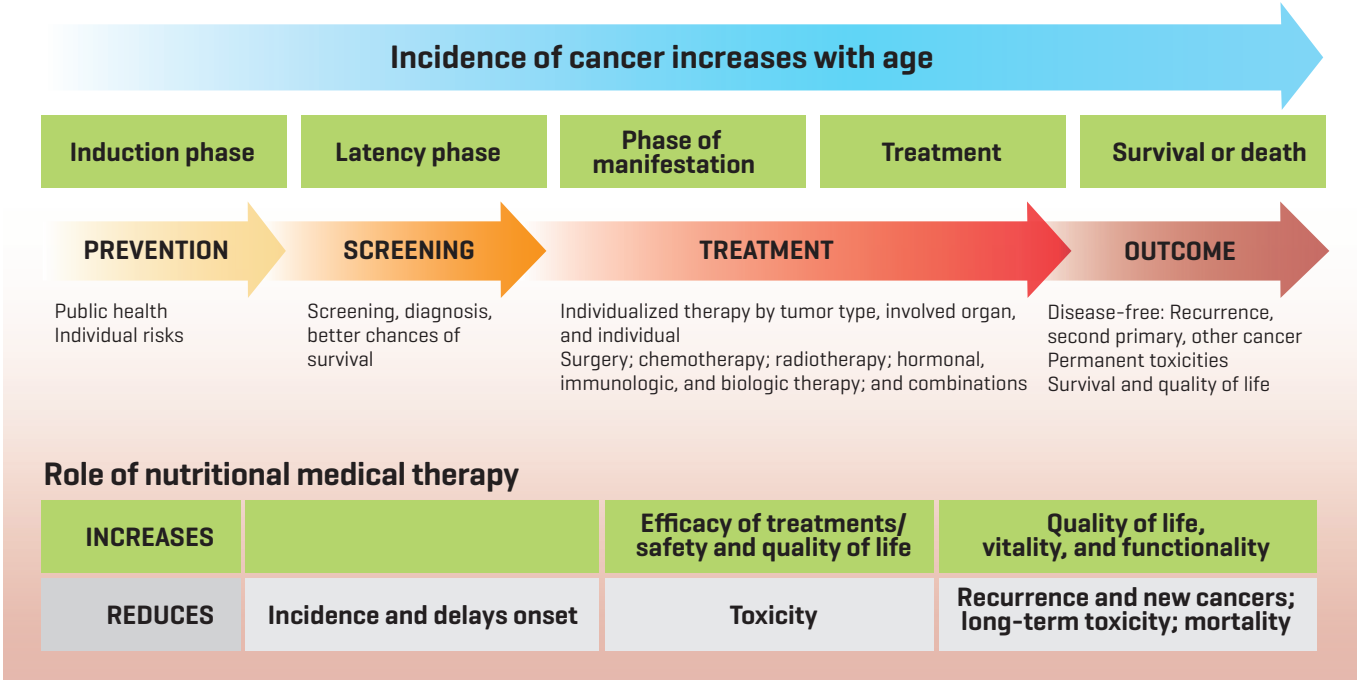
What	Why	How	Questions and actions	
Body weight	- Body weight should remain stable - Involuntary weight loss is a sign of disease-associated malnutrition - Weight loss is an independent risk factor for poor prognosis	**Ask the patient:** *"Have you unintentionally lost weight (5%-10% or more) in the last 3 to 6 months/since the last consultation?"* **Exploratory questions:** - What is your usual weight? - Do your clothes, rings, or dentures fit properly? - Have you made new holes in the belt to shrink it?	YES	**INTERVENTION** Refer to nutrition expert for diagnosis and counseling. The patient may require intervention—refer to ESPEN/ESMO guidelines in cancer patients
			NO	**Follow up closely** - Advise patient to monitor weight - Give counseling on diet and exercise. Emphasize energy/protein consumption
Appetite and intake	- Anorexia or decreased appetite due to cancer and/or treatments - Reduced meal intake independent of anorexia - Nutritional products may be required to meet intake requirements and to slow weight loss	**Ask the patient:** *"Has food intake decreased in the past week/since the last consultation?"* **Exploratory questions:** - Do you have symptoms that prevent you from eating normally, such as mouth ulcers, nausea, vomiting, and taste changes?	YES	**INTERVENTION** Refer to nutrition expert for diagnosis and counseling. The patient may require intervention—refer to ESPEN/ESMO guidelines in cancer patients
			NO	**Follow up closely** - Advise patient to monitor diet intake - Give counseling on diet and exercise. Emphasize energy/protein consumption
Strength and mobility	- Loss of muscle mass and function in cancer is a sign of malnutrition associated with this disease - Muscle mass loss is associated with toxicity to chemotherapy and intolerance to other treatments, decreased life expectancy among others - Use of mixed therapies increases muscle loss and function - Loss of muscle mass can be hidden in overweight and obese patients	**Ask the patient:** *"Have you lost strength or do you feel weaker than usual/since the last consultation?"* **Exploratory questions:** - Have you had difficulty carrying packages, opening bottles, bathing, or other? - Do you feel tired and your muscles weak?	YES	**INTERVENTION** Refer to nutrition expert for diagnosis and counseling. The patient may require intervention—refer to ESPEN/ESMO guidelines in cancer patients
			NO	**Follow up closely** - Advise patient to follow physical activity recommendations - Stay active

Abbreviations: ESMO, European Society for Medical Oncology; ESPEN, European Society for Clinical Nutrition and Metabolism.
Source: Muscaritoli M, Bar-Sela G, Battisti NML, et al.[58]

The GLIM (Global Leadership Initiative on Malnutrition) etiological criteria[59,60] are an international consensus to acilitate the diagnosis of nutritional status that have been validated for the cancer population and that can be used by non-nutrition-expert clinicians. The variables that are in GLIM are: involuntary weight loss, BMI, assessment of muscle mass as phenotypic criteria, and changes in intake and inflammation as etiological criteria. Nutritional diagnosis is made with at least one phenotypic and one etiologic criterion, but the more they are used, the higher the likelihood of appropriate diagnosis. How to assess and interpret the GLIM criteria are discussed further below.

It is imperative to intervene at the source of malnutrition and on the different factors that have influenced the deterioration of nutritional status (**Figure 3**).

Figure 3: Complex Relationships Between Diet, Nutrition, and Cancer



At this stage (screening and nutritional assessment), the intervention of the general nutritionist or specialist is essential for the best therapeutic protocol to be followed. The interpretation of the tools used and the nutritional diagnosis that imposes a challenge for the nutrition professional in the follow-up of these patients is extremely complex. In addition, cancer patients change nutritional status, mobility, diet, metabolic status, inflammatory status, as well as the consequences of treatments occurring in a varied manner and at distinct times. Ongoing nutritional evaluation is then necessary during the clinical course of the disease and treatment in order to achieve the desired outcomes.

The most current recommendations that even the physician or healthcare professional can achieve regarding the nutritional diagnosis are the GLIM etiological criteria (to determine that malnutrition is not just due to anorexia but *involves metabolic stress* and *inflammation* that occurs in cancer. The stages of nutritional deterioration are shown in the following **Table 18**, but not all patients follow the same pathways, nor are there precise biochemical markers to establish the stages of their progression.

Table 18: The Stages of Nutritional Deterioration			
	Phenotypic Criteria		
	Weight loss (%)	**Low BMI (kg/m²)**	**Reduced muscle mass**
Stage 1/moderate malnutrition (requires 1 phenotypic criterion that meets this grade)	5%–10% within the past 6 months OR 10%–20% beyond 6 months	<20 if <70 years <22 if ≥70 years	Mild-to-moderate deficit (per validated assessment methods)
Stage 2/severe malnutrition (requires 1 phenotypic criterion that meets this grade)	>10% within the past 6 months OR >20% beyond 6 months	<18.5 if <70 years <20 if ≥70 years	Severe deficit (per validated assessment methods)

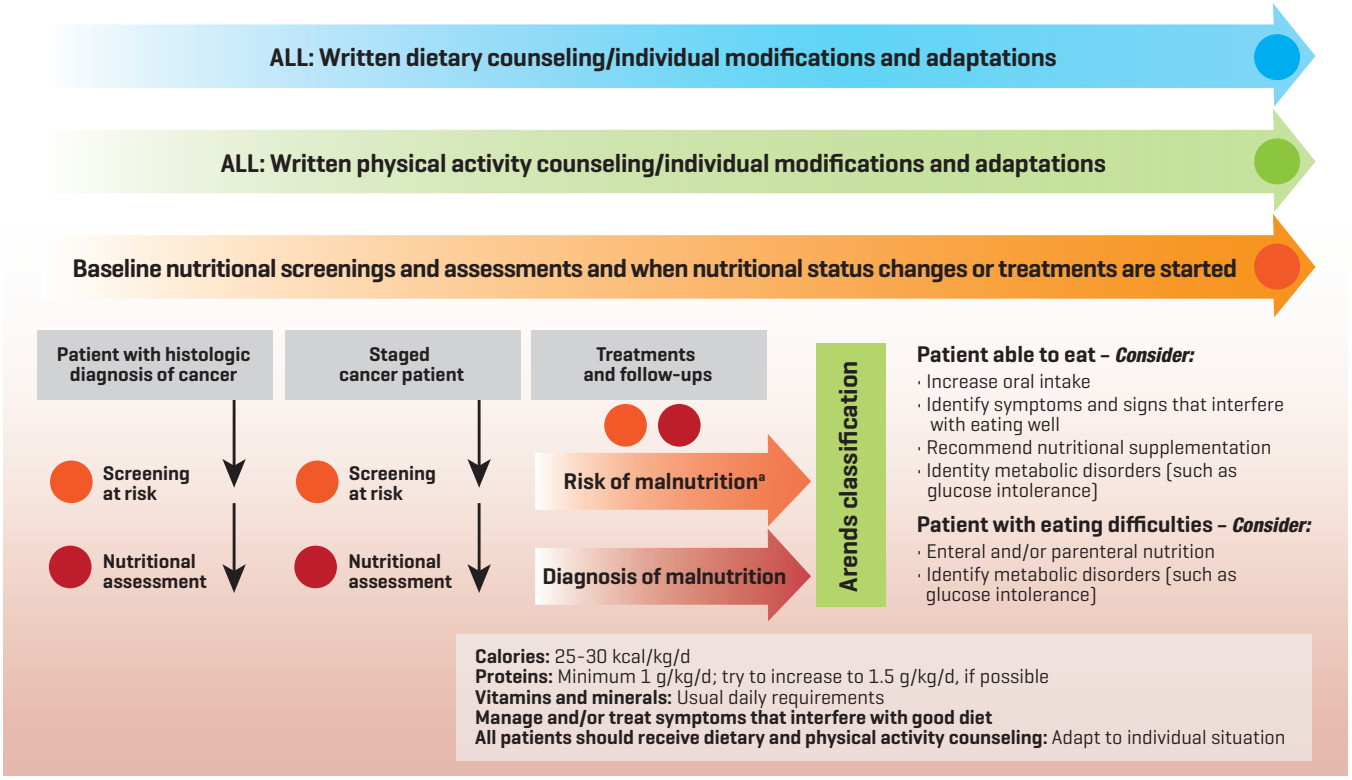
3.7 — Nutritional therapy

Nutritional treatment aims to guarantee adequate nutritional status, help reduce excess catabolism, protect body tissues that are affected by anticancer therapy, specifically the mucosa of the gastrointestinal tract, and also contribute to the effectiveness of anticancer treatment.

It should be noted that nutritional deficiencies are preventable or reversible most of the time, even if metabolic changes exist in the cancer patient caused by the tumor or by treatment that alter the ability to properly use the nutrients in the diet. These changes include inflammation leading to a hypercatabolic state, inefficient metabolic cycles, and anabolic resistance. Thus, the impact of malnutrition on adverse treatment outcomes is primarily due to the decrease in muscle mass.[11] So, nutritional therapy cannot be based solely on administering blocks of nutrients for tissue construction, but it is imperative to act at the source of malnutrition and address the different associated factors that have deteriorated the nutritional status.

The involvement of experts in nutritional therapy, an interdisciplinary team, is essential for the management of these patients' best treatment. A referral to these professionals is highly recommended. **Figure 4** summarizes the nutritional flow that should be adopted for the patient diagnosed with cancer.

Figure 4: A Nutritional Management Algorithm for Patients With Cancer



[a] Initiate nutritional intervention if nutrition service is not available or the consultation is at a time that could affect the nutritional status of the patient.
Adapted from ESMO and ESPEN guidelines for nutritional management in the cancer patient [Muscaritoli M, Arends J, Bachmann P, et al.[61]]

3.8 — Consultation with physician, nutritionist, and other specialist professionals from the interdisciplinary nutrition therapy team

Ideally, the care of any patient requiring nutritional care should be done by an interdisciplinary team of nutritional therapy consisting of physician, nutritionist, nurse, pharmacist, speech therapist and other professionals such as physical therapists, occupational therapists, psychologists, social assistants and physical educators. But that's not the reality in most institutions in the world. Cross-functional work leads to better holistic and comprehensive care that is highly appreciated by the patient[62] and represents a substantial decrease in costs.[63-65] Toward this goal, the following text presents information on nutritional screening and nutritional assessment for non-nutrition-expert practitioners.

3.8.1 — Nutritional screening

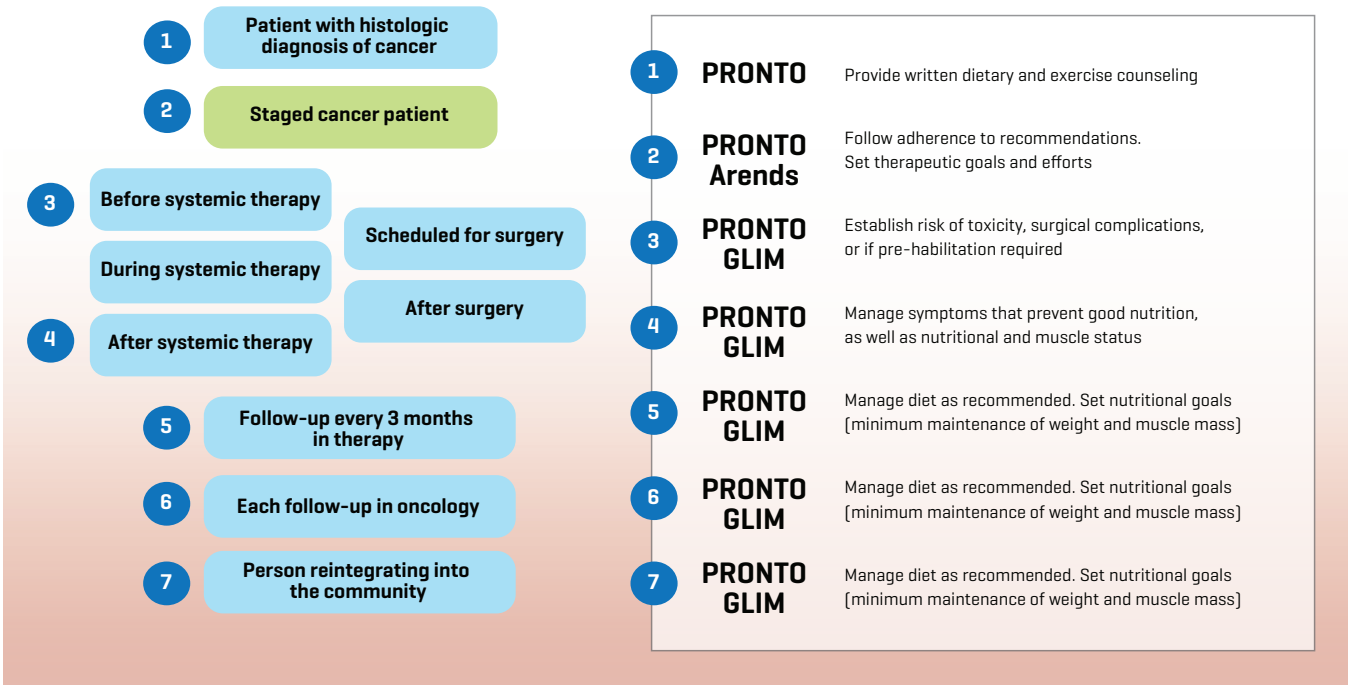
There are multiple screening instruments and no gold standard. The choice of which to use should consider availability of human resources and materials. A key point is that most nutritional screening tools do not consider the routine assessment of muscle mass and function, muscle quality, or the individual's functional status. Note that muscle quantity, quality, and function is an independent predictor of mortality, complications, and health resource use. Muscle mass loss has been associated with the toxicity of systemic antineoplastic therapy interfering with the efficacy of anticancer treatments.[11, 43, 47, 48, 66-70]

Two simple variables are part of the different screening tools: involuntary weight loss and changes in food intake. Below are examples of several instruments used in clinical practice and the reason why the screening should be done ([Table 19](#) and [Figure 5](#)).

Table 19: The Most Frequently Asked Questions the Practitioner Should Ask the Patient

Weight changes	**The goal is to take note of or measure significant weight changes in the past 3 to 6 months. Unintentional weight loss should be asked in terms of the last 3 to 6 months**
	Ask if weight was measured over the past 6 months
	Measure current weight; if there has been weight loss, progression and speed should be estimated
	For those patients who do not give information about weight, ask if their clothing, dentures, watch, or belt fit differently
Changes in appetite and intake	**A simple question: have there been any changes in appetite or food intake in the past week or since the last visit?**
	If the answer is positive, probe further to determine whether the changes are due to the disease or to adverse effects of treatments that influence nutritional status
Changes in strength and function	**One question: have you noticed less strength, weakness, or had difficulty performing your daily activities?**
	If the consultation time allows, the patient may be asked to perform a grip strength test, get up from the chair, or perform a gait speed test. However, the latter is not mandatory during consultation to identify the risk but is part of the functionality assessment

Figure 5: Malnutrition Screening Is a Continuous Process During the Follow-Up of the Person With Cancer

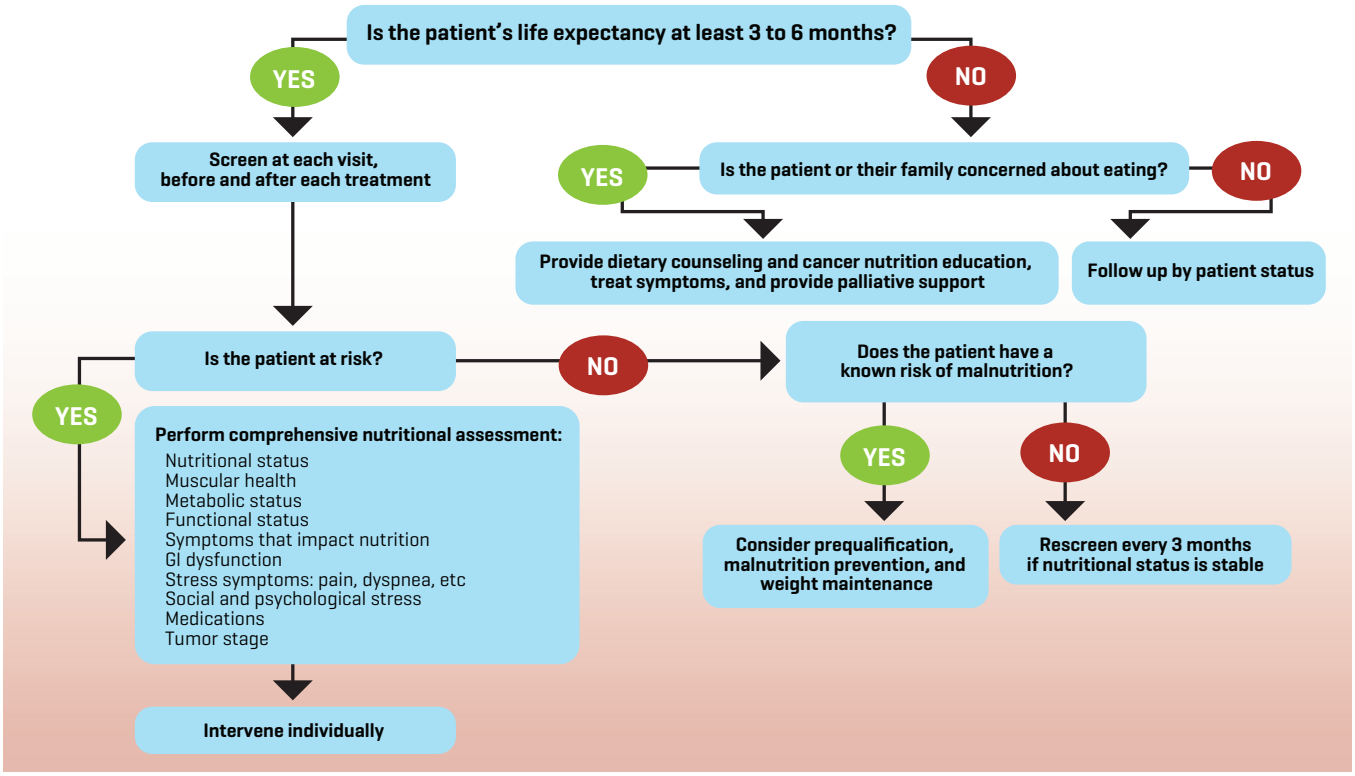


Abbreviations: GLIM, Global Leadership Initiative on Malnutrition.

The identified patient at nutritional risk should be referred to the nutritional therapy team so that they can be thoroughly diagnosed and decide whether or not to require a nutritional intervention. If there is no nutrition professional, the suggested guidelines in ESPEN.[61] On the other hand, patients whose weight loss is less than 5% of the usual weight loss in the last three to six months are recommended to closely monitor weight and patients who are not classified as nutritional risk but are on anticancer treatments should be re-screened every three months or before each initiation of a new therapy offered. **When it is known that therapy, by its modality and intensity, may have an impact on nutritional status such as in surgery, combination therapies, aggressive chemotherapy or agents that produce nausea and vomiting, prophylactic nutritional therapy or the intervention called pre-rehabilitation is recommended.** In addition, dietary counseling should be sought and the level of intake should be maintained or improved to the appropriate level. Likewise, physical activity should be recommended to improve muscle strength, reduce fatigue, anxiety and improve quality of life. Patients who do not report changes in strength, mobility or function should be advised to perform regular exercise routines to reduce the risk of atrophy.

In summary, **Figure 6** summarizes the flow to be adopted for the patient diagnosed with cancer and is supported by international consensus of academic oncology societies.[71] That is, screening is suggested in all newly diagnosed cancer patients before starting anti-cancer therapy including surgical treatment, especially head and neck and upper digestive tract, in addition, when the treatment regimen has changed or at the time of tumor recurrence.

Figure 6: Flowchart for Nutritional Screening in Patients With Cancer



Abbreviation: GI, gastrointestinal.

3.8.2 — Nutritional assessment

All patients diagnosed as being at nutritional risk should be referred to a nutrition expert to evaluate nutritional status, metabolic status, muscle health status, problems with food intake and gastrointestinal tract function. Similarly, on nutritional screening, there are also several nutritional assessment instruments, each with advantages and disadvantages that should be considered.

The most common parameters recommended for measurement that are covered by the GLIM[72] criteria are as follows:

A. Current weight, usual weight and % weight change and time it has occurred;

B. Muscle-mass focused body composition;

C. Nutrient intake, especially protein, but considering dietary variety for vitamins and minerals, in addition to adequate calorie balance;

D. Functional status;

E. Presence and degree of inflammation

The GLIM criteria[72] (**Table 20**) are a global effort on the criteria that should be included for the diagnosis of malnutrition in adults. The variables included in the GLIM were based on the main screening and assay instruments. Three phenotypic criteria (unintentional weight loss, BMI, and muscle mass) associated with etiologic criteria (alterations in dietary intake and/or inflammation) were determined. The cancer patient is defined as being malnourished when positive for at least one phenotypic criterion and one or two of the etiologic criteria. Severity of malnutrition is defined by any of the phenotypic criteria. Since launch, validation of the criteria has been requested in order to make the same language and comparisons possible around the world.

Table 20: Nutritional Diagnostic Tool, GLIM Criteria

	Phenotypic criteria			Etiological criteria	
	Weight loss (%)	**Low BMI (kg/m²)**	**Reduced muscle mass[a]**	**Reduced food intake (or absorption)**	**Inflammation**
Moderate MN	5%-10% in the last 6 months or 10%-20% in more than 6 months	<20 in patients <70 years or <22 in patients >70 years	Mild to moderate deficiency	≤50% of energy requirement, or any reduction for more than 2 weeks, or any gastrointestinal condition affecting food assimilation/ absorption	Due to acute or chronic disease or injury
Severe MN	>10% in the last 6 months or >20% in more than 6 months	<18.5 in patients <70 years or <20 in patients >70 years	Severe deficit		

Abbreviations: BMI, body mass index; CC, calf circumference; GLIM, Global Leadership Initiative on Malnutrition; MN, malnutrition; MUAC, mid upper arm circumference.
[a]Grip strength, MUAC, CC, and physical examination were measured. The following cutoff points were considered to determine "reduced muscle mass":
- Decreased grip strength: <-2 SD according to the sex and age of the dynamometer used.
- Decreased MUAC: mild to moderate between percentiles 5 and 10, and severe with percentiles <5.
- Decreased CC: ≤30.5 cm.

To differentiate between mildly/moderately reduced and severely reduced muscle mass, where anthropometric measures performed have values belonging to different categories, the patient's physical examination was considered and the final categorization was made at the interviewer's own professional discretion.
Source: Cederholm T, Jensen GL.[72]

The GLIM criteria have been considered more accurate in diagnosing malnutrition and correlating with clinical outcomes and prognosis.[49] In the systematic review by Matsui et al,[73] 2023, infectious complications, fistulas, and postoperative pneumonia can be predicted to some extent by the degree of malnutrition measured by the GLIM. Weight loss and, as a consequence, decrease of BMI, and loss of muscle mass are predictors of these complications. Loss of more than 10% of weight in the past six months was predictive of mortality after performing pancreatoduodectomy, total gastrectomy, and esophagectomy. The Balci et al study[74] recruited 267 cancer patients. The authors used two patient classification systems of the PG-SGA and GLIM. The large majority of the study population had advanced cancer 60.4% in stages III-V, and the mean BMI was 26.8kg/m^2. The prevalence of malnutrition by GLIM criteria was 60.3% and the PG-SGA was 53.6%. Classification using the GLIM scale was shown to be appropriate for patient grading and thus survival prediction.

3.8.2.1 — How to assess and interpret the GLIM criteria

Unintentional weight loss

It is common for the cancer patient to lose unintentional weight and data suggest that the vast majority reach the physician with this condition.[75] However, an isolated weight measurement cannot be considered diagnostic or predictive, unless the patient is below the normal weight for their height, age, and sex as demonstrated by some authors.[55] Some patients still don't know how much weight they've lost, then you can question how their clothes or belt fit. It is important to emphasize that some may report loss with subsequent gain, for which you should observe if it is due to the presence of edema.

In addition, it is important to have the ability to measure the intensity of changes over time.

Weight loss over time has an independent value in predicting treatment toxicity, morbidity, and reduced survival.[55, 57, 76, 77]

Body mass index (BMI)

This criterion has been included in the GLIM because of the ease of collecting this information, but it has to be carefully considered that, with the spread of being overweight and obese, large numbers of patients are in the range considered normal without really being normal. In particular, because it considers weight and height as a crude measure of nutritional status, it is not the best parameter for determining body composition, as will be discussed below. Thus, this is the criterion least recommended to be used for nutritional diagnosis.[78]

Muscle mass - measurement of body composition

SARC-F

One of the instruments that has been recommended by the European Working Group on Sarcopenia in Older People (EWG-SOP) to determine the risk of muscle loss among older adults is the SARC-F questionnaire.[79] This is composed of five simple questions, easy for the patient or family member to answer and can be done even by telephone. The SARC-F has been validated in different populations and has good sensitivity and specificity to predict functional and mortality variables.

The SARC-F questions include: strength, need for walking aids, ability to rise from a chair, climb stairs, and number of falls that occurred in the past year (**Table 21**). The questionnaire has been translated into and validated in Spanish.[80]

Table 21: SARC-F Scale Spanish Version – Mexico		
Item	**Questions**	**Score**
1. Strength	How much difficulty do you have carrying 4.5 kilograms?	None = 0 Some = 1 Lots or unable = 2
2. Walking aid	How much difficulty do you have walking across a room?	None = 0 Some = 1 Lots, using aids, or unable = 2
3. Standing up from a chair	How much difficulty do you have getting up from a chair or bed?	None = 0 Some = 1 Lots or unable unaided = 2
4. Climbing stairs	How much difficulty do you have climbing 10 stairs?	None = 0 Some = 1 Lots or unable = 2
5. Falls	How many times have you fallen in the past year?	None = 0 1 to 3 falls = 1 4 or more falls = 2

If the total score is ≥4 points, it is defined as sarcopenia.
Source: Parra-Rodríguez L, Szlejf C, García-González AI, Malmstrom TK, Cruz-Arenas E, Rosas-Carrasco O.[80]

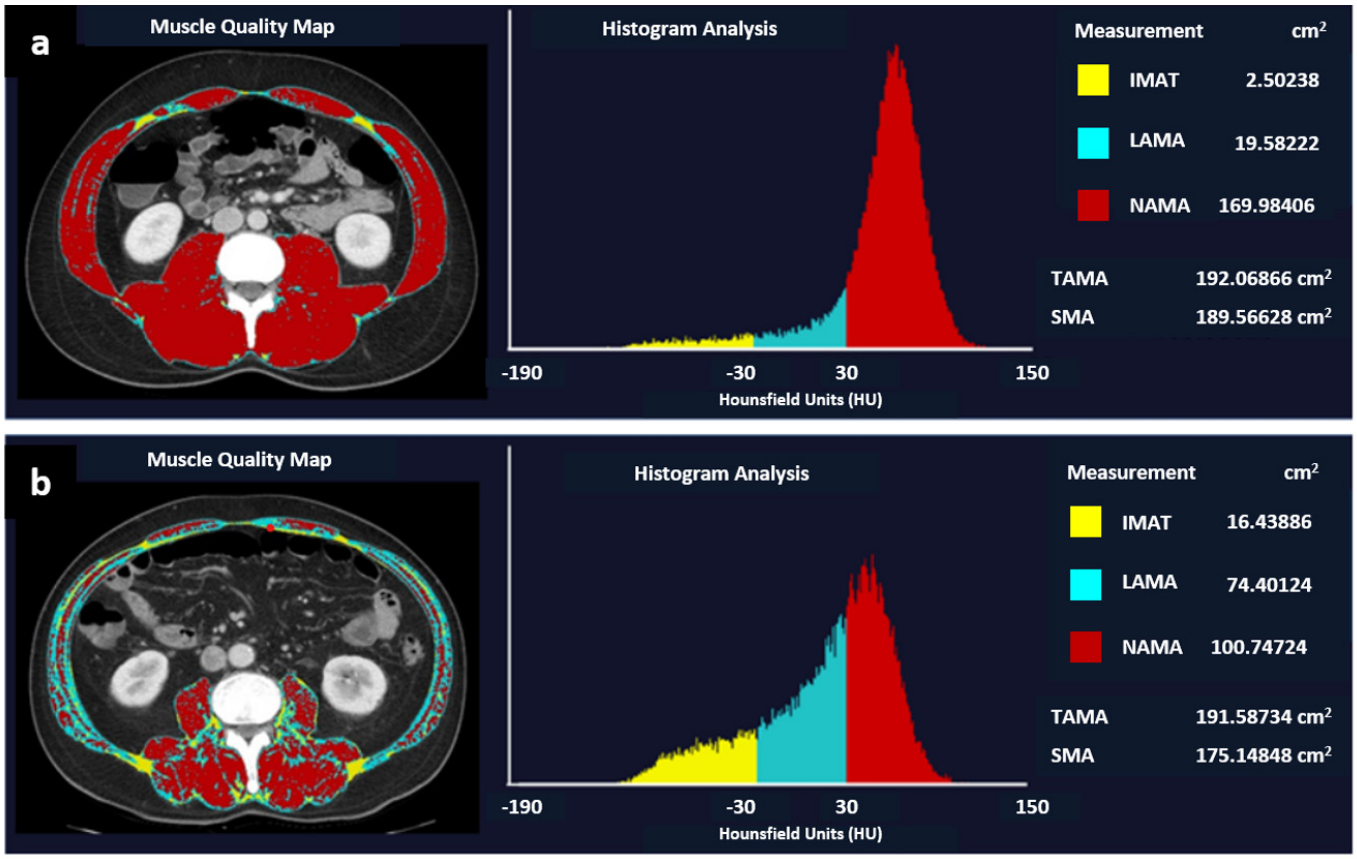
In patients with cancer, it has been used and is able to predict quality of life, number of visits to emergency rooms and decreased life expectancy.[81]

Tomography

The loss of any percentage of muscle mass is already considered a criterion for the diagnosis of malnutrition. This loss can be seen, in some individuals, even before the onset of weight loss and has more serious implications than this, especially in the cancer patient, because it is associated with mortality, surgical complications and toxicity to systemic therapies.[82] It should be emphasized that among overweight and obese patients, muscle loss is not clinically visible and may occur before weight loss is reported. One in four obese patients is estimated to have muscle loss when they have advanced cancer. This loss of muscle mass is usually independent of the change in BMI and can occur with both unintentional weight loss, which occurs frequently, as well as stable or even increased BMI. For this reason, it is important to advise on the status of muscle mass, its quantity, quality and function, independent of weight changes.

Measurement of muscle mass and fat mass is very important in the cancer patient, as the decrease in a short period of time is associated with toxicity to systemic therapies, morbidity and a worse prognosis. This measure is now recommended by scientific associations such as ESPEN, ASPEN, ASCO and ESMO. The pattern for measuring muscle mass is the measurement of the amount and density of muscle by computerized tomography, at the level of the third lumbar vertebrae. This measure allows not only muscle mass volume, but also muscle quality with the presence of myostatosis (intramuscular fat).

Figure 7: Examples of Good and Low Muscle Mass and Quality of Muscle



a) Good muscle mass and quality of muscle, b) Low muscle mass and quality of muscle.
Abbreviations: IMAT, inter/intramuscular adipose tissue area; LAMA, low attenuation muscle area; NAMA, normal attenuation muscle area; SMA, skeletal muscle area; TAMA, total area of abdominal muscles.
Adapted from Kim DW, Kim KW, Ko Y, et al. JMIR Med Inform. 2020;8(10):e23049.

However, systematic measurement by CT scan of muscle mass even if more sensitive and specific, is costly, takes time, is not always available, requires specific software and training to interpret, and, is designed for other diagnostic purposes. The use of measuring muscle mass is when the patient is being studied for other reasons and the muscle mass is being measured for the study. Inclusion in nutritional assessment protocols is not routinely recommended for costs. Thus, when there is no possibility of using CT scans, it is suggested to use other measures such as DEXA, bioimpedance or the use of calf circumference that is associated with mortality.[83]

At the National Institute of Health (NIH) meeting in July, 2022, the importance of assessing muscle quality was presented. CT scans performed for other purposes are usually used to measure muscle volume and density. Low-density muscle suggests myostatosis which is fatty infiltration of muscle tissue. This portion of fat reduces the effective volume of the muscle and can compromise function. The prevalence of muscle loss and myostatosis in cancer is high.[84] **Table 22** records the loss and low muscle density in patients with different types of cancer.

Table 22: Loss of Muscle Mass and Muscle Density According to Cancer Site		
Cancer site	**Loss of muscle mass (%)**	**Low muscle density (%)**
Breast	34	37-60
Pancreatic	51-63	38
Gallbladder	29-69	
Liver	51-66	43-85
Lung	43-52	53
Colorectal	42	19-76

Sources: Caan BJ, Cespedes Feliciano EM, Prado CM, et al and Caan BJ, Meyerhardt JA, Kroenke CH, et al.[82]

Tumors such as the pancreatic, upper gastrointestinal, liver, and respiratory tract are at increased risk of muscle mass depletion. A French study found muscle loss in 18.3% in breast cancer and 49.5% in those with upper digestive tract tumors.[85] For this reason, muscle loss should be actively looked for in this type of tumor and in systemic therapies that are associated with muscle loss. **Table 23** lists the conditions are associated with larger muscle loss and complications.

Table 23: Conditions Associated With Larger Muscle Loss and Complications
Lung, pancreas, colorectal, liver, kidney, esophagus, bladder, metastatic breast lymphoma, non-Hodgkin's lymphoma, gastric, and genitourinary
Chemotherapy/medication regimens associated with low muscle mass toxicity: 5-FU, fluoropyrimidine, oxaliplatin or irinotecan, cisplatin, carboplatin, epirubicin, taxane, sorafenib, sunitinib, safeni, vandetanib, pemetrexed, gemcitabine, vinorelbine, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone
Patients treated with immunotherapy: poor outcomes with low response and duration less than planned, and survival is limited (PD-1 or PD-L1 inhibitors)

Abbreviations: FU, fluorouracil; PD-1, programmed death-1; PD-L1, programmed death ligand-1.

Aleixo et al, in a meta-analysis, showed that patients with breast cancer and muscle loss had a 68% increased risk of death, 56% more toxicity, and the time to tumor progression was shorter for these patients.[86]

The GLIM group has published work on how to assess muscle mass, and suggests that when CT scans are not available, simpler methods can also be used.[87] For example, the use of standardized calf circumference (CC) has been used as a useful approximation in geriatric patients.[88, 89]

On the other hand, the GLIM group indicates that the measure of function should not be used as a direct measure of muscle mass characterization.[87]

Functionality

Loss of function, although not considered by GLIM as a measure of muscle mass[87] is one of the most common complaints in people with cancer. Reduced strength and mobility are common among cancer patients, and may help identify those with low muscle mass potential. This is identified when the patient is limited to performing his/her activities of daily living such as opening bottles, getting up from a chair, climbing stairs, carrying heavy objects and other activities that he/she could usually perform in the past. It is estimated that about 50% of people diagnosed with cancer already have some deterioration of muscle function.

Measurement of hand grip strength is part of the function assessment and diagnosis of muscle strength in general and muscle loss.[31, 90-92] It can predict not only muscle mass and physical activity, but also is part of routine nutritional assessment, quality of life, instrumental and daily living activities, independence, hospital stay, vitamin D and E deficiencies, and even of mortality.

The European consensus group[93] on sarcopenia of the elderly recommends measurement as the first step in the detection of sarcopenia that, if normal, no other measures are required. Measurement cut-off points vary with sex, age, and race of individuals, and in the Asian population, updated to <28 kg for males and 17.7 kg for females. The National Institutes of Health Foundation provides us with other cutoff points that are suggested for the 26 kg Latin American population for men and 16 kg for women.[94] The validation information of the measures should be sought locally to be more accurate in the interpretation of the results. It is usually done in the person's dominant hand with maximum strength and measured by a dynamometer.

New technology is emerging to measure with digital instruments and connected to others who can read and interpret the measure. Note that grip strength is the measurement of upper limb strength and other tools are used to measure lower limb strength indirectly and will be suggested later. An insufficient measure for cut-off points is associated with an increased risk of mortality[95] or as a predictor of toxicity to chemotherapy.[96, 97] These risks were detected by the need to delay chemotherapy, use lower doses, be unable to administer chemotherapy, need for hospitalization, and increased mortality. These findings are complemented by those found using the "Short Physical Performance Battery" (SPPB) tool which will be described later.[98, 99]

Measuring independence in activities of daily living - Scales for measuring activities of daily living have been suggested so that the focus of care is on the person and their function, dignity and independence. Measurement of a person's basic functioning in their daily activities that allows for independence or the need to recommend a caregiver may be assessed by the most widely used scale in rehabilitation that is Barthel's and created in 1965[100] [**Table 24**]. Applying this scale aims to focus all interventions on the cancer patient to preserve or improve abilities by helping with independence and improving quality of life, apart from tumor status. On the other hand, this scale can determine the need for a caregiver when there is a loss of independence in the ability to perform daily activities, as has been shown in a study published in 2022 by researchers from Brazil.[101] The tool validation is sought in people with cancer and with an average age of 55 years, confirming that Barthel is a reliable scale with adequate and valid internal consistency to measure late-stage cancer patient independence. Application as a baseline is important and modifications in follow-up will be able to alert the professional as to how and why to intervene from a nutritional point of view with the fundamental goal of approach to impact functionality. Barthel online scale with calculator included: https://www.rccc.eu/ppc/indicadores/Neuro/Barthel.html

Table 24: Barthel Index: Basic Activities of Daily Living		
Parameter	**Patient situation**	**Score**
TOTAL:		
Eating	- Completely independent	10
	- Needs help cutting meat, bread, etc	5
	- Dependent	0
Hygiene	- Independent: enters and exits the bathroom alone	5
	- Dependent	0
Dressing	- Independent: able to dress and undress, do up buttons, tie shoes	10
	- Needs help	5
	- Dependent	0
Grooming	- Independent: able to wash face and hands, style hair, shave, apply makeup, etc	5
	- Dependent	0
Stool (please rate the previous week)	- Normal continence	10
	- Occasional episode of incontinence, or needs help administering suppositories or enemas	5
	- Incontinence	0
Urination (please rate the previous week)	- Normal continence, or able to care for the catheter if it is inserted	10
	- At most 1 episode of incontinence per day, or needs help caring for the catheter	5
	- Incontinence	0
Using the toilet	- **Independent: able to go to the toilet, dress and undress, etc**	10

Source: Mahoney FI, Barthel DW.[100]

Short Physical Performance Battery – SPPB - The abnormal SPPB test (Appendix 1) has been defined as a score equal to or less than nine points as a total score. This gives the 92% sensitivity test and 80% specificity for identifying fragile older adults and is associated with all causes of mortality.[102-104] In the publication, by Almugbel et al., 2022,[105] grip strength behavior and SPPB, in 85 geriatric patients scheduled for chemotherapy were evaluated. There were 33% with abnormal data for grip strength and 55% for SPPB, and one or the other at 67.1%. In logistic regression adjusting for comorbidities, age, sex, social support, and medication optimization, the grip strength or abnormal SPPB was OR 7.58 (95% CI 1.77, 32.43), but when these two tests were measured separately, the predictor power of grip strength lost statistical significance. This suggests that both examinations are complementary as predictors of tolerance to chemotherapy.

Options for how to assess functionality are found in **Table 25**

Table 25: Short Physical Performance Battery

Balance test	Gait speed test	Chair stand test
a. One foot next to the other b. Semi-tandem position c. Tandem position	4 m (best time of 2 attempts)	5 repeats, straight back, sitting, and holding arms crossed

Assessment of dietary habits and patterns

People's diet is, to some extent, involved in the development of chronic diseases and among these, cancer.[106-109] A high-quality diet has been shown to reduce the risk of mortality in people with cancer, and also poor food consumption influences tumor progression, management, and overall prognosis.[110]

Diet assessment is based on established parameters, which facilitates management and understanding.[111] Assessment and follow-up of diet in cancer patients is critically important and will help make appropriate and timely decisions to improve outcomes in disease management and treatments. Another goal is to look for underlying causes that can alter dietary consumption, digestion and absorption and affect the quantity, diversity and quality of foods consumed.

The amount of food consumed by each individual should be estimated using the history from the past six months and the use of the Meal Block Frequency Questionnaire (FFQ) is recommended.[112] This information is used to calculate the healthy eating index (2010 HEI), which is a validated indicator of diet quality, in order to achieve an overall score, and the particular analysis of imbalances in healthy diet components. The latest version of this tool is the 2020 revision and is available on the National Cancer Institute page (https://epi.grants.cancer.gov/dhq3/).

It should be noted that people with cancer live in the community and are therefore subject to common conditions such as food insecurity as prevalent in Latin America.[113-114] It is suggested to identify this condition with two simple phrases at the level of the household where the patient lives, with a standardized clinical measure:

1. In the past 12 months, we were concerned that our food would not be enough until we got the money to buy more food;
2. In the last 12 months, the foods we bought were not enough to feed us and we had no money to buy more.

Another very simple and easy-to-understand option for determining eating habits and the amount of food the patient eats is the one used by NutritionDay.[115] In this case, figures with a plate are used for each meal, and the patient marks the amount he/she has ingested on that day and by doing so, the amount is estimated in percent relative to the individual nutritional needs. However, it does not indicate quality and variety, but indirectly and simply indicates quantity.

Inflammation

Inflammation is an etiological factor associated with a large number of diseases, if not the majority. In the late 20th century, the role of inflammatory cytokines was recognized as a risk factor for catabolism in cancer patients and cause of weight loss in patients with other conditions. The inflammation is then significantly associated with the risk and severity of malnutrition. Correia et al, demonstrated in patients with cancer of the esophagus, stomach and colon[116-117] those with inflammation identified by the Glasgow prognostic score[36] had more complications during cancer treatment.

Inflammation promotes anorexia, leading to decreased intake, changes in disease and tumor metabolism, increasing energy expenditure and muscle loss.[118, 119] There are also changes in micronutrient levels such as iron, zinc, selenium, vitamin D and A. Thus, severe and recurrent inflammation increases the severity of the deterioration of nutritional status.[120-123] In addition, it influences nutritional treatment and response to it.[124]

Negative nitrogen balance may persist despite nutritional treatment, and in patients with C-reactive protein above 100 mg/dL, nutritional therapy did not influence 30-day mortality.[120] It is then important to treat the root cause of inflammation in conjunction with nutritional therapy.

The GLIM consensus is in the process of publishing guidance on how to classify inflammation and its severity, once this variable is one of the etiological criteria.

3.8.3 — Dysphagia identification and management

Swallowing is a vital motor function in maintaining life and is critical for good hydration, nutrition, secretion management and medication consumption. It is also directly related to quality of life in order to enjoy eating, social interaction and the cultural experience of meals. Dysphagia, which is the difficulty swallowing mainly in the oropharyngeal and esophageal phases. Dysphagia is common in patients with head and neck tumors, in whom 50% of those with cancer in the pharynx is present.[125] It is also common in malnourished patients.[126]

Acute dysphagia commonly occurs due to tissue inflammation, edema, pain, mucus production, and xerostomia. The consequences of dysphagia are relevant and impact the health and effectiveness of treatments, because it worsens nutritional status and decreases quality of life. In addition, these patients are at increased risk of aspiration, pneumonia, and sepsis.[127, 128] In extreme cases when enteral nasal catheter is used, there is an increased risk of atrophy of the swallowing muscles.[129-131] Odynophagia is the most common dysphagia-related symptom and in mediastinal radiotherapy, and generally presents after two months of treatment. Dysphagia is difficult to manage, and, in patients with head and neck cancer, it has been reported that 32% improve, 48% do not improve and 20% worsen.[132]

The suggested M.D. Anderson Dysphagia Inventory (MDADI)[133] (**Table 26**) has been recommended among the reported scales for assessing dysphagia in people with cancer. However, there are no validated tools for screening, but evaluation is recommended in all head and neck cancer patients before starting therapies and in undernourished, especially in the elderly.[134]

Table 26: MD Anderson Dysphagia Inventory

**This questionnaire asks for your views about your swallowing ability.
This information will help us understand how you feel about swallowing.
The following statements have been made by people who have problems with their swallowing.
Some of the statements may apply to you.**

Please read each statement and circle the response which best reflects your experience in the past week.

1= Strongly agree 2 = Agree 3 = No opinion 4 = Disagree 5 = Strongly disagree

My swallowing ability limits my day-to-day activities	0 1 2 3 4 5
I am embarrassed by my eating habits	0 1 2 3 4 5
People have difficulty cooking for me	0 1 2 3 4 5
Swallowing is more difficult at the end of the day	0 1 2 3 4 5
I do not feel self-conscious when I eat	0 1 2 3 4 5
I am upset by my swallowing problem	0 1 2 3 4 5
Swallowing takes great effort	0 1 2 3 4 5
I do not go out because of my swallowing problem	0 1 2 3 4 5
My swallowing difficulty has caused me to lose income	0 1 2 3 4 5
It takes me longer to eat because of my swallowing problem	0 1 2 3 4 5
People ask me "Why can't you eat that?"	0 1 2 3 4 5
Other people are irritated by my swallowing problem	0 1 2 3 4 5
I cough when I try to drink liquids	0 1 2 3 4 5
My swallowing problems limit my social and personal life	0 1 2 3 4 5
I feel free to go out to eat with my friends, neighbors, and relatives	0 1 2 3 4 5
I limit my food intake because of my swallowing difficulty	0 1 2 3 4 5
I cannot maintain my weight because of my swallowing problem	0 1 2 3 4 5
I have low self-esteem because of my swallowing problem	0 1 2 3 4 5
I feel that I am swallowing a huge amount of food	0 1 2 3 4 5
I feel excluded because of my eating habits	0 1 2 3 4 5

Source: Chen AY, Frankowski R, Bishop-Leone J, et al.[135]

All patients at risk should be screened for dysphagia, primarily if they have signs, symptoms or a history of having developed dysphagia, inhalation or aspiration, or pneumonia during diagnosis or treatment. The risk of aspiration can be eliminated by the use of postures, maneuvers, and modifications of the size and consistency of the meal, which are defined by the swallowing specialist.

Swallowing should be routinely evaluated by the swallowing professional, but if this professional is not available, the nutrition expert can do the screening. The swallowing assessment is done by medical record, history, seeing the patient swallowing, video fluorography assessment, or endoscopy. This specialized assessment should be targeted to establish:

A. Aspiration hazard identification. The risks of suffering from dysphagia among patients with head and neck cancer that reached consensus were:

a) patient factors such as age, malnutrition present before treatment, rural location, alcohol abuse, cranial neuropathies, dementia and dependence on catheter feeding;

b) tumor factors such as recurrence, advanced stage, location in the hypopharynx; treatment factors such as tracheostomy, simultaneous chemotherapy and radiotherapy, multimodal treatments[136];

B. Recommend compensatory maneuvers and dietary modifications;

C. Establish treatment plan.

Importantly, any patient at risk of complications due to dysphagia should be evaluated by the expert professional in the area, in addition to the nutritionist.

NUTRITION IN CANCER FOR OTHER HEALTH CARE PROFESSIONALS AND ADMINISTRATORS

The care of the cancer patient should involve other healthcare professionals who have not been mentioned or are not part of the multidisciplinary team, but who have direct involvement in the care process, especially hospital and outpatient administrators. Support for all professionals involved in caring for the cancer patient and their family will be much more effective if the other professionals understand and support all cross-functional initiatives. It has been well demonstrated that investment in the various holistic and integrated care processes leads to savings, or is cost effective.

An evaluation of the effectiveness and costs of an intervention should consider not only whether a treatment is effective for what it is indicated and whether the costs can be justified but also whether the intervention improves quality of life, reduces hospital readmissions, reduces use of health resources, leads to fewer emergency department visits, enables a more rapid return to routine life and when treatment should be discontinued. For this reason, it is important for administrators to know that investing first in multimodal equipment and therapies often leads to better outcomes, especially when discussed with cancer patients in whom the prevalence of malnutrition is very high. Then, early diagnosis and treating malnutrition is an important part of caring for these patients. So we recommend the reading of the introduction and dedicated sessions to the patient and family members, as well as the oncologist and the non-expert nutrition specialist.

4.1 — Cancer, nutritional status, and cost-effectiveness testing of nutritional therapy

Medicine has changed greatly with the availability of new diagnostic methods and treatments. In cancer patient care, this has represented new highly sophisticated technologies and medicines. Patients with cancer still have high levels of disease-associated malnutrition and treatments, inadequately treated. So, malnutrition is the most prevalent disease in hospitals (> 50% in the world) and while it will continue to exist while there is the disease, what cannot happen is not recognizing it early on to prevent or treat it. One of the causes for inadequate nutritional treatment is the lack of recognition of the problem by doctors[137] due to lack of training in college and residency programs[138] as well as the lack of knowledge of health administrators.[139] Another key point has been the lack of administrative support to ensure the action of interdisciplinary teams already recognized as contributing to the reduction of adverse events related to nutritional therapy.[140, 141] This in turn can change the course of the disease and the treatment of the cancer patient.

Nutritional treatment, like other treatments, should be individualized, and therefore it is essential that the identification of nutritional risk be done routinely and when the person at risk is identified, the patient is evaluated so that they can be treated early. This is not yet the reality, and several authors have described it, such as Tobert et al.[142] who identified that in 5,896,792 hospitalizations in 105 American institutions, only 5% had the nutritional diagnosis recorded.

The authors showed that hospitals best classified by patients were those where more patients were found with nutritional diagnosis. Malnutrition has a high cost once undernourished patients have an increase in complications, length of stay, and mortality, as well as more readmissions to health services.[143-146] Early treatment is then cost-effective.

In Australia, Banks et al[147-148] used a predictive model, demonstrating that initiating enteral nutritional therapy early for all patients at risk of malnutrition prevented pressure injury and saved the number of beds/day. The model achieved prediction of 2,896 avoided lesions and 13,397 more beds available to other patients. Buitrago et al.,[145] in Colombia, also using a cost-effective model, showed the impact of initiating nutritional therapy early in malnourished patients. The authors indicated that patients who received delayed nutrition represented a cost of US$3,770, while those who started early treatment the cost was US$2,419, representing a savings of 35.8%. The difference is explained by decreased spending with hospitalization time, readmissions, and complications. In Brazil, Correia et al.[144] used a cost-effectiveness model considering all at-risk patients admitted to public hospitals for a period of one year. If these patients received early oral supplementation, it would represent cost-effectiveness of US$92.24, US$544.59, US$1,848.12, and US $3,698.92 or each day of hospital stay avoided, for additional patients having access to hospitalization, as well as for preventing hospital readmission and death prevention, respectively.

A more meticulous economic assessment of the impact of malnutrition on cancer patients and the necessity of adequate and timely nutritional intervention remains pending. Incurred expenses associated with the management of cancer, including those related to exertional efforts, should be factored in and accounted for when patients experience poor responses due to their nutritional status or when they are forced to discontinue treatments due to malnutrition-induced intolerance or toxicity. These costs should also encompass surgical procedures when undernourished patients have complications, as well as systemic therapies necessitating modification or suspension due to individual nutritional status, thereby altering the intervention's intended outcome. Only by integrating such data can we accurately discern the pivotal role of nutritional care in the management of cancer patients.

For instance, a poster presented at the 2022 ASPEN documented findings from a comprehensive, nutrition-focused quality improvement initiative within a subset of cancer patients participating in the SALUD study.[149] The outcomes revealed that outpatient nutrition-focused care provided to older adults with cancer who were either at risk of malnutrition or already malnourished was correlated with enhancements in both nutritional and functional parameters, alongside a reduction in healthcare resource utilization. These findings underscore the significance of comprehensive nutrition interventions, including the administration of specific oral nutritional supplements containing β-hydroxy-β-methylbutyrate, in mitigating the clinical and economic burdens associated with cancer and malnutrition.

In summary, preventing and treating malnutrition significantly impacts the clinical course of cancer, patients in terms of length of stay, mortality, costs and quality of life. Thus supporting and encouraging interdisciplinary teams that can care for the cancer patient is recommended. More importantly, the patient has the right to be treated as a premise of the right to health, as being one of the principles of human rights.[150]

Cardenas et al.[18] have raised the issue of the need for a global call for action against malnutrition through the Vienna Declaration, signed during the 44th European Society for Parenteral and Enteral Nutrition Congress, Vienna, 2022. The group has advocated for the implementation of nutrition programs that are supported by clinical nutrition societies to reach governments and authorities, non-governmental organizations and other scientific societies, such as avoiding and treating malnutrition.

MEDICAL NUTRITION TREATMENT: INFORMATION FOR NUTRITION EXPERTS

Early establishment of nutritional therapy in the cancer patient is recommended to the extent that it will contribute to a better prognosis, disease progression, and quality of life, as well as being associated with lower healthcare expenses. The first step is to establish the patient's nutritional diagnosis and needs, which will be subject to change throughout treatment.

5.1 — General guidelines

It is important that the patients eat a diet that can be shared socially with their family or their environment.[151] Nevertheless, in the presence of persistent inflammation, it becomes necessary to implement specific nutritional adaptations, whether through dietary adjustments, supplementation, or enteral/parenteral nutrition. In any clinical or health condition, all nutritional recommendations must be accompanied by physical activity, and in the cancer patient, this is no exception.

While the presence of inflammation and insulin resistance alters the use of carbohydrates, the use of fats, nutrients high in caloric density and low in volume, should be considered and increased.[152] An isocaloric, isonitrogenous, low-carbohydrate, and higher-lipid diet is recommended, capable of maintaining nitrogen balance and decreasing protein catabolism. There is some evidence with this type of diet (more fats to control and improve fat-free weight compared to conventional diet.[153, 154]

Dietary counseling has been shown to be effective in improving symptoms, quality of life, and treatment tolerance.[153, 155] In clinical practice, oral nutrition is always the priority. The cancer patient should be taught that the goal is to keep the same weight and maintain function and to know the amount and type of food to eat. This information is used to develop an individualized diet plan, with a detailed description of the red flags indicating the need to consult with the nutrition professional as soon as possible.

Dietary modifications should be based on the individual's preferences so that they can be maintained for as long as possible. When the patients cannot meet their nutritional needs through diet, modification and enrichment, oral supplementation or enteral/parenteral nutrition should be considered. An accepted guide for making decisions according to intake is that less than 75% of estimated intake is insufficient and will have visible consequences after two weeks and that less than 50% will have consequences after one week. Patients who consume between 75% and 90% of the estimated intake should be followed more closely for intervention decisions, and those who consume more than 90% are considered to be at low risk for inadequate intake. Those with oral intake below 50% to75% should be closely followed, as enteral nutrition may be the most adequate feeding route. Parenteral nutrition is reserved for those with a non-functional gastrointestinal tract.

Another key point in counseling these patients is to identify interactions between foods, oral nutritional supplements and enteral nutrition with medications. The involvement of the pharmacist is essential to help identify which medications the patients consume that have interactions with food, indicating options or other strategies to ensure that these are avoided. The most well-known medications with food interaction are:

- Phenytoin
- Levothyroxine
- Levodopa
- Omeprazole
- Warfarin

5.2 — Establishing nutritional requirements in the adult patient with cancer

Nutritional requirements include calories, proteins, minerals and vitamins, and must be individually established based on age, physical activity, previous deficiencies and magnitude of stress associated with the main disease.

The ideal instrument for determining caloric needs is indirect calorimetry, which is not a reality in most medical centers around the world, and almost certainly not in Latin America. Indirect calorimetry establishes the components of resting energy expenditure (REE), which is the energy necessary to maintain vital functions, the energy expended to digest and absorb dietary nutrients. On the other hand, total energy expenditure adds energy spent on physical activity.

In people with acute or chronic illness, there is generally an increase in REE due to hypermetabolism, but muscle loss determines the final value, which is usually decreased. Thus, body composition influences energy expenditure and should be considered for calculations. Energy requirements are usually calculated by multiplying an estimate of needs per kilogram of current weight for individuals without being overweight or obese. For patients with excess weight, the ideal weight should be calculated. The recommended energy requirements are in the range of 20-35 kcal/kg weight per day depending on the nutritional status and clinical condition.[156] Another crucial consideration is the necessity to reassess these calculations whenever there are alterations in the patient's condition throughout the course of treatment. During various treatment modalities such as surgery, chemotherapy, and radiotherapy, healthcare professionals may anticipate or identify instances of hypermetabolism or catabolism. In periods of heightened stress (metabolic, inflammatory, and immunological changes), this often leads to peripheral insulin resistance, elevating the risk of hyperglycemia. Moreover, in malnourished patients, there exists a high risk of re-feeding syndrome, necessitating a cautious approach of calorie provision to minimize potential complications. It is upon healthcare professionals, now recognized as experts in nutrition, to remain vigilant in order to prevent nutritional imbalances while simultaneously averting complications associated with nutritional therapy.

The calculation of protein needs is around 1.5 g/kg/d and, if necessary, can be increased to 2.0 g/kg/d according to metabolic demand such as when fistulas and infections are present, if renal and hepatic functions are not altered.

It is recommended that patients with not change their usual eating habits, but that they be recognized and adaptations be introduced according to current individual needs. For this reason, the ESMO guidelines recommend,[157] at baseline, that usual nutritional habits and feeding times be maintained, especially if the patient has not lost significant weight. On the other hand, many of the symptoms and signs involved with good nutrition act as indicators of nutritional intervention to improve them and, in parallel, to improve nutritional status.[158] With this information, precise, individual nutritional intervention can be initiated, initially treating the symptoms and signs that are known to impact the nutri-

tional status and taking into account other aspects such as social support or financial difficulties so that nutritional status improves. Furthermore, dietary modifications are a very important part of the patient's nutritional intervention, but these modifications may not be feasible for patients with food insecurity at home, which is a limitation that the healthcare professional should know in advance. NOT everyone HAS access to a healthy and sufficient diet even if they are sick.

The next step of the modification is a diet designed specifically for the person with cancer at nutritional risk or malnourished. Dietary modifications in people with cancer are a fundamental and essential step, in conjunction and aligned with anti-cancer treatment.

5.3 — Criteria to consider for nutritional and metabolic interventions in cancer patients

It is imperative to meticulously consider the precise timing for patients with cancer as they traverse various stages throughout the clinical course of the disease and its corresponding treatments. Any broad-spectrum recommendations risk being unsubstantiated if this is overlooked. Therefore, it is incumbent upon oncologists to assess the patient's overall condition, disease stage, and life expectancy and share it with the nutritional therapy team. Additionally, it is crucial to ascertain which anti-cancer therapies will be administered to anticipate potential adverse effects.

Understanding certain disease-related aspects is paramount, including determining whether the patient is in the terminal stages of the disease, the presence and severity of refractory inflammation, the status of remission or cancer progression, and whether the nutritional intervention is likely to yield the desired effects within the anticipated timeframe. Moreover, assessing the patients' commitment to interventions and perceived challenges versus benefits, willingness to engage in physical activities, and ability to adhere to recommended dietary regimens are also essential. These considerations aid in making informed decisions and allow for the anticipation of potential success or failure of interventions.

When contemplating the initiation of any nutritional intervention, priorities must be determined based on the various treatment modalities and respective goals, while considering the unique characteristics of each patient. The initial focus should be on mitigating factors that impede standard or modified dietary intake. Efforts should be directed towards promoting patient independence in oral feeding and dietary modifications. However, if nutritional requirements remain unmet despite these adaptations, then medical nutritional therapy should be initiated.

In comparison to patients with other diseases, the supply of energy and nutrients in the cancer patient may be not sufficient. Attempts should be made to modulate metabolism disorders, which are more complex and challenging, as well as to alleviate the symptoms and signs often experienced by these patients. Among the most frequent disorders that cancer patients present are insulin resistance[159] and anabolic resistance,[133] which prevent them from maintaining good muscle health. One of the measures to decrease catabolism and improve anabolism is the supply of some nutrients, such as beta-hydroxy-methyl-butyrate (HMB), in addition to adequate energy and proteins of high biological value, as well as muscle training. Pharmacological interventions to increase appetite, decrease inflammation, and stimulate muscle mass growth should be evaluated, as well as psychological support to decrease stress.

The multimodal treatment of cancer patients is extremely important, and alongside monitoring nutritional intake, attention should also be paid to preserving or enhancing muscle strength and function to uphold or enhance quality of life. However, ongoing assessment of the patient's prognosis is crucial, as the aforementioned approach may become less applicable for those nearing end-of-life. In such instances, emphasis should be placed on minimizing stress through strategies such as enhancing comfort, and fostering empathetic communication with both the patient and

their family. It is essential to recognize that in the presence of cachexia in end-of-life patients, this is a refractory stage, where no intervention can reverse the nutritional status. For patients with a life expectancy of less than six weeks, the treatment generally focuses on alleviating symptoms such as thirst, nausea, vomiting, and dysphagia, while providing vital psychological support.

In cases where determining the optimal approach proves challenging, it is advisable to implement interventions for a limited duration and assess the patient's progression over time. For patients with a life expectancy exceeding six months, proactive measures should be taken to prevent nutritional, functional, muscular, and psychological deterioration. Vigorous efforts should be made to ensure these patients achieve sufficient energy and adequate nutrient intake to meet their needs with the various medical nutrition therapy according to the gastrointestinal function (**Table 27**). On the other hand, in patients with an estimated life expectancy of less than six months, nutritional counseling and oral supplementation are the strategies available; however, they should also be addressed on an individual basis, contemplating the patients' desires and beliefs. Parenteral nutrition in these cases, based on evidence, does not improve nutritional status or improve quality of life while the risk of complications increases, but it should be evaluated individually considering different aspects, including psychological and ethical aspects.[109]

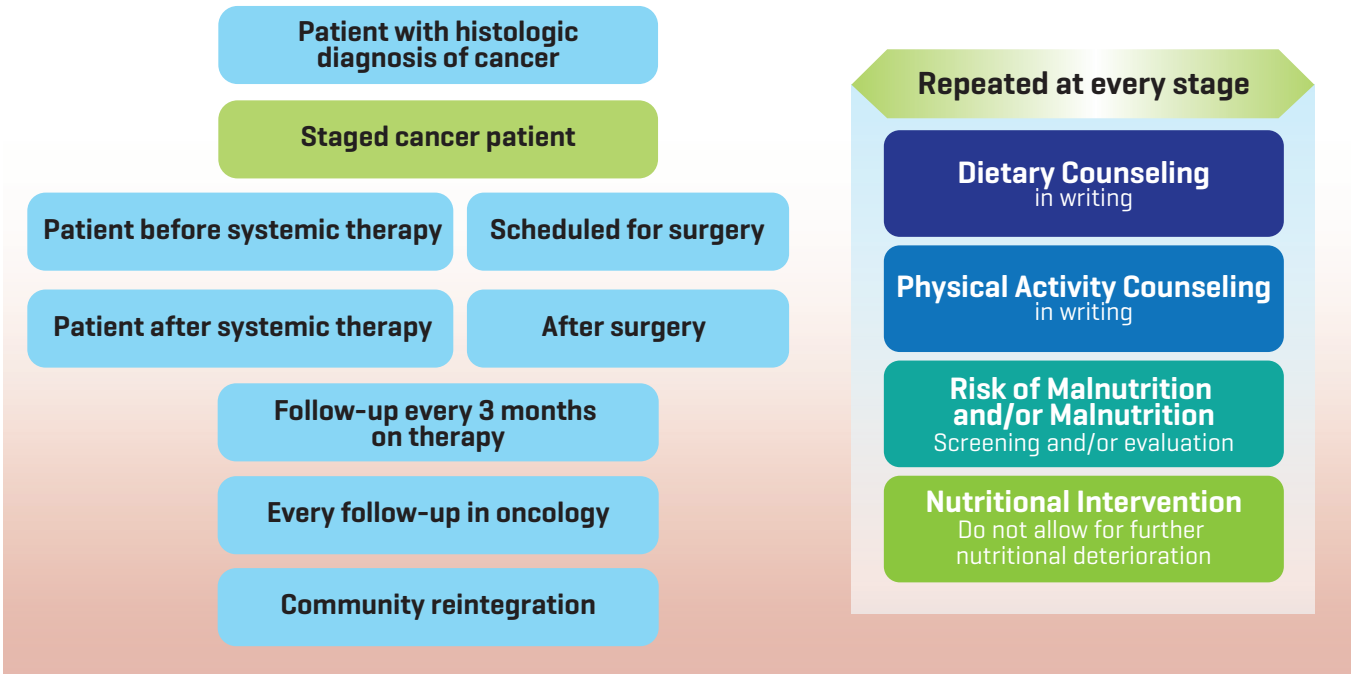
Table 27: Important Recommendations
▪ Mitigate signs and symptoms that interfere with proper eating
▪ Calculate the individual's current nutritional requirements, which may change during the clinical course of the disease
▪ Adjust and/or modify the patient's diet to meet nutritional needs after relieving the patient's symptoms. It is incumbent on the clinician to assess and anticipate nutritional goals or to begin nutritional intervention to prevent nutritional and muscular deterioration
▪ Use specific nutrients to enrich the diet when the patient is able and willing to eat (fats and proteins)
▪ Decide whether oral supplementation should be initiated
▪ Transition to enteral nutrition via tube, parenteral nutrition, or mixed nutrition if the patient's needs cannot be met through other means

5.4 — Medical nutritional interventions after diet modification

Patients, upon receiving a cancer diagnosis, are often overloaded with information that fundamentally alters their lives. Typically, healthcare professionals concentrate on elucidating the significance of the diagnosis, potential treatment options, and the possible ramifications of both the cancer and its treatments, extending beyond cancer treatment to encompass broader health implications. Unfortunately, the critical role of nutrition and functional status, which profoundly influence treatment outcomes and disease progression, is frequently overlooked in these discussions. Conversely, patients often embark on dietary modifications independently, mostly adopting restrictive diets or following advice from ill-equipped sources, thereby missing the opportunity to potentially influence the clinical trajectory of the illness. Therefore, it is advisable to provide fundamental dietary recommendations or counseling at the outset, ideally in written form. This enables patients and their families to review and tailor the guidance to the unique circumstances of the individual patient, the specific cancer type, and any comorbidities they may have. Moreover, cancer patients may

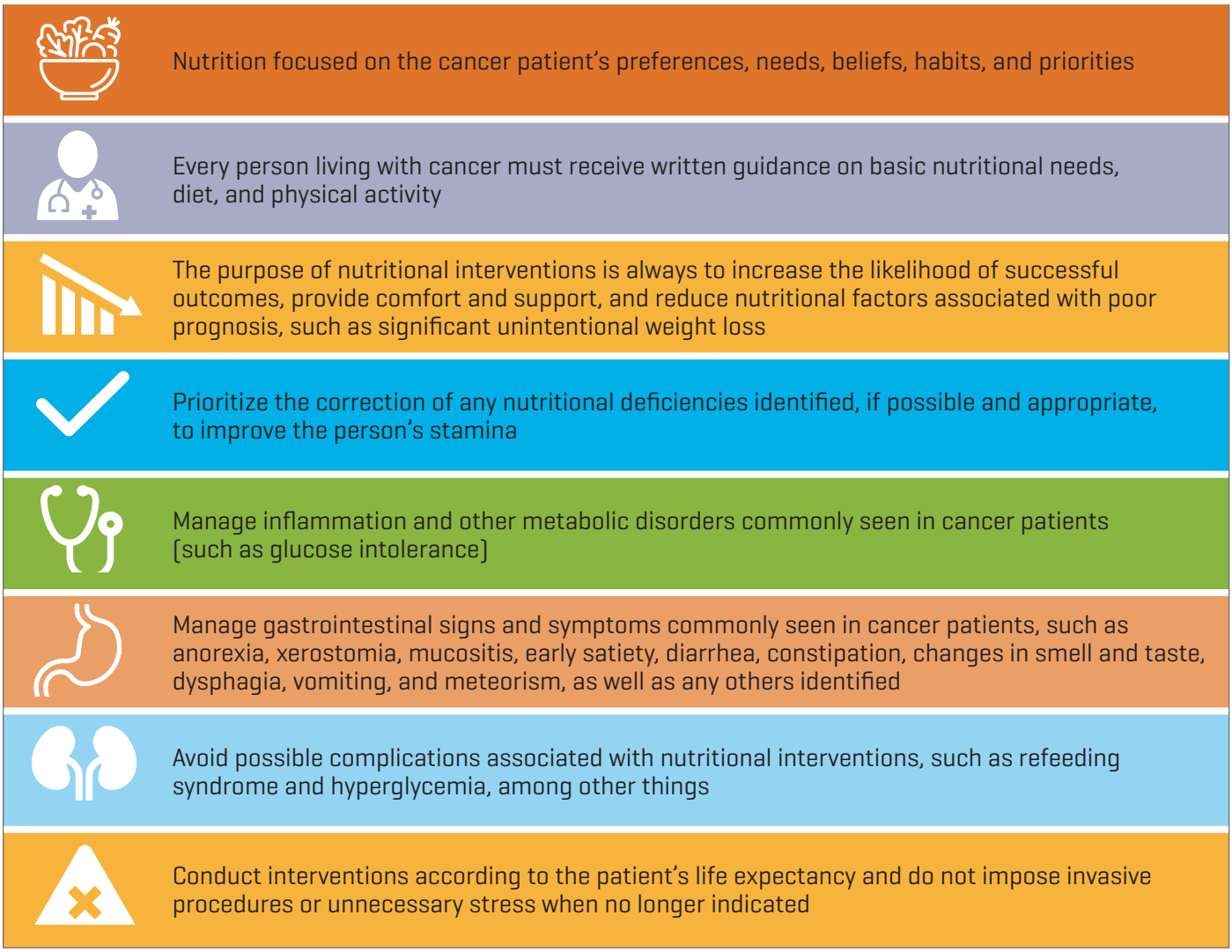
identify symptoms indicative of nutritional decline that necessitate specialized management by adequately trained professionals. Similarly, written recommendations regarding physical activity should be provided to encourage early and appropriate self-care in maintaining functional abilities [**Figure 8**].

Figure 8: Steps in Nutritional Intervention for Every Cancer Stage



From the moment the patient is diagnosed with cancer, symptoms and signs that impact nutritional status can be changed at any time. However, timely intervention is very important to maintain the best possible quality of life. In addition, the treatments and the tumor also interfere with the disease course. Certain key assumptions are crucial to establish to make nutritional recommendations, and it is important to focus on the desired goals of the chosen interventions [**Figure 9**].

Figure 9: Key Assumptions in the Nutritional Management of Patients With Cancer



Good nutrition is key for people with cancer, therefore, healthy eating habits will allow nutritional needs to be met during the diagnosis process, treatment and afterwards, if the person has them as a rule of life, but that is not the reality for most patients.[160] Furthermore, general problems in people with cancer are common and can affect good nutrition, and in turn, the associated treatments lead to worse effects among the malnourished. That means there is a vicious cycle in which malnutrition affects tolerance and increases the toxicity and adverse events of chemotherapy, hormone therapy, radiotherapy, surgery, immunotherapy, and stem cell transplantation, and vice-versa. The goals of a healthy diet and physical activity guidelines are to maintain "healthy weight" and to have good function and independence, which is what today has been defined as good VITALITY.

Establishing a healthy dietary pattern and advocating it for cancer patients across all stages of the disease is essential. This is the cornerstone upon which healthcare professionals build, adapt, enhance, and make dietary interventions appealing as an integral component of patient care. However, it is crucial to emphasize that the initial dietary counseling and physical activity guidance provided are not intended to supplant the directives of the healthcare professional overseeing the individual's care.

Subsequently, the next pivotal step involves delineating the specific dietary requirements of each patient and devising strategies to attain or maintain these goals. These needs should be tailored to encompass the appropriate quantities of protein, fats, carbohydrates, water, vitamins, and minerals essential for optimal nutrition.

5.5 — Re-feeding syndrome and risk identification

The re-feeding syndrome has been defined as a series of clinical and electrolyte changes in response to the introduction or increase in energy in malnourished individuals or after significant periods of starvation, or low-energy diets.[161]

The American Society for Parenteral and Enteral Nutrition (ASPEN) issued a consensus on the identification and management of this syndrome.[162] The diagnostic criterion is characterized by a decrease of at least 10% in plasma levels of phosphorus, magnesium, and potassium compared to baseline, sustained over a period of five days following the initiation of nutritional intervention. Severity is stratified based on the degree of decline, with mild cases defined as decreases between 10 and 20%, moderate cases between 20 and 30%, and severe cases exceeding 30%, often accompanied by organ failure.

Patients with certain diseases and conditions are at an elevated risk of developing re-feeding syndrome, including those with: acquired immunodeficiency syndrome (AIDS); a history of alcohol or other substance abuse; dysphagia or esophageal motility disorders; eating disorders; food insecurity; recent major surgery; gastrointestinal disorders such as malabsorption, inadequate digestion, or chronic constipation; prolonged fasting; complications from surgery; and previous malnutrition. Energy deprivation resulting from starvation and malnutrition significantly increases the susceptibility to this syndrome, as the body's ability to conserve available energy reserves becomes compromised. When coupled with deficiencies in vitamins and electrolytes, these compromised reserves, along with additional factors such as fluid and electrolyte losses from conditions like diarrhea, fistulas, vomiting, increased drainage of body fluids, or the use of diuretics, exacerbate the problem. Furthermore, elevated blood glucose levels trigger insulin production, causing the already depleted electrolytes to enter cells alongside glucose for metabolism, further reducing their levels to potentially life-threatening degrees.

These imbalances mainly affect phosphorus, given its crucial role in oxidative phosphorylation and as a key component of adenosine triphosphate (ATP), the primary energy reserve in humans. Phosphorus deficiency can lead to impaired muscle function, notably respiratory function, potentially culminating in respiratory failure in severe cases. Additionally, it can result in reduced cardiac contractility, conduction abnormalities leading to arrhythmias, and diminished production of 2,3-diphosphoglycerate, which increases oxygen affinity to hemoglobin, thereby reducing tissue oxygen delivery and causing hypoxia.

The decrease in potassium levels is attributed to insulin-stimulated activation of the Na/K ATPase pump, causing potassium to move into cells while sodium exits. Potassium is essential for muscle contraction and nerve impulse transmission. Severe hypokalemia poses a risk of arrhythmias and even death. Weakness, hyporeflexia, respiratory depression, and paralysis may also manifest.

Magnesium deficiency has been associated with the re-feeding syndrome when prioritized by the kidney in exchange with potassium; thus worsening plasma potassium deficiency.

Thiamine deficiency has also been associated with this syndrome because demands are increased during the transition from starvation to feeding, as it involves several steps in glucose metabolism. The severe deficiency is manifested by neurological disorders, confusion, encephalopathy (Wernicke's syndrome and Korsakoff's psychosis), oculomotor abnormalities, hypothermia and even coma.[163-165] Thiamine is involved in the conversion of lactate to pyruvate, and metabolic acidemia can occur without liver damage. Thiamine deficiency also decreases ATP production in the cardiomyocytes and may lead to congestive heart failure, or to dry beriberi. Thiamine may also lead to vasodilation and decreased diastolic blood pressure, by means of increased plasma adenosine.

The clinical manifestations of the deficiencies are shown in **Table 28**:

Table 28: The Clinical Manifestations of the Deficiencies of Ions and Thiamine

Nutrient	Clinical Manefestations
Hypophosphatemia	▪ Neurological signs, paresthesias, weakness, delirium, disorientation, encephalopathy, paralysis with areflexia, convulsions, coma, tetany, hypotension, shock, compromised cardiac volumes, increased preload, diaphragm weakness, respiratory failure, dyspnea, hemolysis, thrombocytopenia and alterations in leukocyte function.
Hypokalemia	▪ Neurological signs, paralysis, weakness, cardiac arrhythmias, cardiac volume compromise, respiratory failure, nausea, vomiting, constipation, rhabdomyolysis, muscle necrosis.
Hypomagnesemia	▪ Neurological signs, weakness, tremor, muscle pain, mental changes, tetany, seizures, arrhythmias, anorexia, nausea, vomiting, and constipation.
Thiamine deficiency	▪ Encephalopathy, lactic acidosis, nystagmus, neuropathy, dementia, Wernike's syndrome, Korsakoff's psychosis, and dry and moist Beriberi.
Sodium retention	▪ Fluid overload, pulmonary edema and cardiac decompensation.

The literature presents varying data regarding the true incidence and prevalence of re-feeding syndrome. What can be established, however, is that in populations where the syndrome is not actively monitored due to its perceived rarity as a nutritional event, a significant number of patients may be placed at risk. Although the risks of complications and mortality associated with re-feeding syndrome are substantial, they are largely preventable. Cancer patients, particularly those experiencing prolonged starvation, malnutrition or electrolyte loss, are particularly susceptible to this syndrome.

The criteria for identifying risk factors proposed by ASPEN are in **Table 29**.[161]

Table 29: ASPEN Consensus on Criteria for Identifying Adult Patients at Risk of Refeeding Syndrome

	Moderate risk: minimum of 2 criteria required	High risk: 1 criterion required
BMI	16-18.5 kg/m^2	<16 kg/m^2
Weight loss	5% in 1 month	7.5% in 3 months or >10% in 6 months
Calorie intake	Nothing or <50% for 5-6 days ***or*** <75% for >7 days with acute illness ***or*** <75% for > 1 month	Nothing or very little for >7 days ***or*** <50% for >5 days with acute illness ***or*** < 50% for >1 month
Abnormal plasma levels of K, P, or Mg before feeding	Minimal deficiency with few intervention needs	Need for formal intervention to restore plasma levels
Loss of subcutaneous fat	Moderate loss	Severe loss
Loss of muscle mass	Mild to moderate loss	Severe loss
Comorbidities	Moderate disease	Advanced disease

Abbreviations: BMI, body mass index; K, potassium; Mg, magnesium; P, phosphorus.
Source: Adapted from da Silva JSV, Seres DS, Sabino K, et al.[162]

The best way to prevent refeeding syndrome is to start nutritional therapy progressively. **Table 30** has the recommendations regarding the amount of initial calories, increasing feeding according to the nutritional requirements, and other recommendations.

Table 30: Published Recommendations for Initiation and Progression of Nutrition for Patients With Refeeding Syndrome Risk

	Initial calories	Feeding progression	Other recommendations
NICE[166]	▪ Maximum 10 kcal/kg/d ▪ 5 kcal/kg/d in end-of-life cases (examples, BMI <14 kg/m^2 or negligible intake for >15 days)	▪ Slowly to meet or exceed breaking needs in 4-7 days	▪ Restore circulatory volume
IrSPEN[167]	▪ Extreme risk 5 kcal/kg/d ▪ High risk: 10 kcal/kg ▪ Moderate risk: 20 kcal/kg	▪ Slow onset of feeding in the nested category	▪ Check electrolyte levels ▪ Electrolyte replacement to correct deficiencies ▪ Monitor fluid balance
CNSG[168]	▪ Extreme risk: consider contributing only 5 kcal/kg/d ▪ High risk: initiate nutritional support with a maximum of 10 kcal/kg body weight ▪ Moderate risk: enter a maximum of 50% of the requirements for the first 2 days	▪ Extreme or high risk: slowly over 4-7 days as clinical and biochemical follow-up allows ▪ Moderate risk: increase energy intake only when clinical conditions and electrolyte results permit	▪ Energy and fluid should be introduced very gradually ▪ Check potassium, magnesium, and phosphorus ▪ Do not discontinue feeding if electrolyte levels decrease ▪ When serum potassium, magnesium, or phosphorus levels are significantly low, feeding should not progress further until supplementation has occurred
Cray[169]	▪ ≈10 kcal/kg/d for severe cases ▪ 15-20 kcal/kg for others	▪ Increase calories with caution in a staggered manner by 200-300 kcal every 2-3 days	▪ Consider all sources of calories and fluids in your calculations (including dextrose) ▪ Check reference electrolytes (especially phosphorus, potassium, and magnesium) before starting nutritional support, and replace low levels immediately ▪ Unless hemodynamically unstable, maintain sodium-containing IV fluids at ≈1 L/d initially in patients with severe malnutrition, such as those with anorexia nervosa, who may have a component of cardiomyopathy
Friedli[170]	▪ 5-25 kcal/kg/d based on severity of RS risk	▪ Nutritional therapy should be initiated with reduced caloric goals and a slow increase to total caloric goals for 5 to 10 days, according to the individual risk category for RS ▪ Fluid overload should be prevented by restricted use of fluids and a sodium-restricted diet within the first 7 days	▪ Patients at high risk of RS should receive electrolyte replacement below normal or in a low normal range ▪ Prophylactic electrolyte supplementation

Abbreviations: BMI, body mass index; CNSG, Clinical Nutrition Steering Group; IrSPEN, Irish Society for Clinical Nutrition and Metabolism; IV, intravenous; NICE, National Institute for Health and Care Excellence; RS, refeeding syndrome.
Source: da Silva JSV, Seres DS, Sabino K, et al.[162]

The treatment of Refeeding syndrome according to ASPEN 2020[161] is recorded in **Table 31**.

Table 31: ASPEN Consensus Recommendations to Prevent and Treat RS in At-Risk Adults

Appearance of care	Recommendations
Calorie initiation	▪ Start with 100-150 g dextrose or 10-20 kcal/kg for the first 24 hours; progress by 33% of goal every 1 or 2 days. This includes enteral and parenteral glucose. ▪ In patients with moderate to high RS risk with low electrolytes, maintain baseline or consider increased calories until electrolytes are supplemented and/or normalized. ▪ Initiation of or increase in calories should be delayed in patients with very low phosphorus, potassium, or magnesium levels until corrected. ▪ Calories from IV dextrose solutions and medications infused with dextrose should be considered at the above limits and/or initiated with caution in patients with moderate to severe risk of RS. If a patient has received significant amounts of dextrose for several days, from maintenance IV fluids and/or medications in dextrose, and has been asymptomatic with stable electrolytes, the calories from nutrition may be reintroduced in an amount higher than those recommended above.
Fluid restriction	▪ No recommendation
Sodium restriction	▪ No recommendation
Protein restriction	▪ No recommendation
Electrolytes	▪ Verify serum potassium, magnesium, and phosphorus before starting nutrition. ▪ Monitor every 12 hours for the first 3 days in high-risk patients. Frequency may be higher depending on the clinical presentation. ▪ Replenish electrolytes based on established standards of care. ▪ No recommendation can be made about whether prophylactic electrolyte dosing should be administered if prefeeding levels are normal. ▪ If electrolytes become difficult to correct or decrease precipitously during the initiation of nutrition, reduce calories/grams of dextrose by 50% and advance dextrose calories by approximately 33% of goal every 1-2 days based on clinical presentation. Recommendations may be modified based on physician judgment and clinical presentation, and cessation of nutritional support may be considered when electrolyte levels are severely and/or life-threateningly low or decline precipitously.
Thiamine and multivitamins	▪ Supplement with 100 mg of thiamine before feeding or before starting IV fluids containing dextrose in at-risk patients. ▪ Supplement with 100 mg/day of thiamine for 5-7 days or more in patients with severe starvation, alcoholism, or other high risk of thiamine deficiency and/or signs of thiamine deficiency. ▪ Routine thiamine levels are unlikely to be of value. ▪ Add MVI to PN daily unless contraindicated, provided PN is continued. For patients receiving oral/enteral nutrition, add a full oral/enteral multivitamin once daily for 10 days or more, depending on clinical status and mode of therapy.
Monitoring and long-term care	▪ Measurement of vital signs every 4 hours for the first 24 hours after the start of calorie intake is recommended in at-risk patients. ▪ Cardiorespiratory monitoring is recommended in patients who are unstable or have severe deficiencies, based on established standards of care. ▪ Measure weight daily and monitor intake and output. ▪ Assess short- and long-term goals for nutritional care daily for the first few days until the patient is considered stabilized (eg, no need for electrolyte supplementation for 2 days) and then based on institutional standards of care.

Abbreviations: ASPEN, American Society for Parenteral and Enteral Nutrition; IV, intravenous; MVI, multivitamin injection; PN, parenteral nutrition; RS, refeeding syndrome.

Source: da Silva JSV, Seres DS, Sabino K, et al.[162]

Lastly, it is advisable that when a patient commences nutritional intervention and is deemed to be at moderate to severe risk of re-feeding syndrome, the therapy should ideally occur in or in close proximity to a hospital setting, especially for those at high risk, necessitating vigilant monitoring. Implementing such measures can help mitigate the incidence of re-feeding syndrome.

5.6 — Nutritional management of the non-malnourished patients

This group of patients has been defined as having no imbalance between intake and demand, but as cancer patients, they are always at risk of malnutrition in the course of the disease and its therapy. As such, early intervention is paramount, therefore, more frequent nutritional screenings and timely adapted interventions should be considered. In this regard, when symptoms and signs impede adequate dietary intake or inadequate food availability, more aggressive treatments should be adopted to alleviate these risk factors. In particular, individuals aged 65 and above, those residing in rural areas, those with cancer types associated with higher rates of malnutrition (such as liver, pancreas, stomach, lung, and head and neck cancers), ethnic groups exhibiting more aggressive cancer progression, people with comorbidities that impact food metabolism, those with obesity, and individuals facing educational or financial constraints are to be carefully followed.

It is important to note that the average age in the United States of people diagnosed with cancer is 67 years.[171] The aging process among people is very heterogeneous and when they have cancer, many of them use multiple medications, have comorbidities, functional, psychological and cognitive deficits and are prone to presenting primary sarcopenia. The consequences of malnutrition are greater in this group of people.[172] In addition to compromising the life expectancy of these patients, functionality, independence, psychological status, and decreased tolerance to treatments with greater toxicity to systemic therapies is common.

5.7 — Nutritional interventions for cancer-associated symptoms/signs

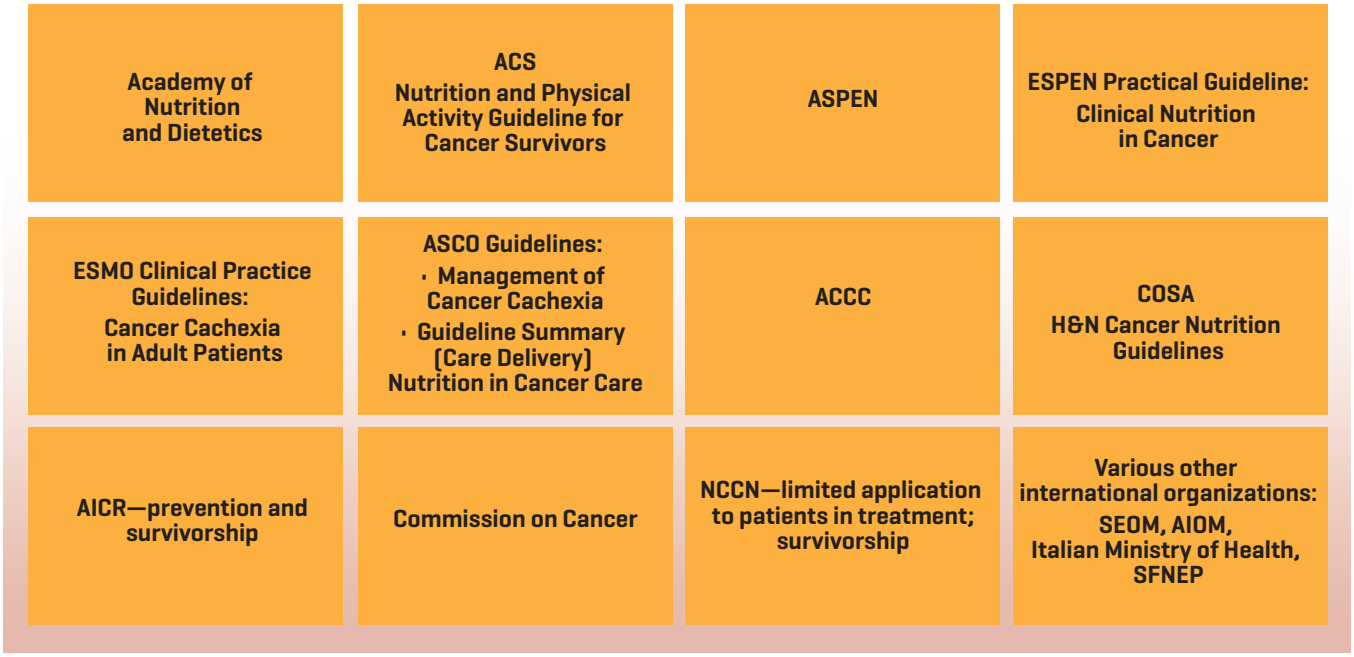
Cancer patients typically present with symptoms/signs that interfere with good eating, and the incidence is very common, above 80% of cancer patients who are on anti-cancer therapy. Among these stand out: constipation - observed between 50 and 95%; anorexia that occurs in 50% at the time of diagnosis and rises to 65% during more advanced stages; nausea in 35%; vomiting in 70% and more than 40% of patients undergoing chemotherapy; meteorism in 21%; reflux and indigestion in 21%; early satiety between 13 and 62%; diarrhea in 14% and 50% in patients with gastrointestinal tumors; changes in taste and smell during chemotherapy in 70% and in head and neck radiotherapy in 90%; mucositis between 20 and 40% in chemotherapy, 80% in patients with bone marrow transplant and 100% in head and neck radiotherapy; dysphagia in 46% in esophageal tumors and between 65-70% in head and neck tumors; xerostomia - 90 to 100% of patients with head and neck tumors; discomfort with odors in 25% of patients.

Specialized nutritional approach — Medical Nutrition Therapy — for cancer patients should be led by an interdisciplinary team to address:

- **A.** A person-focused nutritional care and disease management. It must be based on available evidence regarding diagnosis and intervention;
- **B.** An individualized approach based on medical history and physical examination;
- **C.** The diagnosis of the nutritional status to adequately indicate the type of nutritional therapy to be followed;
- **D.** An intervention plan starting with individualized dietary counseling and specialized intervention according to the etiology of malnutrition;
- **E.** Behavioral changes towards healthier and more specific nutritional habits.

There are currently several guidelines for nutritional intervention in cancer (**Figure 10**).

Figure 10: Current Guidelines



Abbreviations: ACCC, Association of Community Cancer Centers; ACS, American Cancer Society; AICR, American Institute for Cancer Research; AIOM, Italian Association of Medical Oncology; ASCO, American Society of Clinical Oncology; ASPEN, American Society for Parenteral and Enteral Nutrition; COSA, Clinical Oncological Society of Australia; ESMO, European Society for Medical Oncology; ESPEN, European Society for Clinical Nutrition and Metabolism; H&N, head and neck; NCCN, National Comprehensive Cancer Network; SEOM, Spanish Society of Medical Oncology; SFNEP, French Speaking Society of Clinical Nutrition and Metabolism.

5.8 — Hydration for the cancer patient

Hydration in cancer patients must not be overlooked, as dehydration tends to be frequent and more pronounced during systemic therapies, waiting periods for diagnostic studies, and in the terminal stage of the disease. Numerous factors contribute to greater fluid loss, proper fluid intake or failure to achieve homeostasis. Common causes include a diminished sensation of thirst, fever, vomiting, diarrhea, excessive sweating, or insufficient attention to hydration needs during prolonged fasting periods.

Body water is indispensable for numerous physiological functions and plays a vital role in enhancing the tolerance and efficacy of treatments. Moreover, dehydration can precipitate potentially fatal complications, including kidney failure, electrolyte imbalances, cognitive changes, and adversely impact overall well-being. Therefore, ensuring adequate hydration is essential for optimizing the health outcomes and comfort of individuals undergoing cancer treatment.

Chemotherapy and radiotherapy frequently cause damage to the upper digestive tract, such as mucositis, which causes people not to drink enough fluids. These therapies may also cause vomiting and diarrhea that lead to losses of fluids and electrolytes, which are often not replaced adequately. Chemotherapy can also affect kidney function, leading to loss of extra urine. On the other hand, radiation therapy causes salivation disorders producing dry mouth that is very bothersome to the person, as well as causing swallowing problems. Furthermore, certain medications used for pain control may cause cognitive disorders as well as nausea and vomiting.

Recommendations to be made for people with cancer who are at risk of dehydration are:

A. Drinking fluids during treatment is very important to avoid dehydration. The general recommendation should be 30 – 50 mL of fluids per kg/day. This should be adjusted individually according to age, health condition, and type of treatment:

   a. It is recommended to have a bottle of water permanently throughout the day;
   b. Reminders for fluid intake should be kept regularly;
   c. Other fluid sources that the patients like, and the addition of fruits should be ensured.

B. Consuming water-rich fruits and legumes such as watermelon, melon, cucember, lettuce, celery, and citrus fruits. Including soups in the diet that offer additional fluids. Fruit juices with fruit that the person likes are recommended. These elements should be included in the healthy diet plan;

C. Ingesting low amount of caffeine and alcohol as they act as diuretics and contribute to dehydration;

D. Using electrolyte beverages to replace abnormal losses. In the event of diarrhea and vomiting, electrolytes are lost and must be supplied in drinks containing them;

E. Balancing fluids when the risk of dehydration is identified and for the necessary time. Urine color should be assessed as an indicator of hydration while taking into account medications and meals that may change. Similarly, acute weight loss may be due to dehydration.

5.9 — Specific nutrients for cancer patients

5.9.1 — HMB

β-Hydroxy β-methylbutyrate (HMB) is produced endogenously by the body in small amounts as a metabolite of leucine.[173, 174] However, Leucin does not provide large amounts of HMB; only a small portion, equivalent to approximately 5% of leucine, is catabolized and metabolized as in HMB.[174, 175] Therefore, although dietary leucine by itself may lead to a modest stimulation of protein synthesis through the production of small amounts of HMB, direct ingestion of HMB more potently affects such signaling, resulting in an increase in muscle mass.[176, 177] As described by Prado et al.,[142] several pathways have been proposed to explain the effects of HMB on muscle health. These include increased muscle protein synthesis and decreased muscle protein breakdown.[178, 179] Prado et al.[142] further explain that "HMB stimulates muscle protein synthesis by activating the mechanistic target of rapamycin (mTOR) and the growth hormone/insulin-like growth hormone factor axis".[172, 179] HMB also reduces muscle proteolysis and apoptosis of myonuclei, and these effects are via the ubiquitin-proteasome and the autophagy-lysosome system, respectively.[178]

HMB has an anti-inflammatory effect by reducing the production of TNFα and IFN-γ and also by blocking some IL-6 mediated pathways in cancer patients with systemic inflammation, negative protein balance, and involuntary loss of lean body mass, with or without adipose tissue wasting, which helps control them.[180] Additionally, the cancer patient has impaired myogenic regeneration, thus contributing to the decrease and weakness of the muscles. This process falls under the satellite cell domain.

HMB stimulates the proliferation, differentiation, and fusion of human myo-satellite cells in vitro, thereby potentially increasing skeletal muscle regenerative capacity.[178] A systematic review and meta-analysis carried out by Prado et al, in 2022, in cancer patients, showed that HMB supplementation can be beneficial once 4/4 studies demonstrated benefits in maintaining or increasing muscle mass, 2/2 improved strength, therefore better muscle function, 3/3 indicated the reduction of hospitalization and 5/7 showed improved survival.[174]

5.9.2 — Eicosapentaenoic acid (EPA)

Omega-3 fatty acids are known for the anti-inflammatory effects once they help immunomodulate the pro-inflammatory response. However, evidence of these effects in the cancer patient with cachexia remains controversial, despite having been used in various clinical studies. In Mexico, Solís-Martínez et al., used an omega-3 polymeric diet (EPA - 2g/day) in patients with head and neck cancer, for six weeks prior to cancer treatment. The authors evaluated body composition with BIA, in addition to measuring inflammatory markers. The EPA group had decreased inflammatory markers, while showing improvements in markers of body composition and quality of life.[181] Castro et al., at the beginning of 2022, published a systematic review and meta-analysis, aimed at evaluating the reported effects of n-3 supplementation on body weight and inflammatory markers in cancer patients.[182] No differences were found regarding the effect of omega-3 on levels of markers as interleukin-6, C-reactive protein and albumin. Poor evidence and poor quality of the studies prevented a more robust analysis in this meta-analysis. However, Jin et al, at the end of 2022, published another meta-analysis with omega-3 intervention comparing body weight, lean body weight, inflammatory factors, quality of life and survival time.[183] There was no difference in weight variables or inflammatory cytokines; in contrast, improvement in quality of life and increase in mean survival were observed. The dose used in most studies ranges from 2-7 g/day, but clinical evidence has been shown with 2 g/day.

5.10 — Pharmacological interventions

Several medications have been studied that could influence the course of the severely undernourished patient. Among these, steroids and progestin have demonstrated efficacy that affect appetite and body weight, but with side effects that limit wide recommendation. The most commonly used corticosteroids include prednisolone, methylprednisolone, and dexamethasone, and their actions are due to the anti-inflammatory capacity.[184] Toxicity is low if these medications are used for a limited time, whereas with prolonged use, they are associated with significant muscle mass loss, insulin resistance, and increased infections such as candidiasis along with stomatitis.[184] Steroids are often recommended to fight fatigue[157] and there appears to be a temporary beneficial effect on appetite after a few weeks, but weight and prognosis are not improved.[185]

Medroxyprogesterone acetate and megestrol have been shown to increase appetite and decrease the inflammatory status. In a Cochrane systematic review including 23 studies, it was found that megestrol increased appetite [relative risk (RR) 2.57 and weight gain, RR 1.55].[186] This study did not measure the effect on muscle or quality of life and used doses in the range of 160-800 mg/d for on average eight weeks. Megestrol has been associated with thromboembolic events, fluid retention, adrenal insufficiency, and hypogonadism in males.

The use of cannabinoids is not supported by studies reporting effectiveness on increasing appetite and/or weight and quality of life. In all studies, adverse effects were noted to be low, but the dose in most reports is below those used for other purposes.

Olanzapine has been indicated to treat chronic nausea.[187] Nonsteroidal anti-inflammatory medications (NSAIDs) have been studied to stabilize weight loss and can be used for pain.

The European Society for Medical Oncology (ESMO) recommendations on pharmacological interventions in cancer are excerpted below[188] (using levels of evidence and grades of recommendation adapted from the Infectious Diseases Society of America-United States Public Health Service Grading System) [**Table 32**].

Table 32: Recommendations for Pharmacological Interventions in Cancer

Drug	Effects
Corticosteroids	▪ May be used to increase appetite for a short period of up to 2-3 weeks. Effects on appetite usually disappear with longer treatment [I, B].
Progestins	▪ May be used to increase appetite and [body weight], but not muscle mass, QoL or physical function in patients with cancer cachexia [I, B]. The risk of serious side effects, including thromboembolic events, must be considered.
Medical cannabis	▪ There is insufficient evidence to support the use of medical cannabis or its derivatives to alleviate anorexia or early satiety in patients with cancer cachexia [II, C].
Olanzapine	▪ There is moderate evidence to suggest considering the use of olanzapine to treat appetite and nausea in patients with advanced cancer [II, B].
NSAIDs	▪ There is insufficient evidence to recommend the use of NSAIDs alone to treat cancer cachexia [III, C].
Metoclopramide or domperidone	▪ There is insufficient evidence to recommend the use of metoclopramide or domperidone alone to treat cancer cachexia [II, C].
Androgens	▪ As there is evidence of no beneficial effect in terms of improvement in muscle mass, androgens are not recommended [II, D].

ASCO recommendations[189] for medication use as well as nutritional interventions are summarized in **Table 33**.

Table 33: Summary of Recommendations for the Treatment of Cancer Cachexia in Patients With Advanced Cancer

Intervention	Strength of recommendation	Strength of the evidence	Benefits[a]	Harms[a]
Nutritional interventions				
Dietary counseling	Moderate in favor	Low	Moderate	Low
Parenteral or enteral nutrition (routine use)	Moderate against	Low	Low	Moderate to high
Omega-3 fatty acids	No recommendation	Low	Low	Low
Vitamins, minerals, and other dietary supplements	No recommendation	Low	Low	Low
Pharmacologic interventions				
Progesterone analogs	Moderate in favor	Intermediate	Moderate	Moderate
Corticosteroids	Moderate in favor	Intermediate	Moderate	Moderate
Anamorelin	No recommendation (not commercially available)	Intermediate	Moderate	Low
Olanzapine	No recommendation	Low	Moderate	Low
Androgens	No recommendation	Low	Moderate	Low
Thalidomide	No recommendation	Low	Low	Low
NSAIDs	No recommendation	Low	Low	Low
Cyproheptadine	No recommendation	Low	None	Low
Cannabinoids	Weak against	Low	None	Low
Melatonin	Weak against	Low	None	Low
TNF inhibitors	Moderate against	Intermediate	None	Moderate
Hydrazine sulfate	Strong against	Intermediate	None	Moderate
Other interventions				
Exercise	No recommendation	Low	Unknown	Unknown

Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; TNF, tumor necrosis factor.
[a] Categorization of benefits and harms was based on use of the intervention for cancer cachexia in the populations that were enrolled in randomized controlled trials.
Source: Roeland EJ, Bohlke K, Baracos VE, et al.[189]

5.11 — Physical activity

Prior to the 1990s, individuals with cancer were often advised to rest and avoid physical activity. However, the recognition of the benefits of physical activity before, during, and after cancer treatments has grown significantly. In 2010, the American College of Sports Medicine convened round table discussions involving cancer and exercise experts, leading to the development of the first exercise guide specifically tailored for cancer survivors.[190] Several critical assumptions were made, including the safety and tolerability of exercise before, during, and after anticancer treatments, as well as its potential to enhance specific health outcomes. Substantial evidence existed indicating that exercise improves physical function, quality of life, and cancer-related fatigue. Consequently, recommendations emerged advocating for a minimum of 150 minutes per week of aerobic exercise, along with two or more days of resistance exercise, and incorporating stretching exercises whenever feasible. Since then, there has been a surge in publications detailing exercise programs aimed at substantiating the benefits of integrating exercise into cancer management protocols.

In March 2018[191] a roundtable of experts was held to review the information generated in recent years, and the experts were asked to establish the benefits of physical activity in cancer management in the following areas:

1. The role of exercise in cancer prevention and control;
2. The effectiveness of exercise in improving clinical outcomes in cancer progression and treatments;
3. The translation of evidence into clinical practice and for the general community.

The results of this review and evaluation[192] regarding the strength of the benefits of exercise during and after cancer treatment are listed below according to the panel classification:

a) **Strong evidence:**

1. **Anxiety** - Moderate aerobic activity three times a week for 12 weeks or twice a week combined with endurance exercise for 6-12 weeks may reduce people's anxiety during cancer treatment[193-195];
2. **Depressive symptoms** – Moderate-intensity aerobic exercise three times a week for 12 weeks or combined with resistance exercise significantly reduces depressive symptoms[196];
3. **Fatigue** - Moderate-intensity aerobic exercise for at least 12 weeks can significantly reduce cancer-related fatigue during and after treatments[197];
4. **Health-related quality of life** – Moderate aerobic exercise, two to three times a week for at least 12 weeks, improves health-related quality of life during and after treatment[195];
5. **Lymphedema** - There is evidence that lymphedema can be managed in breast cancer patients with specific and safe exercises[198];
6. **Physical function** – moderate aerobic exercise significantly improves the patient's reporting of function in a significant way.[199]

b) **Moderate evidence:**

1. **Bone health** - Two systematic reviews on improvement in bone health with exercise are inconsistent.[200, 201] However, clinical experiments in which bone health was one of the primary outcomes of one of the studies did find evidence of improvement[202];
2. **Sleep** - Results are controversial about improving sleep with exercise either aerobic or resistance in cancer patients.[203, 204] However, evidence in healthy individuals of the effect of exercise on sleep is well established.

c) **Insufficient evidence** (when the specific outcome has not been studied in research or because the results of the studies are controversial or simply because the studied population was insufficient to be able to see significant results). These include cardiotoxicity to chemotherapy, peripheral neuropathy, cognitive function, falls, nausea, pain, sexual function, or tolerance to treatments.

In summary, current recommendations for exercise, derived from the observed benefits for individuals before, during, and after cancer treatments, include engaging in moderate-intensity aerobic exercise (such as continuous walking) at least three times a week for a minimum of 30 minutes, over a period of eight to 12 weeks. Additionally, incorporating endurance exercises at least twice a week, involving two sets of 8 to 15 repetitions, with a workload of at least 60% of the maximum repetitions, is advised.

5.11.1 — During treatment

Moderate physical exercise is safe, when advised by an expert professional, in patients with malnutrition, and is recommended to maintain muscle mass. Cancer patients should be encouraged to perform resistance exercises two to three times a week and aerobic exercises. Aerobic, endurance, flexibility, and balance exercises are recommended. Among the recommendations of the American Society of Oncology, aerobic and resistance exercise should be done during treatment with curative intent to mitigate the adverse effects of anticancer treatments.[193, 205-207] A meta-analysis by Seet-Lee et al[208] showed that aerobic exercise improves overall blood flow (including to the tumor) which improves the medication effect. Of note, the authors indicate that exercise per se had a direct anticancer effect.

Exercise decreases myostatosis and improves muscle mass. Furthermore, exercise influences the residual abilities of organs and systems such as the cardiovascular and respiratory systems, and improves the health status of the person. Finally, exercise is a healthy habit that enables stress management and a sense of well-being.

The ASCO guidelines[209] include physical activity recommendations as part of the comprehensive management of people with cancer because physical activity attenuates the adverse effects of treatments and reduces mortality as reported in breast, prostate, and colorectal cancer patients. Sufficient evidence was presented during a roundtable led by the American College of Sports Medicine, in 2018, to promote an accurate and detailed prescription of exercise, including frequency, intensity, times and type of exercise.[192]

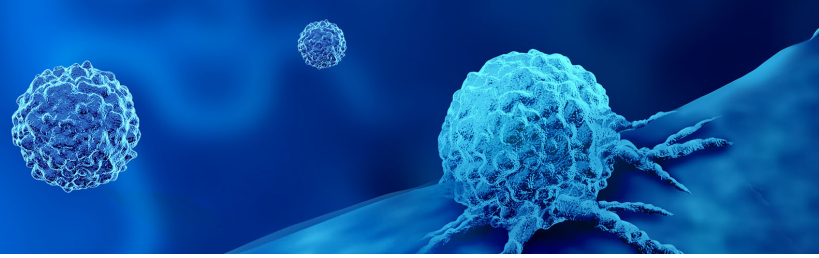
5.11.2 — Post-treatment

Advancements in early detection and improved treatments have brought forth new health needs among individuals post-treatment. For instance, fatigue may persist in up to 25% of individuals who have undergone anti-cancer treatment for several years following its completion, hindering their ability to resume work, maintain independence, and sustain a satisfactory quality of life. Furthermore, certain cancer treatments may introduce additional risk factors for cardiovascular disease, which stands as one of the foremost causes of mortality among cancer survivors.

The American Cancer Society recommendations on nutrition and physical activity for cancer patients and survivors are:

- Return to normal daily activities as soon as possible;
- Participate regularly in physical activity, preferably multiple times per week for at least 10 minutes each time;
- Increase physical activity gradually, working up to 150 to 300 minutes of moderate-intensity physical activity each week (or 75-150 minutes of vigorous-intensity physical activity);
- Include resistance training exercises for at least 2 days;
- Include stretching exercises for at least 2 days.

REFERENCES



1. Seitz K, Cohen J, Deliens L, Cartin A, Castañeda de la Lanza C, Cardozo EA, et al. Place of death and associated factors in 12 Latin American countries: A total population study using death certificate data. *J Glob Health.* 2022;12:04031.
2. World Health A. Cancer prevention and control in the context of an integrated approach. Geneva: World Health Organization; 2017.
3. Organization WH. Cancer 2022 [Available from: https://www.who.int/es/news-room/fact-sheets/detail/cancer.
4. Piñeros M, Laversanne M, Barrios E, Cancela MC, de Vries E, Pardo C, Bray F. An updated profile of the cancer burden, patterns and trends in Latin America and the Caribbean. *Lancet Reg Health Am.* 2022;13:None.
5. López-Kostner F, Zárate AJ, Ponce A, Kronberg U, Kawachi H, Okada T, et al. [Results of a multicentric colorectal cancer screening program in Chile]. *Rev Med Chil.* 2018;146(6):685-92.
6. Barrios CH, Werutsky G, Mohar A, Ferrigno AS, Müller BG, Bychkovsky BL, et al. Cancer control in Latin America and the Caribbean: recent advances and opportunities to move forward. *Lancet Oncol.* 2021;22(11):e474-e87.
7. Villarreal-Garza C, Lopez-Martinez EA, Muñoz-Lozano JF, Unger-Saldaña K. Locally advanced breast cancer in young women in Latin America. *Ecancermedicalscience.* 2019;13:894.
8. Dos-Santos-Silva I, De Stavola BL, Renna NLJ, Nogueira MC, Aquino EML, Bustamante-Teixeira MT, Azevedo ESG. Ethnoracial and social trends in breast cancer staging at diagnosis in Brazil, 2001-14: a case only analysis. *Lancet Glob Health.* 2019;7(6):e784-e97.
9. Organization WH. Integrated care for older people ⁽ICOPE⁾ : guidance for person-centred assessment and pathways in primary care 2019 [Available from: https://www.who.int/publications/i/item/WHO-FWC-ALC-19.1.
10. Muscaritoli M, Imbimbo G, Jager-Wittenaar H, Cederholm T, Rothenberg E, di Girolamo FG, et al. Disease-related malnutrition with inflammation and cachexia. *Clin Nutr.* 2023;42(8):1475-9.
11. Baracos VE. Cancer-associated malnutrition. *Eur J Clin Nutr.* 2018;72(9):1255-9.
12. Maia FCP, Silva TA, Generoso SV, Correia M. Malnutrition is associated with poor health-related quality of life in surgical patients with gastrointestinal cancer. Nutrition. 2020;75-76:110769.
13. Kadakia KC, Symanowski JT, Aktas A, Szafranski ML, Salo JC, Meadors PL, Walsh D. Malnutrition risk at solid tumor diagnosis: the malnutrition screening tool in a large US cancer institute. *Support Care Cancer.* 2022;30(3):2237-44.
14. Muscaritoli M, Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, et al. ESPEN practical guideline: Clinical Nutrition in cancer. *Clin Nutr.* 2021;40(5):2898-913.
15. Anderson RM, Funnell MM. Patient empowerment: myths and misconceptions. *Patient Educ Couns.* 2010;79(3):277-82.
16. Chen MF, Hung SL, Chen SL. Empowerment Program for People With Prediabetes: A Randomized Controlled Trial. *J Nurs Res.* 2017;25(2):99-111.
17. Correia MI, Caiaffa WT, da Silva AL, Waitzberg DL. Risk factors for malnutrition in patients undergoing gastroenterological and hernia surgery: an analysis of 374 patients. *Nutr Hosp.* 2001;16(2):59-64.
18. Cardenas D, Correia M, Hardy G, Gramlich L, Cederholm T, Van Ginkel-Res A, et al. The international declaration on the human right to nutritional care: A global commitment to recognize nutritional care as a human right. *Clin Nutr.* 2023;42(6):909-18.
19. Cardenas D, Davisson Correia MIT, Hardy G, Ochoa JB, Barrocas A, Hankard R, et al. Nutritional care is a human right: Translating principles to clinical practice. *Nutr Clin Pract.* 2022.
20. Pin F, Couch ME, Bonetto A. Preservation of muscle mass as a strategy to reduce the toxic effects of cancer chemotherapy on body composition. *Curr Opin Support Palliat Care.* 2018;12(4):420-6.
21. Ballinger TJ, Marques HS, Xue G, Hoffman R, Gatsonis C, Zhao F, et al. Impact of Muscle Measures on Outcome in Patients Receiving Endocrine Therapy for Metastatic Breast Cancer: Analysis of ECOG-ACRIN E2112. *J Natl Compr Canc Netw.* 2023;21(9):915-23.e1.
22. Prado CM, Wilson H, Armet A. Recetario de cocina alto en proteína para mejorar la salud muscular durante el tratamiento del cáncer. 1 ed. Edmonton: University of Alberta Library; 2022 Novembre 2022.
23. Bautmans I, Knoop V, Amuthavalli Thiyagarajan J, Maier AB, Beard JR, Freiberger E, et al. WHO working definition of vitality capacity for healthy longevity monitoring. *Lancet Healthy Longev.* 2022;3(11):e789-e96.
24. Correia M, Perman MI, Waitzberg DL. Hospital malnutrition in Latin America: A systematic review. *Clin Nutr.* 2017;36(4):958-67.
25. Alvarez-Altamirano K, Delgadillo T, García-García A, Alatriste-Ortiz G, Fuchs-Tarlovsky V. [Prevalence of nutritional risk evaluated with NRS-2002 in Mexican oncology population]. *Nutr Hosp.* 2014;30(1):173-8.
26. Fuchs-Tarlovsky V, Castillo Pineda JC, Rodríguez Veintimilla D, Calvo Higuera I, Grijalva Guerrero P, Gómez García A, et al. Cancer-Related Malnutrition: Epidemiological Results from the Latin American Study of Malnutrition in the Oncology Practice. *Nutr Cancer.* 2022;74(7):2479-88.
27. Gallegos Espinosa S, Nicolalde Cifuentes M, Santana Porbén S. State of malnutrition in hospitals of Ecuador. *Nutr Hosp.* 2014;30(2):425-35.

28. Santana Porbén S. State of malnutrition in cuban hospitals; a needed update. *Nutr Hosp.* 2015;31(5):1900-9.
29. Waitzberg DL, De Aguilar-Nascimento JE, Dias MCG, Pinho N, Moura R, Correia M. Hospital and homecare malnutrition and nutritional therapy in Brazil. Strategies for alleviating it: a position paper. *Nutr Hosp.* 2017;34(4):969-75.
30. Martin L, Senesse P, Gioulbasanis I, Antoun S, Bozzetti F, Deans C, et al. Diagnostic criteria for the classification of cancer-associated weight loss. *J Clin Oncol.* 2015;33(1):90-9.
31. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing.* 2019;48(1):16-31.
32. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol.* 2011;12(5):489-95.
33. Prado CM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, Baracos VE. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. *Lancet Oncol.* 2008;9(7):629-35.
34. Ni J, Zhang L. Cancer Cachexia: Definition, Staging, and Emerging Treatments. *Cancer Manag Res.* 2020;12:5597-605.
35. Jensen GL, Mirtallo J, Compher C, Dhaliwal R, Forbes A, Grijalba RF, et al. Adult starvation and disease-related malnutrition: a proposal for etiology-based diagnosis in the clinical practice setting from the International Consensus Guideline Committee. *Clin Nutr.* 2010;29(2):151-3.
36. McMillan DC. The systemic inflammation-based Glasgow Prognostic Score: a decade of experience in patients with cancer. *Cancer Treat Rev.* 2013;39(5):534-40.
37. Prado CM, Baracos VE, McCargar LJ, Mourtzakis M, Mulder KE, Reiman T, et al. Body composition as an independent determinant of 5-fluorouracil-based chemotherapy toxicity. *Clin Cancer Res.* 2007;13(11):3264-8.
38. Barret M, Antoun S, Dalban C, Malka D, Mansourbakht T, Zaanan A, et al. Sarcopenia is linked to treatment toxicity in patients with metastatic colorectal cancer. *Nutr Cancer.* 2014;66(4):583-9.
39. Ali R, Baracos VE, Sawyer MB, Bianchi L, Roberts S, Assenat E, et al. Lean body mass as an independent determinant of dose-limiting toxicity and neuropathy in patients with colon cancer treated with FOLFOX regimens. *Cancer Med.* 2016;5(4):607-16.
40. Jung HW, Kim JW, Kim JY, Kim SW, Yang HK, Lee JW, et al. Effect of muscle mass on toxicity and survival in patients with colon cancer undergoing adjuvant chemotherapy. *Support Care Cancer.* 2015;23(3):687-94.
41. Anandavadivelan P, Brismar TB, Nilsson M, Johar AM, Martin L. Sarcopenic obesity: A probable risk factor for dose limiting toxicity during neo-adjuvant chemotherapy in oesophageal cancer patients. *Clin Nutr.* 2016;35(3):724-30.
42. Tan BH, Brammer K, Randhawa N, Welch NT, Parsons SL, James EJ, Catton JA. Sarcopenia is associated with toxicity in patients undergoing neo-adjuvant chemotherapy for oesophago-gastric cancer. *Eur J Surg Oncol.* 2015;41(3):333-8.
43. Prado CM, Baracos VE, McCargar LJ, Reiman T, Mourtzakis M, Tonkin K, et al. Sarcopenia as a determinant of chemotherapy toxicity and time to tumor progression in metastatic breast cancer patients receiving capecitabine treatment. Clin Cancer Res. 2009;15(8):2920-6.
44. Prado CM, Lima IS, Baracos VE, Bies RR, McCargar LJ, Reiman T, et al. An exploratory study of body composition as a determinant of epirubicin pharmacokinetics and toxicity. *Cancer Chemother Pharmacol.* 2011;67(1):93-101.
45. Shachar SS, Williams GR, Muss HB, Nishijima TF. Prognostic value of sarcopenia in adults with solid tumours: A meta-analysis and systematic review. *Eur J Cancer.* 2016;57:58-67.
46. Antoun S, Birdsell L, Sawyer MB, Venner P, Escudier B, Baracos VE. Association of skeletal muscle wasting with treatment with sorafenib in patients with advanced renal cell carcinoma: results from a placebo-controlled study. *J Clin Oncol.* 2010;28(6):1054-60.
47. Huillard O, Mir O, Peyromaure M, Tlemsani C, Giroux J, Boudou-Rouquette P, et al. Sarcopenia and body mass index predict sunitinib-induced early dose-limiting toxicities in renal cancer patients. *Br J Cancer.* 2013;108(5):1034-41.
48. Cushen SJ, Power DG, Teo MY, MacEneaney P, Maher MM, McDermott R, et al. Body Composition by Computed Tomography as a Predictor of Toxicity in Patients With Renal Cell Carcinoma Treated With Sunitinib. *Am J Clin Oncol.* 2017;40(1):47-52.
49. Huo Z, Chong F, Yin L, Lu Z, Liu J, Xu H. Accuracy of the GLIM criteria for diagnosing malnutrition: A systematic review and meta-analysis. *Clin Nutr.* 2022;41(6):1208-17.
50. Colcord ME, Benbow JH, Trufan S, Gower NL, Byrne ME, Shea RE, et al. Preoperative Muscle Strength Is a Predictor of Outcomes After Esophagectomy. *J Gastrointest Surg.* 2021;25(12):3040-8.
51. Arends J, Baracos V, Bertz H, Bozzetti F, Calder PC, Deutz NEP, et al. ESPEN expert group recommendations for action against cancer-related malnutrition. *Clin Nutr.* 2017;36(5):1187-96.
52. Kimura W, Miyata H, Gotoh M, Hirai I, Kenjo A, Kitagawa Y, et al. A pancreaticoduodenectomy risk model derived from 8575 cases from a national single-race population (Japanese) using a web-based data entry system: the 30-day and in-hospital mortality rates for pancreaticoduodenectomy. *Ann Surg.* 2014;259(4):773-80.
53. Watanabe M, Miyata H, Gotoh M, Baba H, Kimura W, Tomita N, et al. Total gastrectomy risk model: data from 20,011 Japanese patients in a nationwide internet-based database. *Ann Surg.* 2014;260(6):1034-9.
54. Takeuchi H, Miyata H, Gotoh M, Kitagawa Y, Baba H, Kimura W, et al. A risk model for esophagectomy using data of 5354 patients included in a Japanese nationwide web-based database. *Ann Surg.* 2014;260(2):259-66.

55. Mauricio SF, Ribeiro HS, Correia MI. Nutritional Status Parameters as Risk Factors for Mortality in Cancer Patients. *Nutr Cancer.* 2016;68(6):949-57.
56. Ferguson M, Capra S, Bauer J, Banks M. Development of a valid and reliable malnutrition screening tool for adult acute hospital patients. *Nutrition.* 1999;15(6):458-64.
57. Mauricio SF, Xiao J, Prado CM, Gonzalez MC, Correia M. Different nutritional assessment tools as predictors of postoperative complications in patients undergoing colorectal cancer resection. *Clin Nutr.* 2017.
58. Muscaritoli M, Bar-Sela G, Battisti NML, Belev B, Contreras-Martínez J, Cortesi E, et al. Oncology-Led Early Identification of Nutritional Risk: A Pragmatic, Evidence-Based Protocol (PRONTO). *Cancers (Basel).* 2023;15(2).
59. Cederholm T, Jensen GL, Correia M, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition - A consensus report from the global clinical nutrition community. *Clin Nutr.* 2019;38(1):1-9.
60. Jensen GL, Cederholm T, Correia M, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM Criteria for the Diagnosis of Malnutrition: A Consensus Report From the Global Clinical Nutrition Community. *JPEN J Parenter Enteral Nutr.* 2019;43(1):32-40.
61. Muscaritoli M, Arends J, achmann P, Baracos V, Barthelemy N, Bertz H, et al. ESPEN practical guideline: Clinical Nutrition in cancer. *Clin Nutr.* 2021;40:4741-61.
62. Tremblay D, Roberge D, Touati N, Maunsell E, Berbiche D. Effects of interdisciplinary teamwork on patient-reported experience of cancer care. *BMC Health Services Research.* 2017;17(1):218.
63. Yinusa G, Scammell J, Murphy J, Ford G, Baron S. Multidisciplinary Provision of Food and Nutritional Care to Hospitalized Adult In-Patients: A Scoping Review. *J Multidiscip Healthc.* 2021;14:459-91.
64. Waitzberg DL, Correia MI. Strategies for High-Quality Nutrition Therapy in Brazil. *JPEN J Parenter Enteral Nutr.* 2016;40(1):73-82.
65. Barrocas A. Demonstrating the Value of the Nutrition Support Team to the C-Suite in a Value-Based Environment: Rise or Demise of Nutrition Support Teams? *Nutr Clin Pract.* 2019;34(6):806-21.
66. Wendrich AW, Swartz JE, Bril SI, Wegner I, de Graeff A, Smid EJ, et al. Low skeletal muscle mass is a predictive factor for chemotherapy dose-limiting toxicity in patients with locally advanced head and neck cancer. *Oral Oncol.* 2017;71:26-33.
67. Surov A, Pech M, Gessner D, Mikusko M, Fischer T, Alter M, Wienke A. Low skeletal muscle mass is a predictor of treatment related toxicity in oncologic patients. A meta-analysis. *Clin Nutr.* 2021;40(10):5298-310.
68. Palmela C, Velho S, Agostinho L, Branco F, Santos M, Santos MP, et al. Body Composition as a Prognostic Factor of Neoadjuvant Chemotherapy Toxicity and Outcome in Patients with Locally Advanced Gastric Cancer. *J Gastric Cancer.* 2017;17(1):74-87.
69. Massicotte MH, Borget I, Broutin S, Baracos VE, Leboulleux S, Baudin E, et al. Body composition variation and impact of low skeletal muscle mass in patients with advanced medullary thyroid carcinoma treated with vandetanib: results from a placebo-controlled study. *J Clin Endocrinol Metab.* 2013;98(6):2401-8.
70. Antoun S, Baracos VE, Birdsell L, Escudier B, Sawyer MB. Low body mass index and sarcopenia associated with dose-limiting toxicity of sorafenib in patients with renal cell carcinoma. *Ann Oncol.* 2010;21(8):1594-8.
71. Mohile SG, Dale W, Somerfield MR, Schonberg MA, Boyd CM, Burhenn PS, et al. Practical Assessment and Management of Vulnerabilities in Older Patients Receiving Chemotherapy: ASCO Guideline for Geriatric Oncology. *J Clin Oncol.* 2018;36(22):2326-47.
72. Cederholm T, Jensen GL. To create a consensus on malnutrition diagnostic criteria: A report from the Global Leadership Initiative on Malnutrition (GLIM) meeting at the ESPEN Congress 2016. *Clin Nutr.* 2016.
73. Matsui R, Rifu K, Watanabe J, Inaki N, Fukunaga T. Current status of the association between malnutrition defined by the GLIM criteria and postoperative outcomes in gastrointestinal surgery for cancer: a narrative review. *J Cancer Res Clin Oncol.* 2023;149(4):1635-43.
74. Balcı C, Tufan G, Özdemir N, Aksoy S, Öksüzoğlu Ö B, Zengin N, et al. GLIM criteria as a valid tool for nutrition assessment and mortality prediction in treatment-naïve patients with cancer. *Nutr Clin Pract.* 2023;38(4):798-806.
75. Dewys WD, Begg C, Lavin PT, Band PR, Bennett JM, Bertino JR, et al. Prognostic effect of weight loss prior to chemotherapy in cancer patients. Eastern Cooperative Oncology Group. *Am J Med.* 1980;69(4):491-7.
76. Pedersen B, Groenkjaer M, Falkmer U, Delmar C. Understanding the Essential Meaning of Measured Changes in Weight and Body Composition Among Women During and After Adjuvant Treatment for Breast Cancer: A Mixed-Methods Study. *Cancer Nurs.* 2017;40(6):433-44.
77. Nakagawa T, Toyazaki T, Chiba N, Ueda Y, Gotoh M. Prognostic value of body mass index and change in body weight in postoperative outcomes of lung cancer surgery. *Interact Cardiovasc Thorac Surg.* 2016;23(4):560-6.
78. Gonzalez MC, Correia M, Heymsfield SB. A requiem for BMI in the clinical setting. *Curr Opin Clin Nutr Metab Care.* 2017;20(5):314-21.
79. Malmstrom TK, Miller DK, Simonsick EM, Ferrucci L, Morley JE. SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. *J Cachexia Sarcopenia Muscle.* 2016;7(1):28-36.
80. Parra-Rodríguez L, Szlejf C, García-González AI, Malmstrom TK, Cruz-Arenas E, Rosas-Carrasco O. Cross-Cultural Adaptation and Validation of the Spanish-Language Version of the SARC-F to Assess Sarcopenia in Mexican Community-Dwelling Older Adults. *J Am Med Dir Assoc.* 2016;17(12):1142-6.
81. Williams GR, Al-Obaidi M, Dai C, Bhatia S, Giri S. SARC-F for screening of sarcopenia among older adults with cancer. *Cancer.* 2021;127(9):1469-75.

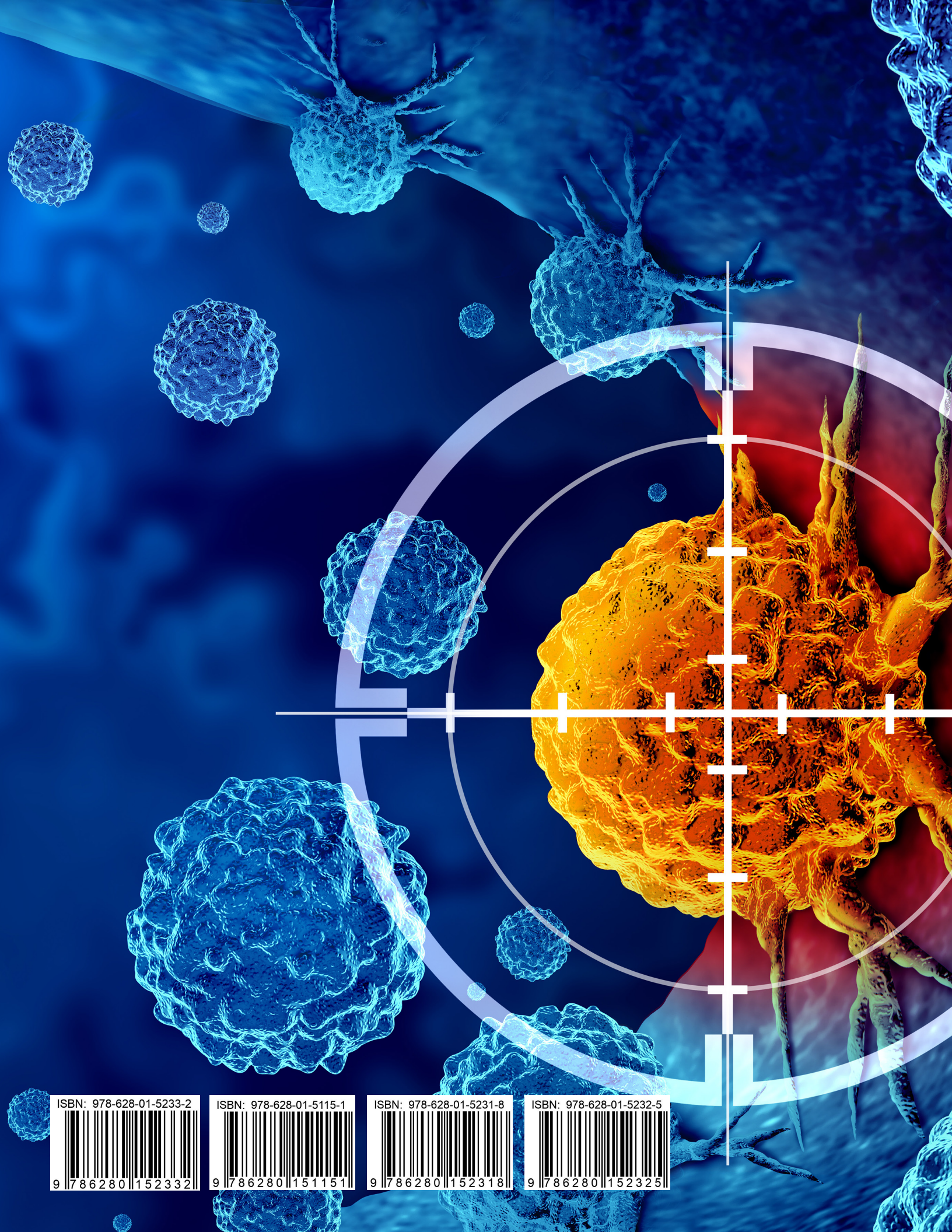
82. Caan BJ, Cespedes Feliciano EM, Prado CM, Alexeeff S, Kroenke CH, Bradshaw P, et al. Association of Muscle and Adiposity Measured by Computed Tomography With Survival in Patients With Nonmetastatic Breast Cancer. *JAMA Oncol.* 2018;4(6):798-804.
83. Santos LP, Gonzalez MC, Orlandi SP, Bielemann RM, Barbosa-Silva TG, Heymsfield SB. New Prediction Equations to Estimate Appendicular Skeletal Muscle Mass Using Calf Circumference: Results From NHANES 1999-2006. *JPEN J Parenter Enteral Nutr.* 2019;43(8):998-1007.
84. Aleixo GFP, Shachar SS, Nyrop KA, Muss HB, Malpica L, Williams GR. Myosteatosis and prognosis in cancer: Systematic review and meta-analysis. *Crit Rev Oncol Hematol.* 2020;145:102839.
85. Pressoir M, Desné S, Berchery D, Rossignol G, Poiree B, Meslier M, et al. Prevalence, risk factors and clinical implications of malnutrition in French Comprehensive Cancer Centres. *Br J Cancer.* 2010;102(6):966-71.
86. Aleixo GFP, Williams GR, Nyrop KA, Muss HB, Shachar SS. Muscle composition and outcomes in patients with breast cancer: meta-analysis and systematic review. *Breast Cancer Res Treat.* 2019;177(3):569-79.
87. Barazzoni R, Jensen GL, Correia M, Gonzalez MC, Higashiguchi T, Shi HP, et al. Guidance for assessment of the muscle mass phenotypic criterion for the Global Leadership Initiative on Malnutrition (GLIM) diagnosis of malnutrition. *Clin Nutr.* 2022;41(6):1425-33.
88. Kawakami R, Murakami H, Sanada K, Tanaka N, Sawada SS, Tabata I, et al. Calf circumference as a surrogate marker of muscle mass for diagnosing sarcopenia in Japanese men and women. *Geriatr Gerontol Int.* 2015;15(8):969-76.
89. Cuervo M, Ansorena D, García A, González Martínez MA, Astiasarán I, Martínez JA. [Assessment of calf circumference as an indicator of the risk for hyponutrition in the elderly]. *Nutr Hosp.* 2009;24(1):63-7.
90. Chen LK, Lee WJ, Peng LN, Liu LK, Arai H, Akishita M. Recent Advances in Sarcopenia Research in Asia: 2016 Update From the Asian Working Group for Sarcopenia. *J Am Med Dir Assoc.* 2016;17(8):767.e1-7.
91. Wiśniowska-Szurlej A, Ćwirlej-Sozańska A, Wołoszyn N, Sozański B, Wilmowska-Pietruszyńska A. Association between Handgrip Strength, Mobility, Leg Strength, Flexibility, and Postural Balance in Older Adults under Long-Term Care Facilities. *Biomed Res Int.* 2019;2019:1042834.
92. Miljkovic N, Lim JY, Miljkovic I, Frontera WR. Aging of skeletal muscle fibers. *Ann Rehabil Med.* 2015;39(2):155-62.
93. Zaragoza-Marti A, Ruiz-Rodenas N, Herranz-Chofre I, Sanchez-SanSegundo M, Serrano Delgado VC, Hurtado-Sanchez JA. Adherence to the Mediterranean Diet in Pregnancy and Its Benefits on Maternal-Fetal Health: A Systematic Review of the Literature. *Front Nutr.* 2022;9:813942.
94. Studenski SA, Peters KW, Alley DE, Cawthon PM, McLean RR, Harris TB, et al. The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. *J Gerontol A Biol Sci Med Sci.* 2014;69(5):547-58.
95. DuMontier C, Loh KP, Bain PA, Silliman RA, Hshieh T, Abel GA, et al. Defining Undertreatment and Overtreatment in Older Adults With Cancer: A Scoping Literature Review. *J Clin Oncol.* 2020;38(22):2558-69.
96. Puts MT, Monette J, Girre V, Pepe C, Monette M, Assouline S, et al. Are frailty markers useful for predicting treatment toxicity and mortality in older newly diagnosed cancer patients? Results from a prospective pilot study. *Crit Rev Oncol Hematol.* 2011;78(2):138-49.
97. Botsen D, Ordan MA, Barbe C, Mazza C, Perrier M, Moreau J, et al. Dynapenia could predict chemotherapy-induced dose-limiting neurotoxicity in digestive cancer patients. *BMC Cancer.* 2018;18(1):955.
98. Judge JO, Schechtman K, Cress E. The relationship between physical performance measures and independence in instrumental activities of daily living. The FICSIT Group. Frailty and Injury: Cooperative Studies of Intervention Trials. *J Am Geriatr Soc.* 1996;44(11):1332-41.
99. Wang DXM, Yao J, Zirek Y, Reijnierse EM, Maier AB. Muscle mass, strength, and physical performance predicting activities of daily living: a meta-analysis. *J Cachexia Sarcopenia Muscle.* 2020;11(1):3-25.
100. Mahoney FI, Barthel DW. FUNCTIONAL EVALUATION: THE BARTHEL INDEX. *Md State Med J.* 1965;14:61-5.
101. Dos Santos Barros V, Bassi-Dibai D, Guedes CLR, Morais DN, Coutinho SM, de Oliveira Simões G, et al. Barthel Index is a valid and reliable tool to measure the functional independence of cancer patients in palliative care. *BMC Palliat Care.* 2022;21(1):124.
102. Owusu C, Margevicius S, Schluchter M, Koroukian SM, Berger NA. Short Physical Performance Battery, usual gait speed, grip strength and Vulnerable Elders Survey each predict functional decline among older women with breast cancer. *J Geriatr Oncol.* 2017;8(5):356-62.
103. da Câmara SM, Alvarado BE, Guralnik JM, Guerra RO, Maciel AC. Using the Short Physical Performance Battery to screen for frailty in young-old adults with distinct socioeconomic conditions. *Geriatr Gerontol Int.* 2013;13(2):421-8.
104. Pavasini R, Guralnik J, Brown JC, di Bari M, Cesari M, Landi F, et al. Short Physical Performance Battery and all-cause mortality: systematic review and meta-analysis. *BMC Med.* 2016;14(1):215.
105. Almugbel FA, Timilshina N, Papadopoulos E, Al-Showbaki L, Alibhai SMH. The role of grip strength and short physical performance battery test in predicting chemotherapy-related outcomes in older adults with cancer. *J Geriatr Oncol.* 2022;13(3):318-24.
106. George SM, Ballard-Barbash R, Manson JE, Reedy J, Shikany JM, Subar AF, et al. Comparing indices of diet quality with chronic disease mortality risk in postmenopausal women in the Women's Health Initiative Observational Study: evidence to inform national dietary guidance. *Am J Epidemiol.* 2014;180(6):616-25.
107. George SM, Irwin ML, Smith AW, Neuhouser ML, Reedy J, McTiernan A, et al. Postdiagnosis diet quality, the combination of diet quality and recreational physical activity, and prognosis after early-stage breast cancer. *Cancer Causes Control.* 2011;22(4):589-98.

108. Reedy J, Krebs-Smith SM, Miller PE, Liese AD, Kahle LL, Park Y, Subar AF. Higher diet quality is associated with decreased risk of all-cause, cardiovascular disease, and cancer mortality among older adults. *J Nutr.* 2014;144(6):881-9.
109. Onvani S, Haghighatdoost F, Surkan PJ, Larijani B, Azadbakht L. Adherence to the Healthy Eating Index and Alternative Healthy Eating Index dietary patterns and mortality from all causes, cardiovascular disease and cancer: a meta-analysis of observational studies. *J Hum Nutr Diet.* 2017;30(2):216-26.
110. Wiseman M. The second World Cancer Research Fund/American Institute for Cancer Research expert report. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. *Proc Nutr Soc.* 2008;67(3):253-6.
111. Jacobs DR, Jr., Steffen LM. Nutrients, foods, and dietary patterns as exposures in research: a framework for food synergy. *Am J Clin Nutr.* 2003;78(3 Suppl):508s-13s.
112. Block G, Woods M, Potosky A, Clifford C. Validation of a self-administered diet history questionnaire using multiple diet records. *J Clin Epidemiol.* 1990;43(12):1327-35.
113. Hager ER, Quigg AM, Black MM, Coleman SM, Heeren T, Rose-Jacobs R, et al. Development and validity of a 2-item screen to identify families at risk for food insecurity. *Pediatrics.* 2010;126(1):e26-32.
114. Gundersen C, Engelhard EE, Crumbaugh AS, Seligman HK. Brief assessment of food insecurity accurately identifies high-risk US adults. *Public Health Nutr.* 2017;20(8):1367-71.
115. Schindler K, Themessl-Huber M, Hiesmayr M, Kosak S, Lainscak M, Laviano A, et al. To eat or not to eat? Indicators for reduced food intake in 91,245 patients hospitalized on nutritionDays 2006-2014 in 56 countries worldwide: a descriptive analysis. *Am J Clin Nutr.* 2016;104(5):1393-402.
116. Maurício SF, da Silva JB, Bering T, Correia MI. Relationship between nutritional status and the Glasgow Prognostic Score in patients with colorectal cancer. *Nutrition.* 2013;29(4):625-9.
117. da Silva JB, Maurício SF, Bering T, Correia MI. The relationship between nutritional status and the Glasgow prognostic score in patients with cancer of the esophagus and stomach. *Nutr Cancer.* 2013;65(1):25-33.
118. Buchmann N, Fielitz J, Spira D, König M, Norman K, Pawelec G, et al. Muscle Mass and Inflammation in Older Adults: Impact of the Metabolic Syndrome. *Gerontology.* 2022;68(9):989-98.
119. Crossland H, Skirrow S, Puthucheary ZA, Constantin-Teodosiu D, Greenhaff PL. The impact of immobilisation and inflammation on the regulation of muscle mass and insulin resistance: different routes to similar end-points. *J Physiol.* 2019;597(5):1259-70.
120. Merker M, Felder M, Gueissaz L, Bolliger R, Tribolet P, Kägi-Braun N, et al. Association of Baseline Inflammation With Effectiveness of Nutritional Support Among Patients With Disease-Related Malnutrition: A Secondary Analysis of a Randomized Clinical Trial. *JAMA Netw Open.* 2020;3(3):e200663.
121. Chasapis CT, Loutsidou AC, Spiliopoulou CA, Stefanidou ME. Zinc and human health: an update. *Arch Toxicol.* 2012;86(4):521-34.
122. Ansemant T, Mahy S, Piroth C, Ornetti P, Ewing S, Guilland JC, et al. Severe hypovitaminosis D correlates with increased inflammatory markers in HIV infected patients. *BMC Infect Dis.* 2013;13:7.
123. Gartner A, Berger J, Bour A, El Ati J, Traissac P, Landais E, et al. Assessment of iron deficiency in the context of the obesity epidemic: importance of correcting serum ferritin concentrations for inflammation. *Am J Clin Nutr.* 2013;98(3):821-6.
124. Stumpf F, Keller B, Gressies C, Schuetz P. Inflammation and Nutrition: Friend or Foe? *Nutrients.* 2023;15(5).
125. Pezdirec M, Strojan P, Boltezar IH. Swallowing disorders after treatment for head and neck cancer. *Radiol Oncol.* 2019;53(2):225-30.
126. Bomze L, Dehom S, Lao WP, Thompson J, Lee N, Cragoe A, et al. Comorbid Dysphagia and Malnutrition in Elderly Hospitalized Patients. *Laryngoscope.* 2021;131(11):2441-7.
127. Raber-Durlacher JE, Brennan MT, Verdonck-de Leeuw IM, Gibson RJ, Eilers JG, Waltimo T, et al. Swallowing dysfunction in cancer patients. *Support Care Cancer.* 2012;20(3):433-43.
128. Jensen K, Lambertsen K, Grau C. Late swallowing dysfunction and dysphagia after radiotherapy for pharynx cancer: frequency, intensity and correlation with dose and volume parameters. *Radiother Oncol.* 2007;85(1):74-82.
129. Rosenthal DI, Lewin JS, Eisbruch A. Prevention and treatment of dysphagia and aspiration after chemoradiation for head and neck cancer. *J Clin Oncol.* 2006;24(17):2636-43.
130. Mekhail TM, Adelstein DJ, Rybicki LA, Larto MA, Saxton JP, Lavertu P. Enteral nutrition during the treatment of head and neck carcinoma: is a percutaneous endoscopic gastrostomy tube preferable to a nasogastric tube? *Cancer.* 2001;91(9):1785-90.
131. Mirabile A, Numico G, Russi EG, Bossi P, Crippa F, Bacigalupo A, et al. Sepsis in head and neck cancer patients treated with chemotherapy and radiation: Literature review and consensus. *Crit Rev Oncol Hematol.* 2015;95(2):191-213.
132. Nguyen NP, Moltz CC, Frank C, Vos P, Smith HJ, Karlsson U, et al. Evolution of chronic dysphagia following treatment for head and neck cancer. *Oral Oncol.* 2006;42(4):374-80.
133. Chen AY, Frankowski R, Bishop-Leone J, Hebert T, Leyk S, Lewin J, Goepfert H. The development and validation of a dysphagia-specific quality-of-life questionnaire for patients with head and neck cancer: the M. D. Anderson dysphagia inventory. *Arch Otolaryngol Head Neck Surg.* 2001;127(7):870-6.

134. Thiyagalingam S, Kulinski AE, Thorsteinsdottir B, Shindelar KL, Takahashi PY. Dysphagia in Older Adults. *Mayo Clin Proc*. 2021;96(2):488-97.
135. Chen AY, Frankowski R, Bishop-Leone J, Hebert T, Leyk S, Lewin J, Goepfert H. The Development and Validation of a Dysphagia-Specific Quality-of-Life Questionnaire for Patients With Head and Neck Cancer: The M. D. Anderson Dysphagia Inventory. *Archives of Otolaryngology–Head & Neck Surgery*. 2001;127(7):870-6.
136. Kuhn MA, Gillespie MB, Ishman SL, Ishii LE, Brody R, Cohen E, et al. Expert Consensus Statement: Management of Dysphagia in Head and Neck Cancer Patients. *Otolaryngol Head Neck Surg*. 2023;168(4):571-92.
137. Waitzberg DL, Correia MI, Echenique M, Ize-Lamache L, Soto JK, Mijares JM, et al. Total nutritional therapy: a nutrition education program for physicians. *Nutr Hosp*. 2004;19(1):28-33.
138. Daley BJ, Cherry-Bukowiec J, Van Way CW, 3rd, Collier B, Gramlich L, McMahon MM, et al. Current Status of Nutrition Training in Graduate Medical Education From a Survey of Residency Program Directors: A Formal Nutrition Education Course Is Necessary. *JPEN J Parenter Enteral Nutr*. 2016;40(1):95-9.
139. Poley MJ. Nutrition and health technology assessment: when two worlds meet. *Front Pharmacol*. 2015;6:232.
140. DeLegge MH, Kelley AT. State of nutrition support teams. *Nutr Clin Pract*. 2013;28(6):691-7.
141. Arenas Moya D, Plascencia Gaitan A, Ornelas Camacho D, Arenas Marquez H. Hospital Malnutrition Related to Fasting and Underfeeding: Is It an Ethical Issue? *Nutr Clin Pract*. 2016;31(3):316-24.
142. Tobert CM, Mott SL, Nepple KG. Malnutrition Diagnosis during Adult Inpatient Hospitalizations: Analysis of a Multi-Institutional Collaborative Database of Academic Medical Centers. *J Acad Nutr Diet*. 2017.
143. Correia MI, Waitzberg DL. The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. *Clin Nutr*. 2003;22(3):235-9.
144. Toulson Davisson Correia MI, Castro M, de Oliveira Toledo D, Farah D, Sansone D, de Morais Andrade TR, et al. Nutrition Therapy Cost-Effectiveness Model Indicating How Nutrition May Contribute to the Efficiency and Financial Sustainability of the Health Systems. *JPEN J Parenter Enteral Nutr*. 2021;45(7):1542-50.
145. Buitrago G, Vargas J, Sulo S, Partridge JS, Guevara-Nieto M, Gomez G, et al. Targeting malnutrition: Nutrition programs yield cost savings for hospitalized patients. *Clin Nutr*. 2020;39(9):2896-901.
146. Correia MI, Castro M, Toledo DDO. A nutrition therapy cost-effectiveness model informs potential cost-savings for healthcare, in Brazil. *Clinical Nutrition ESPEN*. 2020;40:687.
147. Banks MD, Graves N, Bauer JD, Ash S. Cost effectiveness of nutrition support in the prevention of pressure ulcer in hospitals. *Eur J Clin Nutr*. 2013;67(1):42-6.
148. Banks M, Bauer J, Graves N, Ash S. Malnutrition and pressure ulcer risk in adults in Australian health care facilities. *Nutrition*. 2010;26(9):896-901.
149. Cano D, Gomez G, Misas JD, Gracia DA, Brunton C, Sulo S. Nutrition Care Resulting In Improved Outcomes For Colombian Older Adults With Cancer At Malnutrition Risk: Results Of A Quality Improvement Program. *Clin Nutr ESPEN*. 2023;54:579.
150. Cardenas D, Correia M, Ochoa JB, Hardy G, Rodriguez-Ventimilla D, Bermúdez CE, et al. Clinical Nutrition and Human Rights. An International Position Paper. *Nutr Clin Pract*. 2021;36(3):534-44.
151. Garg S, Yoo J, Winquist E. Nutritional support for head and neck cancer patients receiving radiotherapy: a systematic review. *Support Care Cancer*. 2010;18(6):667-77.
152. Körber J, Pricelius S, Heidrich M, Müller MJ. Increased lipid utilization in weight losing and weight stable cancer patients with normal body weight. *Eur J Clin Nutr*. 1999;53(9):740-5.
153. Breitkreutz R, Tesdal K, Jentschura D, Haas O, Leweling H, Holm E. Effects of a high-fat diet on body composition in cancer patients receiving chemotherapy: a randomized controlled study. *Wien Klin Wochenschr*. 2005;117(19-20):685-92.
154. Leistra E, Eerenstein SE, van Aken LH, Jansen F, de van der Schueren MA, Twisk JW, et al. Effect of Early Individualized Dietary Counseling on Weight Loss, Complications, and Length of Hospital Stay in Patients With Head and Neck Cancer: A Comparative Study. *Nutr Cancer*. 2015;67(7):1093-103.
155. Langius JA, Zandbergen MC, Eerenstein SE, van Tulder MW, Leemans CR, Kramer MH, Weijs PJ. Effect of nutritional interventions on nutritional status, quality of life and mortality in patients with head and neck cancer receiving (chemo)radiotherapy: a systematic review. *Clin Nutr*. 2013;32(5):671-8.
156. Cao DX, Wu GH, Zhang B, Quan YJ, Wei J, Jin H, et al. Resting energy expenditure and body composition in patients with newly detected cancer. *Clin Nutr*. 2010;29(1):72-7.
157. Fabi A, Bhargava R, Fatigoni S, Guglielmo M, Horneber M, Roila F, et al. Cancer-related fatigue: ESMO Clinical Practice Guidelines for diagnosis and treatment. *Ann Oncol*. 2020;31(6):713-23.
158. Omlin A, Blum D, Wierecky J, Haile SR, Ottery FD, Strasser F. Nutrition impact symptoms in advanced cancer patients: frequency and specific interventions, a case-control study. *J Cachexia Sarcopenia Muscle*. 2013;4(1):55-61.
159. Dev R, Bruera E, Dalal S. Insulin resistance and body composition in cancer patients. *Ann Oncol*. 2018;29(suppl_2):ii18-ii26.
160. Zhang FF, Cudhea F, Shan Z, Michaud DS, Imamura F, Eom H, et al. Preventable Cancer Burden Associated With Poor Diet in the United States. *JNCI Cancer Spectr*. 2019;3(2):pkz034.

161. Adika E, Jia R, Li J, Seres D, Freedberg DE. Evaluation of the ASPEN guidelines for refeeding syndrome among hospitalized patients receiving enteral nutrition: A retrospective cohort study. *JPEN J Parenter Enteral Nutr.* 2022;46(8):1859-66.
162. da Silva JSV, Seres DS, Sabino K, Adams SC, Berdahl GJ, Citty SW, et al. ASPEN Consensus Recommendations for Refeeding Syndrome. *Nutr Clin Pract.* 2020;35(2):178-95.
163. Hazell AS, Todd KG, Butterworth RF. Mechanisms of neuronal cell death in Wernicke's encephalopathy. *Metab Brain Dis.* 1998;13(2):97-122.
164. Gubler CJ. Studies on the physiological functions of thiamine. I. The effects of thiamine deficiency and thiamine antagonists on the oxidation of alpha-keto acids by rat tissues. *J Biol Chem.* 1961;236:3112-20.
165. Thomson AD. Mechanisms of vitamin deficiency in chronic alcohol misusers and the development of the Wernicke-Korsakoff syndrome. *Alcohol Alcohol Suppl.* 2000;35(1):2-7.
166. Excellence NIfHaC. Nutrition Support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition 2017 [Available from: https://www.nice.org.uk/guidance/cg32/chapter/Introduction#what-to-give-in-hospital-and-the-community.
167. Metabolism ISfCNa. Prevention and Treatment of Refeeding Syndrome in the Acute Care Setting 2013 [Available from: https://www.irspen.ie/wp-content/uploads/2014/10/IrSPEN_Guideline_Document_No1.pdf.
168. Trust ECN. Guidelines for Prevention and Management of Refeeding Syndrome in Adults [Available from: https://cdn.ncpodcast.net/file/NCPodcast/allegati/nc12-LG-CNSG-2019-Sindrome-da-refeeding.pdf.
169. Kraft MD, Btaiche IF, Sacks GS. Review of the refeeding syndrome. *Nutr Clin Pract.* 2005;20(6):625-33.
170. Friedli N, Stanga Z, Culkin A, Crook M, Laviano A, Sobotka L, et al. Management and prevention of refeeding syndrome in medical inpatients: An evidence-based and consensus-supported algorithm. *Nutrition.* 2018;47:13-20.
171. Prevention NIoHOoD. P2P Workshop: Nutrition as Prevention for Improved Cancer Health Outcomes - Day 3 2022 [Available from: https://www.youtube.com/watch?v=ZrFtSgKZRuM.
172. Zhang X, Tang T, Pang L, Sharma SV, Li R, Nyitray AG, Edwards BJ. Malnutrition and overall survival in older adults with cancer: A systematic review and meta-analysis. *J Geriatr Oncol.* 2019;10(6):874-83.
173. Nissen S, Sharp R, Ray M, Rathmacher JA, Rice D, Fuller JC, et al. Effect of leucine metabolite beta-hydroxy-beta-methylbutyrate on muscle metabolism during resistance-exercise training. *J Appl Physiol* (1985). 1996;81(5):2095-104.
174. Prado CM, Orsso CE, Pereira SL, Atherton PJ, Deutz NEP. Effects of β-hydroxy β-methylbutyrate (HMB) supplementation on muscle mass, function, and other outcomes in patients with cancer: a systematic review. *J Cachexia Sarcopenia Muscle.* 2022;13(3):1623-41.
175. Kim JS, Khamoui AV, Jo E, Park BS, Lee WJ. β-Hydroxy-β-methylbutyrate as a countermeasure for cancer cachexia: a cellular and molecular rationale. *Anticancer Agents Med Chem.* 2013;13(8):1188-96.
176. Molfino A, Gioia G, Rossi Fanelli F, Muscaritoli M. Beta-hydroxy-beta-methylbutyrate supplementation in health and disease: a systematic review of randomized trials. *Amino Acids.* 2013;45(6):1273-92.
177. Van Koevering M, Nissen S. Oxidation of leucine and alpha-ketoisocaproate to beta-hydroxy-beta-methylbutyrate in vivo. *Am J Physiol.* 1992;262(1 Pt 1):E27-31.
178. Smith HJ, Mukerji P, Tisdale MJ. Attenuation of proteasome-induced proteolysis in skeletal muscle by {beta}-hydroxy-{beta}-methylbutyrate in cancer-induced muscle loss. *Cancer Res.* 2005;65(1):277-83.
179. Girón MD, Vílchez JD, Salto R, Manzano M, Sevillano N, Campos N, et al. Conversion of leucine to β-hydroxy-β-methylbutyrate by α-keto isocaproate dioxygenase is required for a potent stimulation of protein synthesis in L6 rat myotubes. *J Cachexia Sarcopenia Muscle.* 2016;7(1):68-78.
180. Yakabe M, Ogawa S, Ota H, Iijima K, Eto M, Ouchi Y, Akishita M. Inhibition of interleukin-6 decreases atrogene expression and ameliorates tail suspension-induced skeletal muscle atrophy. *PLoS One.* 2018;13(1):e0191318.
181. Solís-Martínez O, Plasa-Carvalho V, Phillips-Sixtos G, Trujillo-Cabrera Y, Hernández-Cuellar A, Queipo-García GE, et al. Effect of Eicosapentaenoic Acid on Body Composition and Inflammation Markers in Patients with Head and Neck Squamous Cell Cancer from a Public Hospital in Mexico. *Nutr Cancer.* 2018;70(4):663-70.
182. de Castro GS, Andrade MF, Pinto FCS, Faiad JZ, Seelaender M. Omega-3 Fatty Acid Supplementation and Its Impact on Systemic Inflammation and Body Weight in Patients With Cancer Cachexia-A Systematic Review and Meta-Analysis. *Front Nutr.* 2021;8:797513.
183. Jin X, Xu XT, Tian MX, Dai Z. Omega-3 polyunsaterated fatty acids improve quality of life and survival, but not body weight in cancer cachexia: A systematic review and meta-analysis of controlled trials. *Nutr Res.* 2022;107:165-78.
184. Coutinho AE, Chapman KE. The anti-inflammatory and immunosuppressive effects of glucocorticoids, recent developments and mechanistic insights. *Mol Cell Endocrinol.* 2011;335(1):2-13.
185. Yavuzsen T, Davis MP, Walsh D, LeGrand S, Lagman R. Systematic review of the treatment of cancer-associated anorexia and weight loss. *J Clin Oncol.* 2005;23(33):8500-11.
186. Ruiz Garcia V, López-Briz E, Carbonell Sanchis R, Gonzalvez Perales JL, Bort-Marti S. Megestrol acetate for treatment of anorexia-cachexia syndrome. *Cochrane Database Syst Rev.* 2013;2013(3):Cd004310.
187. Naing A, Dalal S, Abdelrahim M, Wheler J, Hess K, Fu S, et al. Olanzapine for cachexia in patients with advanced cancer: an exploratory study of effects on weight and metabolic cytokines. *Support Care Cancer.* 2015;23(9):2649-54.

188. Arends J, Strasser F, Gonella S, Solheim TS, Madeddu C, Ravasco P, et al. Cancer cachexia in adult patients: ESMO Clinical Practice Guidelines(★). *ESMO Open*. 2021;6(3):100092.
189. Roeland EJ, Bohlke K, Baracos VE, Bruera E, Del Fabbro E, Dixon S, et al. Management of Cancer Cachexia: ASCO Guideline. *J Clin Oncol*. 2020;38(21):2438-53.
190. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvão DA, Pinto BM, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc*. 2010;42(7):1409-26.
191. Patel AV, Friedenreich CM, Moore SC, Hayes SC, Silver JK, Campbell KL, et al. American College of Sports Medicine Roundtable Report on Physical Activity, Sedentary Behavior, and Cancer Prevention and Control. *Med Sci Sports Exerc*. 2019;51(11):2391-402.
192. Campbell KL, Winters-Stone KM, Wiskemann J, May AM, Schwartz AL, Courneya KS, et al. Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable. *Med Sci Sports Exerc*. 2019;51(11):2375-90.
193. Mishra SI, Scherer RW, Snyder C, Geigle PM, Berlanstein DR, Topaloglu O. Exercise interventions on health-related quality of life for people with cancer during active treatment. *Cochrane Database Syst Rev*. 2012;2012(8):Cd008465.
194. Persoon S, Kersten MJ, van der Weiden K, Buffart LM, Nollet F, Brug J, Chinapaw MJ. Effects of exercise in patients treated with stem cell transplantation for a hematologic malignancy: a systematic review and meta-analysis. *Cancer Treat Rev*. 2013;39(6):682-90.
195. Lahart IM, Metsios GS, Nevill AM, Carmichael AR. Physical activity for women with breast cancer after adjuvant therapy. *Cochrane Database Syst Rev*. 2018;1(1):Cd011292.
196. Brown JC, Huedo-Medina TB, Pescatello LS, Ryan SM, Pescatello SM, Moker E, et al. The efficacy of exercise in reducing depressive symptoms among cancer survivors: a meta-analysis. *PLoS One*. 2012;7(1):e30955.
197. Cramp F, Byron-Daniel J. Exercise for the management of cancer-related fatigue in adults. *Cochrane Database Syst Rev*. 2012;11(11):Cd006145.
198. Singh B, Disipio T, Peake J, Hayes SC. Systematic Review and Meta-Analysis of the Effects of Exercise for Those With Cancer-Related Lymphedema. *Arch Phys Med Rehabil*. 2016;97(2):302-15.e13.
199. Sweegers MG, Altenburg TM, Chinapaw MJ, Kalter J, Verdonck-de Leeuw IM, Courneya KS, et al. Which exercise prescriptions improve quality of life and physical function in patients with cancer during and following treatment? A systematic review and meta-analysis of randomised controlled trials. *Br J Sports Med*. 2018;52(8):505-13.
200. Dalla Via J, Daly RM, Fraser SF. The effect of exercise on bone mineral density in adult cancer survivors: a systematic review and meta-analysis. *Osteoporos Int*. 2018;29(2):287-303.
201. Fornusek CP, Kilbreath SL. Exercise for improving bone health in women treated for stages I-III breast cancer: a systematic review and meta-analyses. *J Cancer Surviv*. 2017;11(5):525-41.
202. Kohrt WM, Bloomfield SA, Little KD, Nelson ME, Yingling VR. American College of Sports Medicine Position Stand: physical activity and bone health. *Med Sci Sports Exerc*. 2004;36(11):1985-96.
203. Chiu HY, Huang HC, Chen PY, Hou WH, Tsai PS. Walking improves sleep in individuals with cancer: a meta-analysis of randomized, controlled trials. *Oncol Nurs Forum*. 2015;42(2):E54-62.
204. Mercier J, Savard J, Bernard P. Exercise interventions to improve sleep in cancer patients: A systematic review and meta-analysis. *Sleep Med Rev*. 2017;36:43-56.
205. Cave J, Paschalis A, Huang CY, West M, Copson E, Jack S, Grocott MPW. A systematic review of the safety and efficacy of aerobic exercise during cytotoxic chemotherapy treatment. *Support Care Cancer*. 2018;26(10):3337-51.
206. Cormie P, Zopf EM, Zhang X, Schmitz KH. The Impact of Exercise on Cancer Mortality, Recurrence, and Treatment-Related Adverse Effects. *Epidemiol Rev*. 2017;39(1):71-92.
207. Rodríguez-Cañamero S, Cobo-Cuenca AI, Carmona-Torres JM, Pozuelo-Carrascosa DP, Santacruz-Salas E, Rabanales-Sotos JA, et al. Impact of physical exercise in advanced-stage cancer patients: Systematic review and meta-analysis. *Cancer Med*. 2022;11(19):3714-27.
208. Seet-Lee C, Yee J, Morahan H, Ross LS, Edwards KM. The effect of aerobic exercise on tumour blood delivery: a systematic review and meta-analysis. *Support Care Cancer*. 2022;30(11):8637-53.
209. Ligibel JA, Bohlke K, May AM, Clinton SK, Demark-Wahnefried W, Gilchrist SC, et al. Exercise, Diet, and Weight Management During Cancer Treatment: ASCO Guideline. *J Clin Oncol*. 2022;40(22):2491-507.



ISBN: 978-628-01-5233-2
9 786280 152332

ISBN: 978-628-01-5115-1
9 786280 151151

ISBN: 978-628-01-5231-8
9 786280 152318

ISBN: 978-628-01-5232-5
9 786280 152325